A guide to echocardiography for the evaluation of hemodynamics in patients with PAH & PE
Echo Hawaii 2017

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Pulmonary Arterial Hypertension
Echo – Early in the Investigation!

Who to screen? Symptomatic and high risk

- Family members of a patient with heritable pulmonary arterial hypertension (HPAH)
- Patients with systemic sclerosis (SSc) – annually – Khanna (‘level C’)
- Patients with HIV
- Patients with portopulmonary hypertension (PoPH)
- Patients with congenital heart disease
- SYMPTOMS – DYSPNEA
Estimation of pulmonary arterial pressure

Estimation of systolic PA Pressure

RVSP = 4 × TR_{vmax}^2 + estimated RA pressure
Estimation of sPAP by TR Jet

IVC = RAP

RV = MPA = PAP

TRV

RA pressure estimation

<table>
<thead>
<tr>
<th>Collapsibility</th>
<th>Normal (0-5 (3) mmHg)</th>
<th>Intermediate (5-10 (8) mmHg)</th>
<th>High (≥15 mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>25</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Mean RAP, mm Hg</td>
<td>3.4</td>
<td>3.2</td>
<td>3.3</td>
</tr>
<tr>
<td>0-5 cm Hg, %</td>
<td>84</td>
<td>100</td>
<td>67</td>
</tr>
<tr>
<td>5-10 mm Hg, %</td>
<td>12</td>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td>10-15 mm Hg, %</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Traditional RAP classification, mm Hg</td>
<td>0.5</td>
<td>8-10</td>
<td>0.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary indices of elevated RA pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC diameter: ≤2.1 cm, normal; ≤2.1 cm, intermediate; &gt;2.1 cm, high</td>
</tr>
<tr>
<td>Collapse with sniff: &gt;50%, &gt;50%, &lt;50%</td>
</tr>
</tbody>
</table>

IVC, inferior vena cava; MPA, main pulmonary artery; PAP, pulmonary artery pressure; PV, pulmonary valve; sPAP, systolic pulmonary artery pressure; RA, right atrium; RAP, right atrial pressure; RV, right ventricle; TR, tricuspid regurgitation; TRV, tricuspid regurgitant velocity; TV, tricuspid valve.

Pitfalls

Assumption: RVSP = sPAP

RVSP, right ventricular systolic pressure; sPAP, systolic pulmonary artery pressure.
RVSP ≠ sPAP: Pulmonic Stenosis

So... RVSP = 43 + CVP but sPAP = RVSP − PV gradient = 48 − 37 = 11 mmHg ????

TR: When laminar, Echo underestimates!

Watch RAP!
Alignment & Gains are capital

And conversely...
Sometimes you have to take a haircut
FLOW $V = IR$

A. Tricuspid Regurg. Max. Velocity

$V = IR \rightarrow P = Q \times R$

RVSP $> 40$ mmHg in athletes but only at workloads that exceed normal

Athletes, high output, e.g. cirrhosis, anemia, exercise

Pulmonary Vascular Resistance

$R = \frac{V}{I}$ or $PVR = \frac{P}{Q}$

$PVR = 10 \times \frac{2.86}{20.8} + 0.16 = 1.53$ WU

$PVR = 10 \times \frac{3.64}{6.5} + 0.16 = 5.76$ WU

What constitutes a normal RVSP?

- 3790 subjects with ‘normal’ echo
- Age range: 1–89 years
- Mean PASP: 28.3 ± 4.9 mmHg
- 95% CI upper range: 37.2 mmHg
- Age >60 years, 95% upper limit: 42.1 mmHg
- BMI >30 kg/m², 95% upper limit: 40.1 mmHg
- Assumed RA pressure: 10 mmHg

BMI, body mass index; CI, confidence interval; Echo, echocardiography; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; RA, right atrial; RVSP, right ventricular systolic pressure.


What do the guidelines say?

Recommendations: Pulmonary hemodynamics are feasible in a majority of subjects using a variety of validated methods. SPAP should be estimated and reported in all subjects with reliable tricuspid regurgitant jets. The recommended method is by TR velocity, using the simplified Bernoulli equation, adding an estimate of RA pressure as detailed above. In patients with PA hypertension or heart failure, an estimate of PADP from either the mean gradient of the TR jet or from the pulmonary regurgitant jet should be reported. If the estimated SPAP is >35 to 40 mmHg, stronger scrutiny may be warranted to determine if PH is present, factoring in other clinical information.

PA, pulmonary artery; PADP, pulmonary artery diastolic pressure; RA, right atrial; SPAP, systolic pulmonary artery pressure; TR, tricuspid regurgitation.


Echo sPAP vs RHC – Bland and Altman Analysis

DE, Doppler echocardiography; Echo, echocardiography; RHC, right heart catheterization; sPAP, systolic pulmonary artery pressure.
mPAP, dPAP

\[ mPAP = \frac{2}{3} \text{diastolic} + \frac{1}{3} \text{systolic} \]
\[ 4 \times V_{\text{peak}} \text{PR}^2 + \text{RAP} \]
\[ 79 = 0.45 \times \text{AT} \]

MG TR - VTI + RAP

\[ \text{dPAP} = 4 \times \text{end PR}^2 + \text{RAP} \]

Of the 109 patients in the validation cohort, only two patients (1.8%) were classified as having mPAP <25 mmHg using the predictive equation \[ mPAP = 0.61 \times \text{PASP} + 1.95 \text{ mmHg} \], when the observed mPAP at cardiac catheterization for these patients was >25 mmHg.
Etiology: Yes, there’s PH...but why?

sPAP 75 mmHg

sPAP, systolic pulmonary artery pressure.
Don’t forget the left heart

- LV systolic function
- Cardiac Output
- LV diastolic function
- Left-sided valves
Post-capillary PH

Pre-capillary PH
Echocardiographic Parameters to Distinguish Pre-Capillary from Post-Capillary Pulmonary Hypertension.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Favors Pulmonary Arterial Hypertension</th>
<th>Favors Pulmonary Venous Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV size / systolic function</td>
<td>Normal or Small / Normal / Low normal</td>
<td>Enlarged / Reduced</td>
</tr>
<tr>
<td>LA volume</td>
<td>Normal or Small</td>
<td>Moderate-Severely enlarged</td>
</tr>
<tr>
<td>Left Ventricular Diastolic Function</td>
<td>Normal or Mildly impaired E/E’ &lt; 8</td>
<td>Pseudonormal / Restrictive</td>
</tr>
<tr>
<td>Left-sided valvulopathy</td>
<td>Absent / Non-significant</td>
<td>Moderate / Severe Aortic or mitral disease</td>
</tr>
<tr>
<td>RV Size / Shape</td>
<td>Severely enlarged with rounded RV apex</td>
<td>Mildly enlarged or preserved size</td>
</tr>
<tr>
<td>Interventricular Septum</td>
<td>D-shape in systole, Early diastolic septal shift</td>
<td>Normal configuration or subtle flattening</td>
</tr>
<tr>
<td>RVOT flow / Pulmonary Valve motion</td>
<td>Mid-systolic notching of Doppler envelope / notching of m-mode valve tracing</td>
<td>Absence of notching</td>
</tr>
<tr>
<td>Pulmonary Vascular Resistance</td>
<td>Increased</td>
<td>Normal / mildly increased</td>
</tr>
<tr>
<td>PA Acceleration Time</td>
<td>&lt; 80 msec</td>
<td>&gt; 80 msec</td>
</tr>
</tbody>
</table>

A simple echocardiographic method to estimate pulmonary vascular resistance¹

• 3 parameters identified with predictive value:
  – LA size (+1 if parasternal long-axis dimension >42 mm, −1 if <32 mm)
  – Left-sided E/e’ ratio reflective of elevated LA pressure (+1 if E/e’ >10)
  – Presence of RVOT mid-systolic notching or PA acceleration time <80 msec reflective of elevated PVR (−1 if present).

• Scores ranging from −2 (pre-capillary PH most likely) to +2 (post-capillary PH most likely)
  – A score of ≥0 had 100% sensitivity and 62% specificity for post-capillary PH

• Mixed pathophysiology of PH, e.g. systemic sclerosis
  – In these patients, there are often features of elevated LA pressure and elevated PVR
  – Misclassification: improved predictive ability of the score (c-statistic 0.98) after exclusion of subjects with mixed PH pathophysiology
  – Invasive testing with hemodynamic challenge (saline or exercise) is usually required to resolve these cases

LA, left atrial; PA, pulmonary artery; PVR, pulmonary vascular resistance; RVOT, right ventricular outflow tract.

# PASP: Unrelated to prognosis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benza 2010</td>
<td>Reveal Registry</td>
</tr>
<tr>
<td>McLaughlin 2002</td>
<td>Epoprostenol Rx</td>
</tr>
<tr>
<td>McLaughlin 2009</td>
<td>ACCF/AHA consensus</td>
</tr>
<tr>
<td>Galiè 2009</td>
<td>ESC guidelines</td>
</tr>
<tr>
<td>Galiè 2008</td>
<td>Early trial</td>
</tr>
<tr>
<td>Kuhn 2003</td>
<td>Epoprostenol Rx</td>
</tr>
<tr>
<td>Nagaya 2000</td>
<td>Observational (BNP)</td>
</tr>
<tr>
<td>Miyamoto 2000</td>
<td>Observational (BNP)</td>
</tr>
<tr>
<td>Nagaya 1999</td>
<td>Observational (uric acid)</td>
</tr>
</tbody>
</table>

ACCF, American College of Cardiology Foundation; AHA, American Heart Association; BNP, brain natriuretic peptide; ESC, European Society of Cardiology; PASP, pulmonary artery systolic pressure.


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## The RV Focused View

![RV Focused View Diagram](image-url)
Qualitative evaluation of RV

- Normal < 2/3 LV
  - Moderate: when the RV exceeds size of LV

- Severe when RV forms the apex
- But **WATCH** the LV size

LV, left ventricle; RV, right ventricle.

RV systolic function in PH: A challenge

FAC, fractional area change; RV, right ventricle; RVEDA, right ventricular end-diastolic area; RVESA, right ventricular end-systolic area.
RV strain and survival outcomes in the study population

**Strain – 2 D Speckle Tracking**

Abnormal Threshold < -20% **

**Recommendations.** Two-dimensional STE-derived strain, particularly of the RV free wall, appear to be reproducible and feasible for clinical use. Because of the need for additional normative data from large studies involving multivendor equipment, no definite reference ranges are currently recommended for either global or regional RV strain or strain rate.

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RV, right ventricle.
TAPSE – Tricuspid Annular Plane Systolic Excursion

Abnormal TAPSE < 17 mm

RV dp/dt and TAPSE

(dp/dt, Change in pressure/time; RV, right ventricular; TAPSE, tricuspid annular plane systolic excursion.
2D prognostic value

- RA enlargement
- RV eccentricity index
- Pericardial effusion

How Often?

<table>
<thead>
<tr>
<th>Test</th>
<th>At baseline (prior to therapy)</th>
<th>Every 3-6 months</th>
<th>3-4 months after initiation or changes in therapy</th>
<th>In case of clinical worsening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>NT-proBNP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain natriuretic peptide (BNP)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4D Acquisition

Apical 4 chamber view

3D-dataset

Full volume dataset
  • 4-7 consecutive beats
  • Adequate temporal resolution

Save raw data

Tip: don’t forget RV apex!!
Adjust depth and width

Tip: ↑ cardiac cycles, ↑ temporal resolution
Avoid stitching artifact

Step 1

Step 2

Step 3

Courtesy Dr Julia Grapsa

4D Analysis

Endocardial mapping:
  1. RVOT excluded
  2. Trabeculations included to the blood pool

Epicardial mapping

Short axis from base to apex (Simpson’s rule)
  7 mm slices

Myocardial volume

Multiplied with myocardial density (1.05 g/dl) > myocardial mass

Step 1

Step 2

Step 3

Courtesy Dr Julia Grapsa
Morphologic and functional changes are related to the cause of PH and are independent of PH severity at rest.

- PAH results in the greatest degree of RV dilatation and dysfunction
- CTEPH results in lesser dilatation and dysfunction despite greater PVR
- PH secondary to MR shows the least dilatation or dysfunction

CTED, chronic thromboembolic disease; EF, ejection fraction; MR, mitral regurgitation; PVR, pulmonary vascular resistance; RV, right ventricular.


### Knowledge Gaps/Practicalities

- **Simple**
  - RV linear dimension
  - RA "size"
  - Eccentricity
  - Pericardial Effusion
  - 2D strain
  - sPAP

- **Reproducible**
  - Same
  - 3D volumes?
  - 2D Strain

- **Prognostic**
  - RA size, Pericardial effusion
  - Δ RA volume, sphericity
  - RV volume, sphericity
  - 2D strain

- **What do we do?**
  - S’
  - TAPSE
  - MPI
  - RA size
  - Pericardial Effusion
  - sPAP, (mPAP)

  2D strain – free wall only
Can we **follow** patients? - Time: the 4th dimension

What determines a significant change?
- What parameter(s) should we follow?
- Is it a % decrease/increase?
- Is it a simple threshold?
- Is it a % decrease/increase to a significant threshold?
- e.g. Cardio-Oncology

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Role of Echo: What to ask of your Echo Lab

**Diagnosis/screening: prior to therapy**
- Assessment of sPAP by TR jet
- Estimation of mPAP
- RV size and morphology – RA size
- **RV systolic function**
- LV systolic/diastolic function
- LA volume
- Assessment of valvulopathy

**Follow-up: prognosis and response to Tx 3–4 months post initiation of Tx or clinical worsening**
- Quantitation of RV function
  - TAPSE, S', 2D strain, MPI
- RV size
- RA size
- sPAP
- Pericardial effusion

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2D, two-dimensional; Echo, echocardiography; LA, left atrial; LV, left ventricular; mPAP, mean pulmonary arterial pressure; MRI, myocardial performance index; RA, right atrial; RV, right ventricular; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; Tx, treatment.
Future targets

• Avoiding false positives and false negatives
• Best predictors of prognosis
• Best predictors of response to therapy
• Clarifying Echo’s complementary role in work-up and management in era of MRI, BNP, and cost constraints

Key Points

• Echocardiography should be considered early in the evaluation of dyspnea
• PA pressure can be estimated reliably and signs of pulmonary pressure can be sought but attention to detail is required
• Echocardiographic evaluation of right heart size and function can prognosticate and provide insights into patient progress
• Novel techniques such as two-dimensional strain and 3D echocardiography will provide improved new mechanistic and clinical insights in patients with pulmonary hypertension
What’s this?

Acute Pulmonary Embolism
PE continued

“Incidental Finding”
McConnell’s Sign – AJC 1996

- 77% sensitivity, 94% specificity for the diagnosis of acute PE
- Others have shown inability to distinguish vs other acute pathology like RV infarct
- Use in combination with...

The 60/60 Sign – Kurzyna AJC 2002

RV cannot acutely generate very high pressures
RVSP < 60 mmHg

When faced with high Impedance, ejection ends sooner
PA accel time < 60 msec
PE Echo Findings

• Present in 30-40% (*almost all with high risk PE*)
• Increased RV size
• Decreased RV function
• New/worsened TR
• RV Thrombus/PE in transit
• Regional Wall Motion – McConnell’s sign
• Increased PAP – mild or moderate, usually
• Prognostic info – RV dysfunction, Thrombus

Who Said...

• “I Know it When I See It”
• “I am forced to conclude that the concept of ‘…..’ cannot be defined with sufficient specificity and clarity to provide fair notice to persons who ….., to avoid very costly…. (misdiagnoses)
Predictors of Mortality

- R:L EDD ratio HR 2.4
- TAPSE HR 0.53
- RV:RA Gradient HR 1.02

Predictors of ICU Mortality

- RV:LV EDD ratio HR 4.4
- TAPSE HR 0.4
- RVSP HR 1.03
- IVC collapse< 50% HR 4.3

So...

Diagnosis and Prognosis
PE vs. PAH?

Table 6 Diagnostic ability of RV measurements to predict the acuity of pulmonary hypertension

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cutoff</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>AUC</th>
<th>P (vs RVFWS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVFWS</td>
<td>-17.9%</td>
<td>88%</td>
<td>63%</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>RVEDA</td>
<td>18.7 cm²</td>
<td>88%</td>
<td>55%</td>
<td>0.70</td>
<td>.21</td>
</tr>
<tr>
<td>FAC</td>
<td>26.3%</td>
<td>63%</td>
<td>85%</td>
<td>0.74</td>
<td>.55</td>
</tr>
<tr>
<td>PVR</td>
<td>3.34 Wood units</td>
<td>90%</td>
<td>53%</td>
<td>0.72</td>
<td>.33</td>
</tr>
<tr>
<td>PASP</td>
<td>32.5 mm Hg</td>
<td>80%</td>
<td>32%</td>
<td>0.54</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>McConnell sign</td>
<td>45%</td>
<td>86%</td>
<td></td>
<td>0.65</td>
<td>.02</td>
</tr>
</tbody>
</table>

Wright et al JASE 2016

Right Ventricular Systolic Function Responses to Acute and Chronic Pulmonary Hypertension: Assessment with Myocardial Deformation

Leah Wright, BSc, Nathan Dwyer, MBBS, PhD, Janette Power, BSc, Leonard Kritihardes, MBBS, PhD, David Celermajer, MBBS, PhD, and Thomas H. Marwick, MBBS, PhD, MPH, Hobart and Sydney, Australia

JASE 2016

Strain – McConnell’s vs none

Strain PAH vs Acute PE

Higher HR, PVR, Larger RV
Lower %FAC
What’s an Echo worth?

= 50 x

Canadian Society of Echocardiography

19th ANNUAL CANADIAN ECHO WEEKEND
April 20-22, 2017
Toronto Marriott Downtown Eaton Centre Hotel
Toronto, ON

The Annual Canadian Echo Weekend is the premier gathering of professionals committed to the latest development in cardiovascular ultrasound in Canada.