Δευτεροπαθής πνευμονική υπέρταση: Διάγνωση και θεραπεία

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Καμμία σύγκρουση συμφερόντων
WHO – 1975

Primary Pulmonary Hypertension

Secondary Pulmonary Hypertension

2nd (1998) and 5th (2013) World Symposium on Pulmonary Hypertension

- **Group 1:** Pulmonary Arterial Hypertension
  (Heritable, Drugs, Associated Diseases e.g CTD, HIV, CHD, POVD)

- **Group 2:** PHT related to left heart diseases
  (HFrEF, HFpEF, valvulopathies, cardiomyopathies)

- **Group 3:** PHT related to lung diseases and/or hypoxia
  (COPD, interstitial diseases, sleep disorders, altitude, etc)

- **Group 4:** Chronic Thromboembolic Pulmonary hypertension – CTEPH

- **Group 5:** PHT with unclear multifactorial mechanisms
  (hematologic, systemic, metabolic disorders, etc)
Armadale and surrounding regions

Population: 165,450
Female, %: 50.4
Mean age, years: 35

Figure 2. Relationship between sPAP estimated by DE and directly measured by RHC ($r = 0.69$, $p < 0.0001$).
Pitfalls of Right Heart Catheterization

A

Digitized mean
Risk of misclassifying post- as precapillary PH: ≈30% (Ryan et al., 2013)

Expiration

Digitized mean

End-expiratory mean

Inspiration

PAWP Pressure Tracing

End-expiratory
Risk of misclassifying pre- as postcapillary PH: ≈30% (LeVargo et al., 2014)

B

70 year-old patient
HFpEF, volume overload
Body weight 80 kg

Same patient 6 days later
after volume depletion
Body weight 73 kg

PAPm 51 mmHg

PAPm 24 mmHg

PAWP

TPG

Criteria for valid PAWP measurement
PAWP value
Pressure tracing
Respirophasic variations
Catheter position
Aspiration
O2 saturation

Measurement and reading of pressure tracings
Measurement
Zero point
Point of reading
Factors preventing correct interpretation of pressure tracings
Diuretic use
COPD
Atrial fibrillation

High v-wave
Thorax deformities
Abdominal obesity

S. Rosenkranz et al. EHJ 2016
Κλινική Υποψία
- Ιστορικό
- Συμπτώματα
- ΗΚΓ
- CXR

Ηχωκαρδιολογία
Distinguishing between PAH and PH-LHD

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Echocardiography</th>
<th>Other features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65 years</td>
<td>Structural left heart abnormality • Disease of left heart valves • LA enlargement (&gt;4.2 cm) • Bowing of the IAS to the right • LV dysfunction • Concentric LV hypertrophy and/or increased LV mass</td>
<td>ECG • LVH and/or LAH • AF/Afib • LBBB • Presence of Q waves</td>
</tr>
</tbody>
</table>

| Symptoms of left heart failure | Doppler indices of increased filling pressures • Increased E/e’ • >Type 2–3 mitral flow abnormality | Other imaging • Kerley B lines • Pleural effusion • Pulmonary oedema • LA enlargement |

| Features of metabolic syndrome | Absence of • RV dysfunction • Mid systolic notching of the PA flow • Pericardial effusion |

| History of heart disease (past or current) | |
| Persistent atrial fibrillation | |

<table>
<thead>
<tr>
<th>History of</th>
<th>OR (95% CI)</th>
<th>p-value</th>
<th>Risk score #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left heart disease</td>
<td>10.0 (4.0–25.2)</td>
<td>&lt;0.001</td>
<td>22</td>
</tr>
<tr>
<td>ECG SV1+RV6 per mm</td>
<td>1.12 (1.06–1.20)</td>
<td>&lt;0.001</td>
<td>1×(SV1+RV6)</td>
</tr>
<tr>
<td>Echocardiography Left atrial dilation</td>
<td>12.2 (4.1–36.1)</td>
<td>&lt;0.001</td>
<td>20</td>
</tr>
<tr>
<td>Left valve disease worse than mild</td>
<td>7.5 (2.5–22.2)</td>
<td>&lt;0.001</td>
<td>22</td>
</tr>
</tbody>
</table>


ESC/ERS Guidelines 2015
Distinguishing between PAH and PH with HFpEF

Figure 1. LAV Was Significantly Lower in IPAH Than in PH-HFpEF

Only 1 idiopathic pulmonary arterial hypertension (IPAH) patient had a left atrial volume (LAV) >43 ml/m². Dotted pink line represents the LAV threshold of 43 ml/m². PH = pulmonary hypertension; PH-HFpEF = pulmonary hypertension due to heart failure with preserved ejection fraction.
=45-50mmHg

> 90mmHg
Pathophysiological Sequence: Backward Transmission

S. Rosenkranz et al. EHJ 2016
<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   | 1. Pulmonary arterial hypertension  
|                  | Pawp ≤15 mmHg   | 3. PH due to lung diseases        |
| Post-capillary PH| PAPm ≥25 mmHg   | 4. Chronic thromboembolic PH       |
|                  | Pawp >15 mmHg   | 5. PH with unclear and/or multifactorial mechanisms |

RHC is recommended in patients with PH due to left heart disease (group 2) or lung disease (group 3) if organ transplantation is considered

RHC may be considered in patients with suspected PH and left heart disease or lung disease to assist in the differential diagnosis and support treatment decisions
Optimizing therapy for Heart failure
<table>
<thead>
<tr>
<th>Drug</th>
<th>n</th>
<th>Start</th>
<th>End</th>
<th>Duration</th>
<th>Primary endpoint</th>
<th>Secondary endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF with reduced EF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riociguat LEPHT</td>
<td>201</td>
<td>Results available</td>
<td>16 weeks</td>
<td>Change in mPAP from baseline</td>
<td>Haemodynamic and echocardiographic variables, biomarker levels, safety, pharmacokinetics</td>
<td></td>
</tr>
<tr>
<td>Sildenafil Sil-HF (NCT010161381)</td>
<td>210</td>
<td>9/2012</td>
<td>6/2014</td>
<td>24 weeks</td>
<td>Patient Global assessment 6MWD</td>
<td>QoL, Kansas city questionnaire, safety</td>
</tr>
<tr>
<td>Tadalafil PITCH-HF (NCT01910389)</td>
<td>2102</td>
<td>Study terminated February 2014*</td>
<td>Up to 54 months</td>
<td>Time to CV death or 1st HF hospitalization</td>
<td>Biomarkers levels, exercise capacity, QoL, safety</td>
<td></td>
</tr>
<tr>
<td>HF with preserved EF</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sildenafil RELAX</td>
<td>216</td>
<td>Results available</td>
<td>24 weeks</td>
<td>Change in peak VO₂ from baseline</td>
<td>Exercise capacity, clinical status, QoL, safety</td>
<td></td>
</tr>
<tr>
<td>Sildenafil Hoendermis et al</td>
<td>52</td>
<td>Results available</td>
<td>12 weeks</td>
<td>Change in mPAP from baseline</td>
<td>Change in PAWP, cardiac output, peak VO₂</td>
<td></td>
</tr>
<tr>
<td>Riociguat DILATE</td>
<td>48</td>
<td>Results available</td>
<td>16 weeks</td>
<td>Change in mPAP from baseline</td>
<td>Haemodynamic and echocardiographic variables, biomarker levels, safety, pharmacokinetics</td>
<td></td>
</tr>
<tr>
<td>HF with EF &gt; 35%</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Macitentan MELODY-1 (NCT02070991)</td>
<td>60</td>
<td>5/2014</td>
<td>10/2015</td>
<td>12 weeks</td>
<td>Safety and tolerability (fluid retention)</td>
<td>PVR, haemodynamics, changes in TPG and DPG, echocardiographic variables (RV function)</td>
</tr>
</tbody>
</table>
Take Home Messages

- “Secondary” PHT (Nice group 2 & 3) is the commonest type

- Differential Diagnosis with PAH + CTEPH (Nice group 1 & 4) is **crucial** due to specific therapies

- Integrated diagnostic approach – No “miraculous” test

- PHT related to Left Heart Disease could progress to a dominant RV phenotype with worse prognosis and remains an area with limited evidence-based therapies but intense research
Ευχαριστώ για την προσοχή σας!

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