Le Cathétérisme Droit dans l’HTAP: Pourquoi est-ce Indispensable?

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Diagnostic Work-up in Pulmonary Hypertension

- Chest x-ray
- Pulmonary function tests
- Echocardiography
- Laboratory evaluation
- ECG
- Exercise testing
- CT
- Ventilation-perfusion scan
- Angiography
- Right heart catheterization
Hemodynamic Data Obtained with Doppler-Echocardiography

- Volumetric measurements
  - Stroke volume and cardiac output
  - Regurgitation volume and fraction
  - Pulmonary-systemic flow ratio (Qp/Qs)

- Pressure gradients
  - Maximal instantaneous gradient
  - Mean gradient

- Valve area
  - Stenotic valve area
  - Regurgitant orifice area

- Intracardiac pressures
  - Pulmonary artery pressures
  - Left atrial pressure
  - Left ventricular end-diastolic pressure
Problems of Hemodynamic Measurements in Echocardiography

- No absolute pressure
- No direct flow measurement
- Dependent on quality of echo signal
  - PHTN may be underestimated or missed in the presence of a poor signal
- In apical view mitral regurgitation or aortic stenosis signals could be falsely interpreted as tricuspid signals
- Not reliable for PAP measurement in the presence of pulmonary stenosis
How Good is the Estimation of PA Pressure by Tricuspid Regurgitation Velocity?

- $? \text{RVSP} = \text{Gradient}$
- $? \text{RVSP} = \text{Gradient} + 10 \text{ mmHg}$
- $? \text{RVSP} = \text{Gradient} + \text{RAP estimated on clinical grounds}$
- $? \text{RVSP} = \text{Gradient} + \text{RAP estimated by cava index}$
Estimation of RA Pressure Based on Diameter of the IVC

<table>
<thead>
<tr>
<th>IVC Diameter</th>
<th>Changes IVC Diameter with Inspiration</th>
<th>RA Pressure Estimation (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small (&lt;1.5 cm)</td>
<td>Collapse</td>
<td>0-5</td>
</tr>
<tr>
<td>Normal (1.5-2.5 cm)</td>
<td>&gt;50% ↓</td>
<td>5-10</td>
</tr>
<tr>
<td>Normal (1.5-2.5 cm)</td>
<td>&lt;50% ↓</td>
<td>10-15</td>
</tr>
<tr>
<td>Dilated (&gt;2.5 cm)</td>
<td>&lt;50% ↓</td>
<td>15-20</td>
</tr>
<tr>
<td>Dilatation also of the hepatic veins</td>
<td>no change</td>
<td>&gt;20</td>
</tr>
</tbody>
</table>
Correlation Doppler – Invasive Measurement

Currie PJ et al. JACC 1985;6.750-6
Stevenson JG JASE 1989;2:157-71

<table>
<thead>
<tr>
<th>Auteur</th>
<th>n</th>
<th>r</th>
<th>SEE mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yock 1984</td>
<td>62</td>
<td>0.95</td>
<td>7</td>
</tr>
<tr>
<td>Currie 1985</td>
<td>111</td>
<td>0.90</td>
<td>8</td>
</tr>
<tr>
<td>Stevenson 1989</td>
<td>50</td>
<td>0.96</td>
<td>6.9</td>
</tr>
</tbody>
</table>

Estimated pressure 50 mmHg → 95% confidence limits 34-66 mmHg

Tricuspid regurgitant jet estimation
• only in 50-60% of patients with no PHTN
• only in 80-90% of patients with PHTN
Doppler Echocardiography vs Invasive Pressure Measurements

Trans-Tricuspid pressure difference (mmHg) vs mPAP (mmHg) measured invasively

- False positive
- False negative

$r^2 = 0.4515$

Right Heart Catheterization
Cardiac Catheterisation → Essential in the Diagnosis and Management of PHTN

- Diagnostic gold standard
- Confirms the diagnosis of PHTN
- Describes the haemodynamic mechanism (e.g. PAH vs left heart disease)
- Determines severity (CO, RAP, mixed venous oxygen saturation)
- Testing for vasoreactivity
- Overall procedure-related mortality 0.055% (95% CI, 0.01%–0.099%): 4/7218

Right Heart Catheterization

Characteristic intracardiac pressure waveforms during passage through the heart:

- RA: Right atrium
- RV: Right ventricle
- PA: Pulmonary artery
- PCW: Pulmonary capillary wedge pressure

Pressure readings:
- RA: 40 mmHg
- RV: 20 mmHg
Goals of Invasive Assessment

- Confirm non-invasive estimation of pulmonary pressures
- Measurement of pressures and saturations in all heart chambers
- Find etiology of PHTN (e.g., shunts)
- Test vasoreactivity
- Plan therapy
- Assess prognosis
Right Heart Catheterization
→ Insight into Pulmonary Hemodynamics:
   Pressures, Flow State, Resistances

To rule out shunts-droit
Pulmonary Artery Wedge Pressure Measurement

Transpulmonal gradient = mean PAP – mean PCWP
Right Heart Catheter
Transpulmonary Gradient (TPG)
= mean PA pressure – PCWP

\[ TPG = 65 - 9 = 56 \text{ mmHg} \]
Right Heart: Normal Hemodynamics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syst. PA pressure</td>
<td>18 – 25 mmHg</td>
</tr>
<tr>
<td>Diast PA pressure</td>
<td>6 – 10 mmHg</td>
</tr>
<tr>
<td>Mean PAP</td>
<td>12 – 16 mmHg</td>
</tr>
<tr>
<td>PCWP</td>
<td>6 – 10 mmHg</td>
</tr>
</tbody>
</table>

\[
PVR = \frac{\text{Mean PAP} - \text{PCWP}}{\text{Cardiac Output}} \times 80 = 60-120 \text{ dyn.sec.cm}^{-5}
\]
Right Heart Catheterization in PAH

- **Increased mPAP**
  - normal mPAP < 20 mmHg; PAH defined as mPAP > 25 mmHg
- **Normal PCWP**
  - normal range <15 mmHg
- **PVR↑, > 3 Wood units (250 dyn/sec/cm⁻⁵)**
- **Right atrial pressure↑**
  - normal right atrial pressure 2–7 mmHg
- **Cardiac output↓**
  - normal cardiac output 4–8 liters per minute
- **Cardiac index↓**
  - normal cardiac index 2.5–4.0 liters/min/m²

*Gradient DPAP-Wedge < 6mmHg
# Acute vasodilator responsiveness in different forms of PAH

<table>
<thead>
<tr>
<th>Condition</th>
<th>Nº of patients tested*</th>
<th>Acute responders# (n, %)</th>
<th>Long-term responders to CCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sporadic PPH</td>
<td>430</td>
<td>57 (13 %)</td>
<td>27 (6.3 %)</td>
</tr>
<tr>
<td>Appetite suppressant</td>
<td>127</td>
<td>13 (10 %)</td>
<td>10 (7.9 %)</td>
</tr>
<tr>
<td>Connective Tissue D.</td>
<td>166</td>
<td>15 (9 %)</td>
<td>2</td>
</tr>
<tr>
<td>PVOD / PCH</td>
<td>34</td>
<td>3 (9 %)</td>
<td>0</td>
</tr>
<tr>
<td>HIV-associated PAH</td>
<td>123</td>
<td>2 (1.5 %)</td>
<td>1</td>
</tr>
<tr>
<td>Portopulmonary Ht.</td>
<td>153</td>
<td>1 (0.6 %)</td>
<td>0</td>
</tr>
<tr>
<td>Congenital Heart D.</td>
<td>41</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Familial PPH</td>
<td>34</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

* With NO and/or PG I₂  
# fall in mPAP and PVR > 20%  

Personal unpublished data

Sitbon Venice 2003
## Acute Vasodilation Testing

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ROUTE</th>
<th>DOSE</th>
<th>HALF LIFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>inhaled</td>
<td>10-20ppm</td>
<td>15-30s</td>
</tr>
<tr>
<td>Adenosine (USA)</td>
<td>iv</td>
<td>50-200μg/kg/min</td>
<td>5-10s</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>po</td>
<td>10-40mg</td>
<td>2 h</td>
</tr>
<tr>
<td>Epoprostenol</td>
<td>iv</td>
<td>2-20ng/kg/min</td>
<td>3-5min</td>
</tr>
<tr>
<td>Iloprost</td>
<td>inhaled</td>
<td>10-20μg</td>
<td>45 min</td>
</tr>
<tr>
<td>Bosentan</td>
<td>po</td>
<td>62.5-125mg</td>
<td>5 h</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>po</td>
<td>25-100mg</td>
<td>60 min</td>
</tr>
</tbody>
</table>
PHTN: Positive Vasodilator Response

Decrease of mean pulmonary artery pressure by $\geq 10$ mmHg to reach $\leq 40$ mmHg with an increased or unchanged cardiac output.

= new definition (Dana Point 2008)
Importance of Vasoreactivity Testing

- Initiation of vasodilator therapy
- Surgical closure of shunts in congenital disease
- Detection of right ventricular dysfunction
Guidelines for the diagnosis and treatment of pulmonary hypertension

The 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 the International Society of Heart and Lung Transplantation (ISHLT)

Authors/Task Force Members: Nazzareno Galiè (Chairperson) (Italy); Marius M. Hoepfer (Germany); Marc Humbert (France); Adam Torbicki (Poland); Jean-Luc Vachiery (France); Joan Albert Barbera (Spain); Maurice Beghetti (Switzerland); Paul Corris (UK); Sean Gaine (Ireland); J. Simon Gibbs (UK); Miguel Angel Gomez-Sanchez (Spain); Guillaume Jondeau (France); Walter Klepetko (Austria); Christian Opitz (Germany); Andrew Peacock (UK); Lewis Rubin (USA); Michael Zellweger (Switzerland); Gerald Simonneau (France)
### Table 11  Recommendations for right heart catheterization (A) and vasoreactivity testing (B)

<table>
<thead>
<tr>
<th>Class</th>
<th>Level</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RHC is indicated in all patients with PAH to confirm the diagnosis, to evaluate the severity, and when PAH specific drug therapy is considered</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RHC should be performed for confirmation of efficacy of PAH-specific drug therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RHC should be performed for confirmation of clinical deterioration and as baseline for the evaluation of the effect of treatment escalation and/or combination therapy</td>
</tr>
</tbody>
</table>
A positive response to vasoreactivity testing is defined as a reduction of mean PAP ≥10 mmHg to reach an absolute value of mean PAP ≤40 mmHg with an increased or unchanged CO.

Vasoreactivity testing should be performed only in referral centres.

Vasoreactivity testing should be performed using nitric oxide as vasodilator.

**Dedicated interventionalists (HUG → Dr. Keller)**
- Indication for the cath discussed in the multidisciplinary PHT team
- Knows about the patients
- Knows the specific question that the invasive test is suppose to answer
- Is able to integrate the results in the clinical context
Central Role of Cardiac Catheterization and Vasoreactivity Test

Avoid pregnancy (I-C)
Influenza and pneumococcal immunization (I-C)
Supervised rehabilitation (IIa-B)
Psycho-social support (IIa-C)
Avoid excessive physical activity (III-C)

General measures and supportive therapy

Expert Referral (I-C)

Acute vasoreactivity test
(I-C for IPAH)
(IIb-C for APAH)

Diuretics (I-C)
Oxygen* (I-C)
Oral anticoagulants:
IPAH, heritable PAH and PAH
due to anorexigens (IIa-C)
APAH (IIb-C)
Digoxin (IIb-C)

VASOREACTIVE

NONVASOREACTIVE
Goals of Invasive Assessment

- Confirm non-invasive estimation of pulmonary pressures
- Measurement of pressures and saturations in all heart chambers
- Find etiology of PHTN
- Test vasoreactivity
- Plan therapy
- Assess prognosis
### Hemodynamic Classification

<table>
<thead>
<tr>
<th>Class</th>
<th>Symptoms</th>
<th>Echocardiography</th>
<th>RV Catheterization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>NYHA I</td>
<td>Syst. PAP 35-55 mmHg</td>
<td>Mean PAP 21-40 mmHg</td>
</tr>
<tr>
<td>Moderate</td>
<td>NYHA II</td>
<td>Syst PAP &gt; 55 mmHg</td>
<td>Mean PAP &gt; 40 mmHg</td>
</tr>
<tr>
<td>Severe</td>
<td>NYHA III</td>
<td>RV function impaired</td>
<td>SVO₂ &lt; 60 %</td>
</tr>
<tr>
<td>Very severe</td>
<td>NYHA IV</td>
<td>RV function severely impaired</td>
<td>SVO₂ &lt; 50 %</td>
</tr>
</tbody>
</table>
Hemodynamic Adverse Prognostic Indicators in Primary Pulmonary Hypertension

- Pulmonary arterial oxygen saturation < 63%
  - >63%: 55% survival at 3 years
  - < 63%: 17% survival at 3 years

- Cardiac index < 2.1 l/min/m²
  - < 2.1: 17 months median survival

- Right atrial pressure > 10 mmHg
  - < 10 mmHg: 4 years mean survival
  - > 20 mmHg: 1 month mean survival

- Lack of pulmonary vasodilator response to acute challenge
## Prognostic Implications

<table>
<thead>
<tr>
<th>Better prognosis</th>
<th>Determinants of prognosis</th>
<th>Worse prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No</strong></td>
<td>Clinical evidence of RV failure</td>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td><strong>Slow</strong></td>
<td>Rate of progression of symptoms</td>
<td><strong>Rapid</strong></td>
</tr>
<tr>
<td><strong>No</strong></td>
<td>Syncope</td>
<td><strong>Yes</strong></td>
</tr>
<tr>
<td>I, II</td>
<td>WHO-FC</td>
<td>IV</td>
</tr>
<tr>
<td>Longer (&gt;500 m)(^a)</td>
<td>6MWT</td>
<td>Shorter (&lt;300 m)</td>
</tr>
<tr>
<td>Peak O(_2) consumption &gt;15 mL/min/kg</td>
<td>Cardio-pulmonary exercise testing</td>
<td>Peak O(_2) consumption &lt;12 mL/min/kg</td>
</tr>
<tr>
<td>Normal or near-normal</td>
<td>BNP/NT-proBNP plasma levels</td>
<td>Very elevated and rising</td>
</tr>
<tr>
<td>No pericardial effusion TAPSE(^b) &gt;2.0 cm</td>
<td>Echocardiographic findings(^b)</td>
<td>Pericardial effusion TAPSE(^b) &lt;1.5 cm</td>
</tr>
<tr>
<td>RAP &lt;8 mmHg and CI ≥2.5 L/min/m(^2)</td>
<td>Haemodynamics</td>
<td>RAP &gt;15 mmHg or CI ≤2.0 L/min/m(^2)</td>
</tr>
</tbody>
</table>
Conclusions: Why is Right Heart Catheterization Necessary

RHC is indicated in all patients with PAH to confirm the diagnosis, to evaluate the severity, and when PAH specific drug therapy is considered.
Conclusions: Why is Right Heart Catheterization Necessary

- Pressure measurement not estimation
  - On Echo PHTN cannot be estimated in in 50-60% of patients with no PHTN and in 80-90% of patients with PHTN
- Allows to exclude „treatable“ causes of PHTN (shunts)
- Can differentiate PHTN related or not related to LV dysfunction
- Insight into pulmonary hemodynamics: pressures, flow state, resistances
- Invasive, but low complication rates
- Vasoreactivity testing by non-invasive measurements not reliable → Planning of therapy without vasoreactivity test questionable
- Has prognostic implications at the time of diagnosis
- To follow the patient response to vasodilator therapy if the clinical evolution and the echocardiographic parameters are discordant: if PHTN stable or decreasing but also the cardiac output is decreasing the prognosis is poor.
- Prognosis of the patient with severe PAHT unfavorable → the highest degree of accuracy for diagnosis and assessment of vasoreactivity is indicated
Last but not least

- Indication, interpretation, and therapeutic consequences of right heart catheterization and vasoreactivity need to be discussed in a multidisciplinary fashion.

- Right heart catheterization should be done by a « dedicated » interventional cardiologist.

- Cardiac catheterization should be performed in a dedicated pulmonary hypertension center.