Role of Echo for Heart Failure Prognosis
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Echocardiography and Survival in Heart Failure Patients

WHY IS EJECTION FRACTION SO IMPORTANT?
Frank-Starling Curve

LV EJECTION

Stroke Volume

Filling

REMODELING

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Clinical Approach to Heart Failure

HF Reduced EF

- ACE Inhibitors/ARBs
- β-Blockers
- Spironolactone
- Defibrillator
- CRT with Wide QRS
- Ibravidine (New)
- Entresto (New)

HF Preserved EF

- Associated with Hypertensive Heart Disease
- Other CV Risk
- Treat: Hypertension CV Risk

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QUANTITATIVE STANDARD

Modified Simpson’s Rule

Volume = Σ (¼πD²h)

EF = EDV-ESV/EDV

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EJECTION FRACTION AND MORTALITY AFTER ACUTE MYOCARDIAL INFARCTION
ACE Inhibitor Therapy: Enalapril
Study Of Left Ventricular Dysfunction
SOLVD TRIAL II
Asymptomatic LV Dysfunction EF < 35%

<table>
<thead>
<tr>
<th>Drug</th>
<th>Controls (n=2,117)</th>
<th>Enalapril 20 mg/d (n=2,111)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Deaths</td>
<td>334 (15.8%)</td>
<td>313 (14.8%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Death or Hospitalization</td>
<td>518 (24.5%)</td>
<td>434 (20.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>52 (2.5%)</td>
<td>46 (2.2%)</td>
<td>0.74</td>
</tr>
</tbody>
</table>

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DEFIBRILATOR THERAPY TO PREVENT SUDDEN DEATH
MADIT: II Multicenter Automatic Defibrillator Implantation Trial II

\[
\text{Probability of Survival} = \begin{cases} 
1 & \text{Conventional Medical Therapy} \\
0 & \text{Defibrillator + Medical Therapy} 
\end{cases}
\]

Defibrillator + Medical Therapy p<0.05
Conventional Medical Therapy

Bardy et al. N Eng J Med, Jan 2005

SUDDEN CARDIAC DEATH
HEART FAILURE TRIAL
Mortality by Intention-to-treat

\[
\text{Mortality} = \begin{cases} 
0 & \text{Amiodarone Placebo} \\
1 & \text{Defibrillator} 
\end{cases}
\]

n = 2,521
- CHF NYHA II or III
- Nonischemic CMP or CAD
- EF ≤ 35%

23% Reduction in Mortality p=0.007

SELECTION CRITERIA FOR RESYNCHRONIZATION THERAPY
- HEART FAILURE: NYHA Functional Class II, III or IV
- QRS ≥ 120 msec (> 150ms LBBB)
- EF ≤ 35%

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IMPROVEMENTS IN EF BY ECHO
- Continued Refinements in Digital Image Quality
- Echo Contrast Enhancement for poor echo images

Contrast Bolus
Gorcsan J. 2015
3D vs. MRI Volumes

Corsi et al. Circulation. 2005;112(8):1161-70

Bias = 1.4 ml
Agreement ± 20 ml.

"I'm Too Busy to Trace EF!"
"I'm Really an Expert at Eyeballing EF!"
"Eyeballing EF is Good Enough!"

Visual Estimates of the Experts

Cannesson...Gorcsan et al. JACC 2007;49:217

Visual EF: Novice vs. Expert

Cannesson...Gorcsan et al. JACC 2007;49:217

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

Application to Patients Undergoing Cancer Chemotherapy

Thavendiranathan...Marwick et al. JACC 2013; 61:77.

EF Test-Retest Variability

n = 56 patients, Echos at 5 time points: Baseline, 3, 6, 9 and 12 months
WHAT OTHER THAN EF CAN PREDICT PROGNOSIS IN HEART FAILURE?

RESTRICTIVE INFLOW PATTERN
Mitral E Deceleration Time

DECELERATION TIME AND SURVIVAL IN DILATED CARDIOMYOPATHY
DECELERATION TIME AND SURVIVAL IN AMYLOID HEART DISEASE

Klein et al. J Am Coll Cardiol 1996

E’ PREDICTS OUTCOME WITH ABNORMAL EF

- n = 182
- EF < 50%


ASSESSMENT OF LV FILLING PRESSURE

Routine Doppler Mitral Inflow
Tissue Doppler Mitral Annulus

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E/E’ PREDICTS PROGNOSIS AFTER MI

n = 205 with Acute MI

Global Longitudinal Strain & Prognosis in Heart Failure
- 194 heart failure patients
- EF = 26%
- Death, transplant or LVAD over 5 yrs

Global Circumferential Strain & Prognosis in Heart Failure
- 201 HF patients
- EF = 23%
- HF Hospitalization or Death 5 yrs


Motoki...Klein et al. JACC 2012

Cho et al. J Am Coll Cardiol 2009;54:618
Additive Prognostic Value of GLS and GCS in CRT

- 205 HF patients for CRT
- LVEF < 35%, QRS > 120 ms

Additive Prognostic Value of GLS and GCS in CRT

- 205 HF patients for CRT
- LVEF ≤ 35%, QRS > 120 ms

Additive Prognostic Value of GLS and GCS in CRT

- 205 HF patients for CRT
- LVEF ≤ 35%, QRS > 120 ms

Additive Pronostic Value of GCS to EF

- n = 120 HF patients
- EF 25-35% and GCS ≤ 6.5
- EF ≤ 25% and GCS ≤ 6.5
- EF 25-35% and GCS > 6.5
- EF ≤ 25% and GCS > 6.5

Additive Prognostic Value of GCS to EF

- n = 120 HF patients
- EF 25-35% and GCS ≤ 6.5
- EF ≤ 25% and GCS ≤ 6.5
- EF 25-35% and GCS > 6.5
- EF ≤ 25% and GCS > 6.5

Left Atrial Strain Rate

- Positive Peak Strain Rate
- Early Negative Peak Strain Rate
- Late Negative Peak Strain Rate
Left Atrial Strain

Positive Peak Strain

Negative Peak Strain

Total Strain

LA Strain Correlates with Markers of Diastolic Function

Positive Peak Strain

Mitral Inflow Velocity

Mitral Annular Velocity


LA Strain Correlates with Markers of Diastolic Function

Mitral Annular Velocity

Left Atrial Volume


LA Strain and New Onset HF


LA Strain and New Onset HF

Biomarkers and Outcome


LA Strain in Heart Failure Preserved EF (HFP EF)

n = 308 Heart Failure Pts

EF ≥ 50%

LV and LA Reverse Remodeling after CRT


TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSION (TAPSE)

Normal

RV Failure

RV Recovery by TAPSE in Heart Failure

n = 706 Chronic Heart Failure Pts; EF ≤ 45%
Median Follow-Up: 3.3 years
Baseline TAPSE
TAPSE from Baseline to 6 mo.

CASE STUDY
47 yo woman with scleroderma
Pathogenesis of Pulmonary Arterial Hypertension

- Risk Factors and Associated Conditions
- Vascular Injury
- Disease Progression

**NORMAL IRREVERSIBLE DISEASE**


Vascular Injury

- Endothelial dysfunction
  - Loss of response to short-acting vasodilator trial

Disease Progression

- Vascular smooth muscle dysfunction
  - Impaired voltage-gated potassium channel (K_v1.5)
- Smooth muscle hypertrophy
- Adventitial and intimal proliferation
- In situ thrombosis
- Plexiform lesion

Advanced Vascular Lesion

Early intimal proliferation

Thinking Differently About Pulmonary Hypertension

- PAH is not just high pressure and an elevated PVR
- Patients don’t die from high pulmonary pressures; they die from failure to compensate for high pressures
- New focus on RV function and RV/PV interactions

Disease Severity, Stability and Prognosis in Pulmonary Arterial Hypertension

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT)

Authors/Task Force Members: Massimo Galati (ESC Chairperson) (Italy), Marc Humbert (ERS Chairperson) (France), Jean-Luc Vachierry (Belgium), Simon Gibbs (UK), Irene Lang (Austria), Adam Turbick (Poland), Gérard Simonneau (France), Andrew Parrott (UK), Antonio Verzola Nordmeyra (The Netherlands), Maurer Böggen (Switzerland), Andreas Gloor (Germany), Miguel Angel Gomez Sanchez (Spain), Georg Henzmann (Germany), Walter Klopfer (Austria), Patrizio Lanciotti (Belgium), Marco Macucci (Italy), Teresa McDonagh (UK), Luc A. Piaud (Belgium), Pedro T. Trindade (Switzerland), Maurizio Zompatori (Italy) and Marius Hooger (Germany)

European Heart Journal

Pericardial Effusion in Patients with Pulmonary Hypertension

- n = 200
- Survival
- Pericardial Effusion

TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSION (TAPSE)

- Normal
- Severe Pulmonary Hypertension RV Failure

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**TAPSE and Survival in Pulmonary Hypertension**


$n=47$ patients with PAH

Reference Range for Normal RV Strain

N=169 patients with normal TTE

Mean RV free wall strain = \(-25 \pm 15\%\)

Reference Range for Normal RV Strain

Assess RV Function: Speckle Tracking Echocardiography

Frame 1

Frame n + 1

Reference Range for Normal RV Strain

Reference Range for Normal RV Strain

RV free wall strain and outcomes in PH

All-cause mortality

RV global strain in pulmonary hypertension

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 Fine, Kane et al. Circ CV Img 2013

RV Strain Is Additive to Other Echocardiographic Features and Survival in PH

Echo Risk Factors:
- RA > 18 cm²
- Pericardial Effusion
- RV global Strain < -15%

Handa R...Gorcsan J et al. 2015

RV- LV Remodeling in PH

Basal RV to LV Dimension Ratio and Survival In Pulmonary Hypertension

RV D/LV D = 1.34

N=165
P=0.000017
HR = 2.7 (95% CI 1.68-4.34) p<0.0001


RV- LV Remodeling in PH

Limitations of 2D Echocardiography To Assess the Right Ventricle

RV complex geometry: Difficulty in taking the most representative slice

Rudaki JASE 2010

RV 3D SPECKLE TRACKING

Artida Toshiba corp.
Progressive changes in PH patients

Estimation of RV Decompensation


Hemodynamic and RV 3D Echo Data

3D echocardiography was performed immediately before or after right heart catheterization.

- Invasive Hemodynamics
  - Right atrial (RA) pressure, Pulmonary artery pressure (systolic PAP, mean PAP), RV pressure & Pulmonary vascular resistance (PVR).

- 3D Echocardiography
  - RV volume index (EDVI, ESVI), RV ejection fraction (RVEF), RV global area strain.

- Combining Pressure with RV Volume Data to Determine:
  - RV adapted phase; RV remodeling with increasing PA pressures
  - RV adverse remodeled phase; RV remodeling with decreasing PA pressures

Examples of RV 3D Strain and Volume Analysis

PH Patients

Utilizing 3D Echo and Hemodynamics to Determine Right Ventricular Adaptation Versus Adverse Remodeling

RV Pressure Volume Loops Derived from 3D Echo

Hospitalization, Death or Lung Transplantation

6 Month Follow-Up
3D Echo Analysis of RV and LV

RV to LV End-Diastolic volume ratio was used as a biventricular remodeling index.

Normal Value: 1.1 (0.7-1.7) N=30

Goda,...Gorcsan et al. AHA 2015

Pulmonary Hypertension
Patient Examples

Patient A

RV to LV End-diastolic volume ratio = 7.26

3D RV End-Diastolic Volume = 247 ml
3D LV End-Diastolic Volume = 34 ml

Patient B

RV to LV End-diastolic volume ratio = 0.97

3D RV End-Diastolic Volume = 148 ml
3D LV End-Diastolic Volume = 152 ml

Goda,...Gorcsan et al. AHA 2015

RV to LV End-Diastolic Volume Ratio and PH Hospitalization, Death or Lung Transplant

n = 97

P<0.0001

HR=4.8

95% CI 2.2 to 10.4

Effects of Lung Transplantation on 3D Right and Left Ventricular Function

BEFORE TRANSPLANT

AFTER TRANSPLANT

Strain

Ryo K, Champion HC, Gorcsan J.

TAKE HOME MESSAGES

• EJECTION FRACTION
  - Clinically Here To Stay – Quantification Essential
  - Trace EF 2D Biplane is Standard of Care
  - Use Contrast for poor images
  - 3D is best, if available.

• Mitral Inflow Deceleration Time < 150ms

• Tissue Doppler of Mitral Annulus
  - Additive to EF for Prognosis E/E' > 15

• Global Longitudinal Strain (GLS)
  - Normal GLS: -16% to -21%
  - GLS < -6.9 % marker for death, transplant, or LVAD

• Global Circumferential Strain (GCS)
  - Normal GCS -21% to -29%
  - GCS < -10.7 % marker for HF Hospitalization or death
  - GCS < -6.5% marker for death, transplant, or LVAD

• Pulmonary Hypertension:
  - Markers for Poor Prognosis
    - Pericardial Effusion
    - TAPSE < 15 mm
    - RV Mean Longitudinal Strain < -15%
    - RV Free Longitudinal Wall Strain < -19%

• Future Applications Continue to Emerge!