Σύγχρονες απεικονιστικές προσεγγίσεις στην πνευμονική υπέρταση

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Νοσοκομείο Αττικόν
### Table 3  Haemodynamic definitions of pulmonary hypertension

<table>
<thead>
<tr>
<th>Definition</th>
<th>Characteristics</th>
<th>Clinical group(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH</td>
<td>PAPm ≥25 mmHg</td>
<td>All</td>
</tr>
</tbody>
</table>
| Pre-capillary PH            | PAPm ≥25 mmHg, PAWP ≤15 mmHg | 1. Pulmonary arterial hypertension  
2. PH due to left heart disease  
3. PH due to lung diseases  
4. Chronic thromboembolic PH  
5. PH with unclear and/or multifactorial mechanisms |
| Post-capillary PH           | PAPm ≥25 mmHg, PAWP >15 mmHg | 2. PH due to left heart disease  
5. PH with unclear and/or multifactorial mechanisms |
| Isolated post-capillary PH  | DPG <7 mmHg and/or PVR ≤3 WU  | 2. PH due to left heart disease  
5. PH with unclear and/or multifactorial mechanisms |
| Combined post-capillary and pre-capillary PH | DPG ≥7 mmHg and/or PVR >3 WU | 2. PH due to left heart disease  
5. PH with unclear and/or multifactorial mechanisms |

### Table 5  Important pathophysiological and clinical definitions

1. Pulmonary hypertension (PH) is a haemodynamic and pathophysiological condition defined as an increase in mean pulmonary arterial pressure ≥25 mmHg at rest as assessed by right heart catheterization (Table 3). PH can be found in multiple clinical conditions (Table 4).

2. Pulmonary arterial hypertension (PAH, group 1) is a clinical condition characterized by the presence of pre-capillary PH (Table 3) and pulmonary vascular resistance >3 Wood units, in the absence of other causes of pre-capillary PH such as PH due to lung diseases, chronic thromboembolic PH, or other rare diseases (Table 4). PAH includes different forms that share a similar clinical picture and virtually identical pathological changes of the lung microcirculation (Table 4).

3. There is no sufficient data to support the definition of 'PH on exercise'.
Clinical classification of Pulmonary Hypertension (ESC/ERS guidelines 2015)

1. Pulmonary arterial hypertension
   1.1 Idiopathic
   1.2 Heritable
      1.2.1 BMPR2 mutation
   1.2.2 Other mutations
   1.3 Drugs and toxins induced
   1.4 Associated with:
      1.4.1 Connective tissue disease
      1.4.2 Human immunodeficiency virus (HIV) infection
      1.4.3 Portal hypertension
      1.4.4 Congenital heart disease (Table 6)
      1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis
   1'.1 Idiopathic
   1'.2 Heritable
      1'.2.1 EIF2AK4 mutation
   1'.2.2 Other mutations
   1'.3 Drugs, toxins and radiation induced
   1'.4 Associated with:
      1'.4.1 Connective tissue disease
      1'.4.2 HIV infection

1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart disease
   2.1 Left ventricular systolic dysfunction
   2.2 Left ventricular diastolic dysfunction
   2.3 Valvular disease
   2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
   2.5 Congenital / acquired pulmonary veins stenosis

3. Pulmonary hypertension due to lung diseases and/or hypoxia
   3.1 Chronic obstructive pulmonary disease
   3.2 Interstitial lung disease
   3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
   3.4 Sleep-disordered breathing
   3.5 Alveolar hypoventilation disorders
   3.6 Chronic exposure to high altitude
   3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions
   4.1 Chronic thromboembolic pulmonary hypertension
   4.2 Other pulmonary artery obstructions
      4.2.1 Angiosarcoma
      4.2.2 Other intravascular tumors
      4.2.3 Arteritis
      4.2.4 Congenital pulmonary arteries stenoses
      4.2.5 Parasites (hydatidosis)

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms
   5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
   5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
   5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
   5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

Galie N et al.
ESC guidelines 2015
Pulmonary Hypertension groups

- Thromboembolic disease
- Precapillary (arterial)
- IPAH and APAH
- Left-sided heart disease
- Lung disease/hypoxia
- Postcapillary (venous)
GOALS FOR IMAGING IN PH PATIENTS

➢ Assess probability for PH
  ▪ Assessment of LV/RV size, morphology, function
    ➢ SV, CO, EF
    ➢ RV mass, PA distensibility

➢ Specific Diagnosis
  ▪ Non invasive hemodynamic assessment
    ▪ PASP, RAP, mean PAP, PVR

➢ Prognostic markers
  ▪ PA angiography
  ▪ Lung perfusion
  ▪ Lung parenchyma
ROLE OF ECHOCARDIOGRAPHY IN PULMONARY HYPERTENSION

• Screening for PH in high risk populations (FH for genetic mutation, drug exposure, DVT/PE, CTD/vasculitis, liver transplant, post splenectomy)
• Screening based on clinical presentation
• Hemodynamic evaluation of PH (PASP, mPAP, PVR)
• Evaluation of right heart structure and function
• Determine etiology and clinical classification (Diastology, valve dz.)
• Risk stratification and prognostication
• Monitor disease and response to therapy
HEMODYNAMIC EVALUATION OF PH

- Pulmonary Artery Systolic Pressure (PASP)
- Pulmonary Artery Diastolic Pressure (PADP)
- Mean Pulmonary Artery Pressure (MPAP)
- Pulmonary Vascular Resistance (PVR)
### Non Invasive Hemodynamic Evaluation of PH by Echocardiography

<table>
<thead>
<tr>
<th>Key indices (cutoff)</th>
<th>Additional indices (cutoff)</th>
<th>Complementary indices (cutoff)</th>
<th>Research tools</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary hemodynamics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPAP = $4 \times \text{TRV}^2 + \text{RAP}$ (TRV &gt; 2.8–2.9 msec; SPAP 36 mm Hg)</td>
<td>MPAP = TVI_{TR} + RAP$^{13}$ ($\geq 25$ mm Hg)</td>
<td>$\text{AT}_{RVOT} &lt; 100$ msec</td>
<td>PVCAP = SV/4 \times (\text{TRV}^2 - \text{PRV}^2)^{14}$ ($&lt; 0.8$ mL/mm Hg predicts mortality in PAH patients)</td>
</tr>
<tr>
<td>RAP = IVC size and collapsibility $^{16}$ ($\geq 2.1$ cm, collapse $&lt; 50$%; RAP 15 mm Hg)</td>
<td>RV IVRT$^{15}$ (by DTI; $&gt; 65$ msec; SPAP $&gt; 40$ mm Hg; $&lt; 59$ msec; RAP $&gt; 8$ mm Hg)</td>
<td>MPAP = 0.61 \times \text{SPAP} + 2$ mm Hg$^{19}$</td>
<td></td>
</tr>
<tr>
<td>MPAP = $4 \times \text{PRV}^2 + \text{RAP}$ ($\geq 25$ mm Hg)</td>
<td>MPAP = 0.61 \times \text{SPAP} + 2$ mm Hg$^{19}$</td>
<td>MPAP = 90 - 0.62 \times \text{AT}_{RVOT}$</td>
<td></td>
</tr>
<tr>
<td>DPAP = $4 \times (\text{PRV ED})^2 + \text{RAP}$</td>
<td></td>
<td>MPAP = 79 - 0.45 \times \text{AT}_{RVOT}$</td>
<td></td>
</tr>
<tr>
<td>PVR = TRV/TVI_{RVOT} (cm) $\times 10 + 0.16^{21}$ ($&gt; 0.2$: PVR $&gt; 2$ WU; $&lt; 0.15$: normal PVR)</td>
<td>PVR = SPAP/(HR \times TVI_{RVOT})$^{22}$ ($&gt; 0.076$: indexed PVR $&gt; 15$ RU)</td>
<td>$\text{FVE}_{RVOT}^{23}$ (midsystolic &quot;notch&quot;)</td>
<td></td>
</tr>
<tr>
<td>PCWP = $1.9 + 1.24 \times \text{E/E}'$ $^{24}$ ($\text{E/E}' &gt; 15$; PCWP $&gt; 15$ mm Hg)</td>
<td>$\text{LAVI}^{25}$ ($&gt; 31$ mL/m$^2$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impaired RV systolic function</td>
<td>TAPSE ($&lt; 16$ mm)</td>
<td>Tei index: (IVRT + IVCT/ET) $&gt; 0.40$ by PW Doppler; $&gt; 0.55$ by DTI</td>
<td>3D RV EF ($&lt; 44%$)</td>
</tr>
<tr>
<td>TAPSE ($&lt; 16$ mm)</td>
<td>Tei index: (IVRT + IVCT/ET) $&gt; 0.40$ by PW Doppler; $&gt; 0.55$ by DTI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV FAC ($&lt; 35%$)</td>
<td>RV LPSS$^{26}$ ($= -19%$)</td>
<td></td>
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</tr>
</tbody>
</table>
TR JET ESTIMATES OF PASP CAVEATS

- Poor quality signals
- Weak or absent TR jet (enhance using Contrast)
- Inaccurate in pts with very severe TR
- Resting PASP dependent on age, BMI
- Flow dependent variable
- May underestimate or overestimate pulmonary pressures
<table>
<thead>
<tr>
<th>Peak tricuspid regurgitation velocity (m/s)</th>
<th>Presence of other echo ‘PH signs’</th>
<th>Echocardiographic probability of pulmonary hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2.8 or not measurable</td>
<td>No</td>
<td>Low</td>
</tr>
<tr>
<td>≤2.8 or not measurable</td>
<td>Yes</td>
<td>Intermediate</td>
</tr>
<tr>
<td>2.9–3.4</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.9–3.4</td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td>&gt;3.4</td>
<td>Not required</td>
<td></td>
</tr>
</tbody>
</table>
## OTHER ECHO PH SIGNS

<table>
<thead>
<tr>
<th>A: The ventricles</th>
<th>B: Pulmonary artery</th>
<th>C: Inferior vena cava and right atrium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ventricle/ left ventricle basal diameter ratio &gt;1.0</td>
<td>Right ventricular outflow Doppler acceleration time &lt;105 msec and/or midsystolic notching</td>
<td>Inferior cava diameter &gt;21 mm with decreased inspiratory collapse (&lt;50 % with a sniff or &lt;20 % with quiet inspiration)</td>
</tr>
<tr>
<td>Flattening of the interventricular septum (left ventricular eccentricity index &gt;1.1 in systole and/or diastole)</td>
<td>Early diastolic pulmonary regurgitation velocity &gt;2.2 m/sec</td>
<td>Right atrial area (end-systole) &gt;18 cm²</td>
</tr>
<tr>
<td>PA diameter &gt;25 mm.</td>
<td></td>
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</tr>
</tbody>
</table>
Mean PAP = 4PR Vearly2 + RAP

Diastolic PAP = 4PAEDV2 + RAP

Mean PAP = 1/3SPAP + 2/3PADP

J Am Soc Echocardiogr 2010; 23: 685-713
PVR

Distinguish if PAP is due to high flow or high PVR

Good correlation with invasive data

Prognostic marker

PVR = TRVmax/RVOT VTI x 10 + 0.16

JACC; 2003: 41, 6, 1021-1027
Changes (minor):
- RV dimensions
- S’
- TAPSE
- RIMP
• Not indexed to size
RV MEASUREMENTS

General recommendations

- **Parameters that can be measured**
  - RV and RA size
  - RV systolic function
    - FAC
    - DTI derived annular systolic velocity wave
    - TAPSE
    - RV index of myocardial performance
  - **Parameters that could be measured (when feasible)**
    - RV EF and volumes
TIPS FOR RV MEASUREMENTS

➢ Use multiple views for RV diameters

➢ Beware of suboptimal apical views
APICAL 4 CH VIEWS

- RV focused view allows better visualization of the entire free wall
- It is better than a standard 4 CH view
- RV focused view is recommended to measure RV diameters
Tricuspid annular plane systolic excursion (TAPSE)

- RV Base-to-apex shortening during systole measured as the systolic displacement of the lateral portion of the tricuspid annular plane
  - M-mode guided excursion

TAPSE < 17 mm is highly suggestive of RV systolic dysfunction.
Off line analysis by color coded tissue Doppler currently remains a research tool, with less data and wider confidence intervals for normal values.

**Recommendations:**

An $S'$ velocity $< 9.5$ cm/sec measured on the free-wall side indicates RV systolic dysfunction.
**RV Fractional Area Change**

- Endocardial borders of end-systole and end-diastole traced manually
- Avoid trabeculae
- Diastolic-systolic area difference divided by end-diastolic area x 100

RV FAC (%) 49±7

FAC < 35% indicates RV dysfunction
RV FUNCTION

Tei index, MPI, RIMP

**RIMP by Pulse Doppler**

\[
RIMP = \frac{TCO - ET}{ET}
\]

**RIMP by TDI**

\[
RIMP = \frac{IVRT + IVCT}{ET} = \frac{TCO - ET}{ET}
\]

Normal values

\[
\text{≤0.43 (PW)}
\]

\[
\text{≤0.54 (DTI)}
\]

**NOTE !** RIMP may be falsely low in cases of increased RAP
RV strain

RV longitudinal strain should be measured in the RV-focused four-chamber view.

Pooled data (though heavily weighted by a single vendor) suggest that global longitudinal RV free wall strain > -20% (i.e., <20% in absolute value) is likely abnormal.

Caveats:
• Placing the basal reference points too low (i.e., on the atrial side of the tricuspid annulus) might result in artifactually low basal strain values.
• The width of the region of interest should be limited to the myocardium, excluding the pericardium.
RIGHT ATRIUM
VOLUMES PREFERRED

Single plane
25±7ml/m² ♂
21±7ml/m² ♀
Echo indices predictive of survival in PAH

<table>
<thead>
<tr>
<th>Echocardiographic parameters</th>
<th>Worse prognosis</th>
</tr>
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<tbody>
<tr>
<td>Tricuspid annular plane systolic excursion</td>
<td>&lt;15 mm</td>
</tr>
<tr>
<td>Right ventricular Doppler (Tei) index</td>
<td>&gt;0.88</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>Present</td>
</tr>
<tr>
<td>Left ventricular eccentricity index at end-diastole</td>
<td>&gt;1.7</td>
</tr>
<tr>
<td>Right atrial volume</td>
<td>Increasing size</td>
</tr>
<tr>
<td>Right ventricular fractional area change</td>
<td>Decreasing %</td>
</tr>
</tbody>
</table>

Eur Respir Rev 2011; 20: 122, 236–242
<table>
<thead>
<tr>
<th>Determinants of prognosis(^a) (estimated 1-year mortality)</th>
<th>Low risk &lt;5%</th>
<th>Intermediate risk 5–10%</th>
<th>High risk &gt;10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs of right heart failure</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Progression of symptoms</td>
<td>No</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Syncope</td>
<td>No</td>
<td>Occasional syncope(^b)</td>
<td>Repeated syncope(^c)</td>
</tr>
<tr>
<td>WHO functional class</td>
<td>I, II</td>
<td>III</td>
<td>IV</td>
</tr>
<tr>
<td>6MWD</td>
<td>&gt;440 m</td>
<td>165–440 m</td>
<td>&lt;165 m</td>
</tr>
<tr>
<td>Cardiopulmonary exercise testing</td>
<td>Peak VO(_2) &gt;15 ml/min/kg (&gt;65% pred.) VE/VCO(_2) slope &lt;36</td>
<td>Peak VO(_2) 11–15 ml/min/kg (35–65% pred.) VE/VCO(_2) slope 36–44.9</td>
<td>Peak VO(_2) &lt;11 ml/min/kg (&lt;35% pred.) VE/VCO(_2) slope ≥45</td>
</tr>
<tr>
<td>NT-proBNP plasma levels</td>
<td>BNP &lt;50 ng/l</td>
<td>BNP 50–300 ng/l</td>
<td>BNP &gt;300 ng/l</td>
</tr>
<tr>
<td></td>
<td>NT-proBNP &lt;300 ng/l</td>
<td>NT-proBNP 300–1400 ng/l</td>
<td>NT-proBNP &gt;1400 ng/l</td>
</tr>
<tr>
<td>Imaging (echocardiography, CMR imaging)</td>
<td>RA area &lt;18 cm(^2) No pericardial effusion</td>
<td>RA area 18–26 cm(^2) No or minimal, pericardial effusion</td>
<td>RA area &gt;26 cm(^2) Pericardial effusion</td>
</tr>
<tr>
<td>Haemodynamics</td>
<td>RAP &lt;8 mmHg CI ≥2.5 l/min/m(^2) SvO(_2) &gt;65%</td>
<td>RAP 8–14 mmHg CI 2.0–2.4 l/min/m(^2) SvO(_2) 60–65%</td>
<td>RAP &gt;14 mmHg CI &lt;2.0 l/min/m(^2) SvO(_2) &lt;60%</td>
</tr>
</tbody>
</table>
WHEN TO USE CMR AS AN ADJUNCT TO ECHOCARDIOGRAPHY IN CLINICAL PRACTICE IN PATIENTS WITH CONGENITAL HEART DISEASE

- Borderline or ambiguous echo measurements
- CMR data more precise than echocardiography
  - Eval of systemic and pulmonary veins
  - Quantification of RV vol/EF
  - RVOT/RV-PA conduits
  - Quantification of shunts
  - Quantification of PR
  - Evaluation of entire aorta
  - Tissue characterization
Therrien et al. AJC 2005
- RV EDV > 170 ml/m2

Buechel et al. Eur Heart J 2005
- RV EDV > 150 ml/m2

Osterhof et al. Circ 2007
- RVEDV > 160 ml/m2
- RV ESV > 82 ml/
For congenital heart disease involving the right ventricle: contouring error results in threshold values of 15–20 ml/m^2 for right ventricular end-diastolic volume 2.6–3.0% for right ventricular ejection fraction. Serial changes greater than these likely represent true clinical change.
Cardiac magnetic resonance findings predicting mortality in patients with pulmonary arterial hypertension: a systematic review and meta-analysis

Vivian J. M. Baggen1,2 · Tim Leiner3 · Marco C. Post1 · Arie P. van Dijk1 ·
Jolien W. Roos-Hesselink2 · Eric Boersma2,4 · Jesse Habets3 · Gertjan Tj. Sieswerda1
Meta-analysis showed that RV ejection fraction was the strongest predictor of mortality in PAH-pooled HR 1.23 [95% CI 1.07–1.41], p = 0.003) per 5% decrease
RADIOLOGY
NUCLEAR MEDICINE
IMAGING METHODS
MULTIMODALITY IMAGING TEAM FOR PULMONARY HYPERTENSION REFERRAL CENTERS

ΠΓΝ Αττικόν
Διακλινικό Ιατρείο Πνευμονικής Υπέρτασης
What is machine learning?

(derived from artificial intelligence)

- Heterogeneous or unknown population
- Unsupervised machine learning
- Clusters
<table>
<thead>
<tr>
<th></th>
<th>Phenogroup 1 (n = 23)</th>
<th>Phenogroup 2 (n = 29)</th>
<th>Phenogroup 3 (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demography &amp; risk factors</strong></td>
<td>Middle aged, 66yo Female, 39% Systemic hypertension, 78% Sinus rhythm, 61%</td>
<td>Elderly, 73yo Female, 69% Systemic hypertension, 90% Atrial fibrillation, 76%</td>
<td>Younger, 63yo Female, 33% Coronaropathy, 40% Atrial fibrillation, 67%</td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
<td>Mild LV remodeling Preserved LVEF, 60% Preserved RV function Mild bi atrial dilatation</td>
<td>Mild LV remodeling Preserved LVEF, 63% Altered RV function Moderate biatrial dilatation</td>
<td>Severe biventricular remodeling Altered LVEF, 48% Severe RV dysfunction Severe biatrial dilatation</td>
</tr>
<tr>
<td><strong>Hemodynamics</strong></td>
<td>Mild PH, mPAP 34mmHg Normal PVR, 1.9 Woods</td>
<td>Severe PH, mPAP 44mmHg High resistance, 4.7 Woods</td>
<td>Moderate PH, mPAP 39 mmHg Small PVR increase, 2.7 Woods</td>
</tr>
</tbody>
</table>

| Combined post-capillary PH (DPG>7 and/or PVR>3) | 22% | 90% OR = 31.2 IC95% [6.61 – 147.34] p < 0.001 | 27% OR = 1.31 IC95% [0.36 – 4.7] p = 0.68 |
PHENOMAPPING IN PH

Raitier O et al. ESC 2018
University of Rouen, France
From heterogeneous population, machine learning was able to identify patients at:
- High risk of combined postcapillary PH
- High risk of mortality
• However before designing trials with vasodilators, model needs to be improved with larger data

Raitier O et al. ESC 2018
University of Rouen, France
CONCLUSIONS

- Imaging plays a central role in patients with a clinical suspicion of PH

- Echocardiography is a first line imaging test for individual and high-risk group screening
  - Echocardiography directs next steps in diagnostic algorithm for PH
  - CMR is an essential tool for GUCH patients
  - CMR provides useful prognostic information in patients with PAH
  - Multimodality imaging team is essential for PH referral centers

- AI will offer improved identification of subgroups of PH patients for optimal clinical trials design
ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ