No Relevant Disclosure
B.C. earthquake wakes up Vancouver, Victoria-area residents

Quake, 4.3-4.8 in magnitude, centred 20 km north of Victoria at 11:39 p.m PT Tuesday but no damage reported

LEARNING OBJECTIVES

• Clinical contexts and etiologies of pulmonary hypertension (PH)
• Current classification of PH
• Role of echo in pulmonary hypertension
• Echo in pulmonary embolism
CLINICAL CLASSIFICATION OF PH
(DANA POINT, CALIFORNIA 2008)

Group 1: Pulmonary arterial hypertension (PAH)
- Myeloproliferative disorders
- Splenectomy
- Metabolic: glycogen storage, thyroid
- Renal failure, dialysis
- Fibrosing mediastinitis
- Sarcoidosis,
- Pulmonary Langerhans cell histiocytosis,
- Lymphangiomyomatosis

Group 2: Left Heart Disease
- Idiopathic
- Heritable (BMPR2, ALK1, Endoglin)
- Drug, toxins
- Persistent PH of Newborn
- CTD, HIV, portal HTN
- Congenital: ASD, VSD, PDA
- Schistosomiasis
- Chronic hemolytic anemia
- Group 1': Pulmonary venoocclusive disease, pulmonary capillary hemangiomatosis

Group 3: Lung Disease and Hypoxia
- Systolic dysfunction
- Diastolic dysfunction
- Valve disease
- COPD
- ILD
- Mixed restrictive, obstructive
- OSA
- Alveolar hypoventilation
- High altitude
- Developmental abnormalities

Group 4: Thromboembolism

Group 5: Unclear, Multifactorial
- Myeloproliferative disorders
- Splenectomy
- Metabolic: glycogen storage, thyroid
- Renal failure, dialysis
- Fibrosing mediastinitis
- Sarcoidosis,
- Pulmonary Langerhans cell histiocytosis,
- Lymphangiomyomatosis

Simonnereau et al. J Am Coll Cardiol 2009;54: S43–54
WHERE IS THE LESION?

Group I—PAH
Idiopathic PAH
Heritable
  BMPR2
  ALK1, endoglin (with or without HHT)
Unknown
Drug and toxin-induced
PAH associated with:
  Connective tissue diseases
  HIV infection
  Portal hypertension
  Congenital systemic to pulmonary shunts
  Schistosomiasis
  Chronic hemolytic anemia
Persistent pulmonary hypertension of newborn
Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis

Group II—PH owing to left heart disease
Systolic dysfunction
Diastolic dysfunction
Valvular disease

Group III—PH owing to lung diseases and/or hypoxia
Chronic obstructive pulmonary disease
Interstitial lung disease
Other pulmonary diseases with mixed restrictive and obstructive pattern
Sleep-disordered breathing
Alveolar hypoventilation disorder
Chronic exposure to high altitude
Developmental abnormalities

Group IV—Chronic thromboembolic PH

Group V – Others

PAH: relative blood flow obstruction and increased PVR proximal to capillary bed

Pulmonary Arterial Hypertension: histopathological features

Normal:
- Intima
- Endothelium
- Media and smooth muscle
- Adventitia

Intimal and medial thickening:
- Endothelial proliferation
- Intimal fibrosis
- Medial and smooth muscle cell hypertrophy

Intimal fibrosis and in situ thrombosis:
- In situ thrombosis
- Intimal fibrosis

Collateral flux
Plexiform lesion

Direction of blood flow:
- Media
- Intimal fibrosis
- Intimal fibrosis

Actelion PAH-info.com
DEFINITION OF PH AND PAH BY CATH

PH: Mean PAP $\geq 25$ mmHg

PAH: Mean PAP $\geq 25$ mmHg + PCWP $\leq 15$ mmHg

ACCF/AHA: PVR $>3$ WU

McLaughlin et al. J Am Coll Cardiol 2009; 53: 1573-1619
PULMONARY VASCULAR RESISTANCE
PULMONARY WEDGE PRESSURE

PVR: Distinguishing high PAP due to increased flow versus from increased PVR

- PVR by cath: \(\frac{\text{Mean PAP} - \text{PCWP}}{\text{CO}}\)
- PVR by echo: \(\frac{\text{Peak TR/ RVOT TVI}}{10 + 0.16}\)

PCWP by echo: 1.9 + 1.24 x E/E'
NEW PROPOSED DEFINITIONS Mean PAP

- Upper limit of normal: 20 mm Hg
- Borderline PH: 20-24 mm Hg
- Manifest PH: ≥25 mm Hg

SCREENING FOR PH

HISTORY THAT RAISES INDEX OF SUSPICION OF PH

• Family history for IPAH or BMPR2 mutation
• Prior use of appetite suppressants or stimulants (metamphetamines)
• DVT and pulmonary embolism, HIV, sickle cell disease, connective tissue diseases, vasculitis, scleroderma, sarcoidosis, post-splenectomy
• Pre-liver transplant, portal hypertension

SYMPTOMS: dyspnea, chest discomfort, lightheadedness, palpitations, presyncope, syncope, edema, fatigue and reduced exercise tolerance
ROLE OF ECHO IN PH

- Screening for PH in higher risk populations
- Detection of PH, decide who needs right heart cath
- Evaluation of hemodynamics of PH, and structure and function of right heart
- Determine etiology and clinical classification
- Risk stratification and prognostication (severity of PH, right heart size and function, TAPSE, S’, FAC, MPI
- Monitoring disease stability, response to therapies
ECHO FEATURES OF PH

- RA, RV enlargement
- RV hypertrophy
- RV dysfunction
- Abnormal ventricular septum: posterior wall ratio ( >1)
- Ventricular septal flattening, D-shaped LV
- Significant TR and PR
- Reduced RV outflow tract velocity
- Short RVOT acceleration time (<100 msec)
- Dilated IVC and decreased collapsibility
- PFO/ASD (bubble study)
- Dilated pulmonary arteries
- Pericardial effusion
ECHO FEATURES OF PH RELATED TO LEFT HEART PROBLEMS

- LA enlargement
- LVH
- LV diastolic dysfunction
- Right heart enlargement may not yet be present
- Elevated filling pressures by E/e’
- Extent of functional MR at rest and during exercise
- Usually modest pulmonary pressures (SPAP 60s rather than >80 mm Hg)
LIMITATIONS OF ECHO IN PAH

• Images can be limited in some patient populations (lung disease, obesity)
• TR jet may be weak or absent in some patients, thus precluding PASP assessment (can enhance with agitated saline contrast)
• May overestimate or underestimate actual pulmonary pressures

TR VELOCITY AND LIKELIHOOD OF PULMONARY HYPERTENSION

<table>
<thead>
<tr>
<th>TR velocity (m/sec)</th>
<th>Estimated SPAP (mm Hg)</th>
<th>Other Echo signs of PH present</th>
<th>Likelihood of PH</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2.8</td>
<td>&lt;36</td>
<td>No</td>
<td>Unlikely</td>
</tr>
<tr>
<td>&lt;2.8</td>
<td>&lt;36</td>
<td>Yes</td>
<td>Possible</td>
</tr>
<tr>
<td>2-9-3.4</td>
<td>36-50</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>&gt;3.4</td>
<td>&gt;50</td>
<td>Yes</td>
<td>Likely</td>
</tr>
</tbody>
</table>

TR velocity is not representative of pulmonary pressures in the presence of RVOT obstruction or pulmonary stenosis.

ECHO FOR DIAGNOSING AND MONITORING PULMONARY HYPERTENSION

PULMONARY HEMODYNAMICS (elevated pressures)
- Systolic PAP = 4 x TRV^2 + RAP (high >35 mm Hg)
- Mean PAP = 4 x PRVearly^2 + RAP) (PH ≥ 25 mm Hg)
- Diastolic PAP =4 x PRVend^2 + RAP (high >15 mm Hg)
- RAP: (RA>15 mm Hg if IVC>21 mm, inspiratory collapse <50%)
- RVOT acceleration time (PH <100 ms)
- PVR = TRV/RVOT TVI x10 + 0.16 (normal <0.15 WU; PH: >3 WU)
- PCWP=1.9 + 1.24 x E/E’ (high>15 mm Hg)

IMPAIRED RV SYSTOLIC FUNCTION
- TAPSE (Tricuspid annular plane systolic excursion) <16 mm
- Tei index =(IVRT + IVCT)/ET (>0.40 by PW Doppler; >0.55 by DTI)
- RV fractional area change <35%
- S-wave velocity by DTI (<10 cm/sec)
PULMONARY HEMODYNAMICS
ECHO ASSESSMENTS

• Pulmonary pressures

• Pulmonary vascular resistance
SYSTOLIC, MEAN, AND DIASTOLIC PULMONARY ARTERY PRESSURE

Systolic PAP = 4 \times TRV^2 + RAP

- Mean PAP = 4 \times \text{peak PRV early}^2 + RAP
- Diastolic PAP = 4 \times \text{PRVend}^2 + RAP
MEAN PULMONARY ARTERY PRESSURE

- Mean PAP $= 4 \times PRV_{\text{early}}^2 + \text{RAP}$
- Mean PAP $= 0.61 \times \text{SPAP} + 2 \text{ mm Hg}$
- Mean PAP $= \text{VTI of TR jet} + \text{RAP}$
- Mean PAP $= \frac{1}{3}(\text{SPAP}) + \frac{2}{3}(\text{DPAP})$
- Mean PAP $= 79 - 0.45 \times (\text{PAAT})$
- Mean PAP $= 90 - (0.62 \times \text{PAAT})$
- Mean PAP $= 80 - 0.5 \times (\text{PAAT})$

PAAT = pulmonary artery acceleration time (same as RVOT acceleration time)
MEAN PULMONARY ARTERY PRESSURE

Mean PA = Mean systolic Pressure + Estimated RV-RV gradient RA pressure (TVI)

RVOT ACCELERATION TIME

- AT inversely correlates with mean PAP.
- Normal >130 ms
- <100 ms : significant PH
- If AT < 90 msec → SPAP is > 60 mmHg

For estimation of MPAP
- $MPAP = 79 - (0.45 \times RVOT\ AT)$
- $MPAP = 90 - (0.62 \times RVOT\ AT)$
- $MPAP = 80 - (0.50 \times RVOT\ AT)$
American Society of Echocardiography Recommends estimated RA be:

- 3 mmHg, IVC <21mm and >50% collapse
- 8 mmHg, IVC <21 mm and <50% collapse
- 8 mm Hg, IVC >21 mm and >50% collapse
- 15 mmHg, IVC >21mm and <50% collapse

HEPATIC VEIN FLOW IN PH

Hepatic veins
- Normal size 5-11 mm
- Abnormal if A wave > systolic S wave
- Abnormal: Vs/Vd< 1 (High RAP)
- Systolic filling fraction: Vs/(Vs + Vd)< 55%
  Sensitive and specific for increased RAP
PVR = \[(\text{TRV/TVI}_{\text{RVOT}}) \times 10\] + 0.16 (Abbas Formula)*

\[
= (3.9 / 10.2) \times 10 + 0.16 = 3.98 \text{ WU}
\]

\[
\text{PVR}_c = (\text{RVSP} - \text{E/e'}) / \text{VTI}_{\text{RVOT}} \text{ (Corrected Dahiya equation)}#
\]

*Abbas, AE et al. JACC 2003. 41: 1021-1027
RV IMPACT
ECHO ASSESSMENT
QUANTITATIVE ESTIMATE OF RV SIZE

- Length (> 86 mm*)
- Mid diameter (> 35 mm*)
- Basal diameter (> 42 mm*)
- RV area > 28 cm²*

* Measures indicate dilatation

- RV end-diastolic diameter has been identified as a predictor of survival in patients with chronic pulmonary disease

Tips
- Measure at end diastole from an RV focused apical 4-chamber view
- Optimize image to have maximum diameter without foreshortening the ventricle

RV-RA SIZE: QUALITATIVE “EYEBALL” ESTIMATE

- **Normal RV size**
  - RV 2/3 size of LV

- **Mild RVE**
  - RV Similar to LV/ Shares apex

- **Moderate RVE**
  - RV Larger than LV

- **Severe RVE RAE**
  - Very large RV/ Apex forming D shaped septum
RV FAC (FRACTIONAL AREA CHANGE)

RV FAC (%) = \( \frac{RV_{\text{area} \text{ diastole}} - RV_{\text{area} \text{ systole}}}{RV_{\text{area} \text{ diastole}}} \times 100 \)

RV systolic dysfunction if FAC <35%
RV LONGITUDINAL FUNCTION: TAPSE

TAPSE
- Simple, reproducible
- Represents longitudinal function
- Correlates well with radionuclide angiography in determining RV systolic function. Relatively load dependent.
- Normal at least >16 mm (some publications >20 mm Hg)
- TAPSE < 18 mm has negative prognostic implications

TECHNICALLY
- In apical 4C view, place M-Mode cursor through the lateral tricuspid annulus
- Measure excursion from end-diastole to end-systole; average over 3 beats
- Angle and load dependent
- Off-axis views tend to overestimate TAPSE

TV Annular velocity $s'$
- Simple, sensitive, reproducible
- Good indicator of *basal* free wall function
- Angle dependant
- Relatively independent of loading conditions
- Correlated with EF by first pass radionuclide ventriculography
- Normal $> 10$ cm/s

RV Myocardial Performance Index (MPI)
- $\text{MPI} = (\text{TCO} - \text{ET}) / \text{ET}$
  - TCO: TV closure to opening time
  - ET: ejection time
- Normal MPI by TDI $< 0.55$
The RV Index of Myocardial Performance (RIMP) Global Indicator of Systolic and Diastolic Function.

- Needs the measurements of 2 different cardiac cycles (tricuspid inflow and RV outflow by PW Doppler)

- Relatively independent of HR and from loading conditions

- Prognostic in PH

- Normal values below 0.4

- May get pseudonormalized with high RVDP or RAP

\[ MPI = \frac{(IVCT + IVRT)}{ET} = \frac{(a - ET)}{ET} \]


OTHER TECHNIQUES
3D AND STRAIN

INDIRECT SIGNS OF PULMONARY HYPERTENSION
INDIRECT ECHOCARDIOGRAPHIC FINDINGS IN PH

“Flying W” sign by M-Mode (mid-systolic notching)
Due to early closure of pulmonary valve because of high PVR

Dilated coronary sinus
SEPTAL FLATTENING - ECCENTRICITY INDEX

Abnormal eccentricity Index : D1/D2 > 1

E.I = 40/25 = 1.6 (D1/D2)

Primarily in Diastole = volume overload
In Systole as well = volume and pressure overload
PERICARDIAL EFFUSION
A BAD SIGN IN PH

- Associated with greater disease severity
- Increases mortality risk
- Likely reflects high venous pressure and poor lymphatic drainage
## DETERMINANTS OF PROGNOSIS IN PAH

<table>
<thead>
<tr>
<th>DETERMINANTS OF RISK</th>
<th>LOWER RISK</th>
<th>HIGHER RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical evidence of RV failure</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Progression of symptoms</td>
<td>Gradual</td>
<td>Rapid</td>
</tr>
<tr>
<td>WHO class</td>
<td>II, III</td>
<td>IV</td>
</tr>
<tr>
<td>6MWD</td>
<td>Longer (&gt;400 m)</td>
<td>Shorter (&lt;300 m)</td>
</tr>
<tr>
<td>CPET</td>
<td>Peak VO$_2$&gt;10.4 mL/kg/min</td>
<td>Peak VO$_2$&lt;10.4 mL/kg/min</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>Minimal RV dysfunction</td>
<td>Pericardial effusion, significant RV enlargement/dysfunction; RA enlargement (TAPSE in ESC guidelines)</td>
</tr>
<tr>
<td>Hemodynamics</td>
<td>RAP &lt;10 mm Hg; CI &gt;2.5 L/min/m$^2$</td>
<td>RAP &gt;20 mm Hg; CI &lt;2.0 L/min/m$^2$</td>
</tr>
<tr>
<td>BNP</td>
<td>Minimally elevated</td>
<td>Significantly elevated</td>
</tr>
</tbody>
</table>

*Syncope* is poor prognostic sign added in the ESC guidelines

PROGNOSTIC VALUE OF ECHO PARAMETERS IN PULMONARY HYPERTENSION

• 2-year survival = 88% if TAPSE > 18 mm
• 2-year survival = 50% if TAPSE < 18 mm
• Forfia PR – Am J Respir Crit Care Med 2006; 174: 1034


Prognostic value of MPI
YeoTc – Am J Cardiol 1998; 81:1157-61
Tei, C- JASE 1996; 9: 838-47

ECHOCARDIOGRAPHIC PREDICTORS OF OUTCOMES

81 pts prostacyclines vs placebo
F/U 36 months, 20 deaths, 21 transplantations

Right atrial size

- RA size < median
- RA size > median

Survival (%)

Years

81 pts prostacyclines vs placebo
F/U 36 months, 20 deaths, 21 transplantations

Pericardial effusion

- No effusion
- Effusion

Survival (%)

Years

Eccentricity index

- Eccentricity index < median
- Eccentricity index > median

Survival (%)

Years

- Ra size > 20 cm², abnormal; > 27 cm² associated with poor prognosis
- Eccentricity index > 1 abnormal; > 1.7 carries poor prognosis

EXERCISE INDUCED PULMONARY HYPERTENSION

- Slight increase in pulmonary pressures with exercise appeared normal SPAP <40-45 mm Hg
- Athletes SPAP <55-60 mm Hg (due to substantial increase in pulmonary flow)
- Competitive athletes who exercise at high levels of CO and PAP because of an intrinsically steep pressure-flow relationship may be exposed in the long term to RV remodeling and subsequent arrhythmias
ECHO IN PULMONARY EMBOLISM

- 32 year old woman
- Has been on oral contraception
- Healthy, no significant past history
- Presyncope while at school
- Short of breath
- Pleuritic chest pain
- On arrival to ER: BP 78/45 mm Hg,
- HR 130 bpm and regular
- Decreased air entry on left side.
Acute Dilatation Pre-thrombolysis

Post-thrombolysis
ECHO IN PULMONARY EMBOLISM

- Echo low sensitivity for diagnosing pulmonary embolism
- Acute RV and RA dilatation, RV dysfunction
- Elevated pulmonary pressures, dilated IVC
- Intracardiac thrombus (IVC, right heart)
- Thrombus in pulmonary arteries (rare by TTE)
- McConnell’s sign: Akinetic mid RV free wall with sparing of apex

SUMMARY: ECHO ASSESSMENT OF PH

- Bi-ventricular size and function, presence of ventricular hypertrophy, cardiomyopathy, valvular abnormality (MS, MR, AS etc..), pericardial effusion
  - Subjective and quantitative assessment of RV size
  - Subjective and quantitative assessment of RV systolic function
  - Percent fractional area change (% FAC)
  - Tricuspid annular plane systolic excursion (TAPSE)
  - Eccentricity Index / D-shaped LV
  - RV myocardial performance index (MPI) or Tei index
  - TDI systolic velocity of the RV lateral annulus (S’)
- Pulmonary artery pressure estimation / Hemodynamics:
  - Pulmonary artery pressures (Systolic, Mean, Diastolic), PVR
  - RVOT acceleration time and presence of pulmonary valve notching
- Size of both atria
- RA pressure assessment (IVC size and collapse, hepatic veins)
- Assessment of C.O (LVOT diameter and time-velocity integral of aortic flow by PW Doppler)
- Intracardiac shunt, bubble study (Congenital heart disease, PFO/ASD)
- 3D echocardiography, myocardial deformation techniques (strain imaging or speckle-tracking techniques derived from tissue Doppler) if available
SUMMARY: ROLE OF ECHO IN PH

- Echo: Key for initial diagnosis and follow up evaluation of a patient with PH.
- Despite its limitations, it is the most clinically useful noninvasive test for the assessment of the pulmonary circulation
- Echo is reasonably accurate estimate of the RV, and PA pressures and hemodynamics.
- Echo is important for prognostication, monitor progression and response to therapy, independent of clinical and right heart cath data
THANK YOU!