Ο ασθενής με πνευμονική υπέρταση στην εντατική μονάδα

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Σύγκρουση συμφερόντων

- Καμία για τη συγκεκριμένη παρουσίαση
• Right ventricular (RV) failure is the most common cause of death in patients with pulmonary hypertension, and RV function is the major determinant of morbidity and mortality in this patient population.
PAH pt in ICU: the problem

• Because of the rarity of the disease, there are no large trials examining the management of critically ill patients with acute decompensated right ventricular failure.

• Therefore, the recommendations for treatment in this complicated group are, by necessity, guided by our understanding of the physiology of the disease and not by specific data.
Prognostic factors of acute heart failure in patients with pulmonary arterial hypertension


• The first prospective study analysing consecutive patients requiring ICU admission for severe acute right ventricular failure due to decompensated PAH
Prognostic factors of acute heart failure in patients with pulmonary arterial hypertension


<table>
<thead>
<tr>
<th>Age yrs</th>
<th>50.0 (16.2–77.4)</th>
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<tr>
<td>Sex F/M n</td>
<td>2.3/1</td>
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<tr>
<td>BMI kg·m⁻²</td>
<td>20.9 (15.9–33.6)</td>
</tr>
</tbody>
</table>

**Type of PAH n**

- Idiopathic PAH: 24
- Inoperable CTEPH: 7
- Systemic sclerosis-associated PAH: 5
- PAH associated with connective tissue diseases other than scleroderma: 2
- HIV-related PAH: 3
- Portopulmonary hypertension: 3
- PAH associated with congenital heart disease: 2

**NYHA functional class when last stable n**

- II: 5
- III: 26
- IV: 15

**Pulmonary haemodynamic data when last stable**

- $\tilde{P}_{pa}$ mmHg: 52 (32–103)
- PVR dyn·s·cm⁻⁵: 1016 (525–2400)
- $P_{ra}$ mmHg: 12 (0–32)
- CI L·min⁻¹·m⁻²: 2.23 (1.47–5.0)
Prognostic factors of acute heart failure in patients with pulmonary arterial hypertension


- iv prostacyclin alone (9)
- iv prostacyclin in combination with bosentan (10)
- iv prostacyclin in combination with sildenafil (1),
- iv prostacyclin with bosentan and sildenafil (3),
- bosentan alone (10)
- bosentan with sildenafil (7)
Prognostic factors of acute heart failure in patients with pulmonary arterial hypertension

Triggers factors for PAH decompensation: 19/44 pts

- unplanned modification or withdrawal of pulmonary vasodilator therapy (3);
- unplanned withdrawal of diuretics (1);
- septicaemia (5);
- pneumonia (3);
- purulent pleural effusion (1);
- septic state without bacterial documentation(2);
- cardiac arrhythmia (3);
- unplanned pregnancy (1).

There was no difference in outcome according to the identification of a triggering factor.
• **Documented infection** at any time during the ICU stay was the **strongest predictor of death**, occurring in 74% of the non survivors compared with 22% of the survivors ($P = 0.0005$), and underscoring the need for aggressive management of infectious complications in these patients.
The Johns Hopkins group cause for hospitalization

- Decompensated right ventricular failure (56%),
- Infection (16%),
- Bleeding (mostly gastrointestinal, but also hemoptysis) (8%),
- Arrhythmia (6%),
- Syncope (6%)

- ICU stay was required in 16% of cases, and overall hospital mortality was 8.8%.
- Inhospital mortality increased to 14 and 48% if an ICU admission was required.

Worse in-hospital mortality

- Connective tissue disease-related (OR 4.92, P = 0.03),
- Systolic blood pressure <100 mmHg (OR 4.32, P = 0.01),
- Sodium level <136 mEq/L (OR 4.29, P = 0.02) on admission.
Precipitating factors: Arrhythmias

- Ventricular arrhythmias have rarely been reported.
- Atrial tachyarrhythmia (most importantly atrial tachycardia), atrial flutter, and atrial fibrillation are increasingly encountered.
- The management of supraventricular tachyarrhythmia in patients with PH has never been evaluated in clinical trials.
- Rate control alone does not appear to be sufficient and restoration of sinus rhythm seems to be critical.
- Antiarrhythmics or electrical cardioversion may be required when patients are acutely unstable or have a new onset of arrhythmia.
- b-blocking agents and calcium channel blockers should be avoided as they may further impair RV function.
Precipitating factors: sepsis

- Sepsis is a common cause of acute deterioration, and an elevated C-reactive protein (CRP) should lead to a careful search for a focus of infection. Broad-spectrum antibiotics may be indicated, even in the absence of a clear source, when infection is suspected.

- Patients receiving continuous i.v. prostanoid are at risk of developing a catheter-related bloodstream infection (CRBSI). Patients with a CRBSI will often have no external signs of line infection and may present with non-specific worsening of breathlessness. An elevated, unexplained, CRP in such patients should lead to exclusion of a line infection with peripheral and central blood cultures and antibiotic therapy to cover gram-positive and gram-negative organisms while cultures are pending.
Major surgery - pregnancy

• Improved outcomes, but with maternal mortality still between 10 and 20%.

• Early elective delivery at 34–36 weeks via Caesarean section using a combined spinal–epidural approach (to minimize the effect on the SVR).

• Oxytocin may increase PVR and reduce SVR
RV afterload increase

1. RV volume overload
2. Loss of RV-PA Coupling
3. Tricuspid regurgitation
4. RV dilatation
5. Increased RV wall stress
6. Normal cardiac output

Ongoing RV ischaemia

Diastolic VV interaction (pericardium and IVS)

High right-sided filling pressures

Oedema; Organ congestion

Reduced coronary perfusion

Reduced RV output

Low aortic root pressure

RCA perfusion limited to systole

Compensatory tachycardia

Avoid hypoxemia - hypercapnia
The effect of positive thoracic pressure

• Every attempt should be made to avoid endotracheal intubation of patients with RV failure.

• Intubation of these patients is often problematic owing to effects of sedatives on cardiac function and nonselective vasodilation leading to systemic hypotension and hemodynamic collapse.
The effect of positive thoracic pressure

• If intubation and mechanical ventilation are unavoidable, hypotension and loss of RV contractility must be prevented and the administration of catecholamines before anesthesia should be considered.

• Despite the lack of controlled clinical trials, etomidate is the preferred drug for induction of general anesthesia as it has little effect on cardiac contractility and vascular tone.
A Technique of Awake Bronchoscopic Endotracheal Intubation for Respiratory Failure in Patients With Right Heart Failure and Pulmonary Hypertension

Jimmy Johannes, MD¹; David A. Berlin, MD²; Parimal Patel, MD²; Edward J. Schenck, MD²; Frances Mae West, MD³; Rajan Saggar, MD¹; Igor Z. Barjaktarevic, MD, PhD¹

CCM 2017
• 3,130 PAH patients between 1997 and 2000 in 17 referral centers in Europe and in the United States.
• **513** patients had circulatory arrest and CPR was attempted in **132** (26%).
• Although 96% of the CPR attempts took place in hospitalized patients (74% in intensive care units or equally equipped facilities) and although there was only minimal delay between collapse and initiation of CPR, resuscitation efforts were primarily unsuccessful in **104** patients (79%).
• Only **eight** patients (6%) survived for more than 90 d.
Fluid management of these patients is often difficult, as both hypovolemia and hypervolemia can have detrimental effects on blood pressure, organ perfusion, and cardiac function. Fluid loading may improve hemodynamics in patients with acute PE, but unmonitored fluid challenge may further impair RV function. In most, but not all, cases, RV failure is associated with fluid overload and negative fluid balance is the key to successful therapy. However, fluid removal may reduce the already low cardiac output and may thereby further impair end organ function.
• Renal congestion attributable to RV failure is also associated with the development of worsened renal function.

• Patients with peripheral edema attributable to RV failure therefore benefit from diuresis with a combination of loop diuretics, aldosterone antagonists, and sometimes thiazide diuretics.

• Often a continuous infusion of loop diuretic is used, although evidence to demonstrate superiority over a bolus approach is lacking.

• Continuous venovenous haemofiltration (CVVH) should be considered in selected instances of resistant heart failure.
RV afterload increase

1. RV volume overload
2. Tricuspid regurgitation
3. High right-sided filling pressures
4. Oedema; Organ congestion

Diastolic VV interaction (pericardium and IVS)

Loss of RV-PA Coupling
RV dilatation
Increased RV wall stress
Reduced right coronary perfusion
RV ischaemia
Reduced RV output

Ongoing RV ischaemia

Ongoing RV ischaemia

Low aortic root pressure
RCA perfusion limited to systole
Compensatory tachycardia

Normal cardiac output

4. Ventricular interdependence
5. Reduction in overall CO

Treat precipitating factors

Optimize RV preload
- Diuretics
- Fluids

Improve RV contractility

Reduce RV afterload

Maintain perfusion pressures
Reduce RV afterload

- Epoprostenol 2 ng/kg/min to start with, and increase by 1 ng/kg/min every 6 or 8 h until the goal dose is reached or until the titration is limited by side effects or hypotension.
- I.V. sildenafil is available for patients where the enteral route is not possible.
- Inhaled nitric oxide (NO) can be an effective way of reducing RV afterload, but its use may be limited by lack of availability, the development of methaemaglobinaemia, and rebound pulmonary hypertension on cessation.
- Nebulized prostanoid therapy may also be considered, especially in the presence of coexisting lung disease.
- Accurate dosing and administration in the acutely unwell patient may be challenging.
Intensive Care Unit Management of Patients with Severe Pulmonary Hypertension and Right Heart Failure

1. Treat triggering factors and provide supportive care
   - Treat infections, anemia, arrhythmias, comorbidities
   - Rule out pulmonary embolism, myocardial infarction, other conditions
   - Oxygen (SpO₂ > 90%)
   - Avoid intubation, if possible
   - Contact PH referral center

2. Optimize fluid balance
   - Administer fluids if hypovolemia is present/suspected
   - Administer IV diuretics (or use hemofiltration) if fluid excess is present

3. Reduce RV afterload
   - IV prostanoids (epoprostenol, treprostinil, iloprost) are treatment of choice
   - Alternatives include IV or oral PDE-5 inhibitors or inhaled vasodilators (NO, iloprost)
   - If 1-3 are insufficient:
     - Dobutamine
     - Norepinephrine or vasopressin

4. Optimize cardiac output
   - ScvO₂ > 70%, SvO₂ > 65%, CI > 2.0 l/min/m²
   - Alternatives include levosimendan or PDE-3 inhibitors (may cause systemic hypotension)
   - If 1-4 are insufficient:
     - Intropes
     - Inotilators

5. Optimize perfusion pressure
   - If 1-5 are insufficient:
     - Lung transplantation possible?
     - Consider extracorporeal life support

6. Consider lung transplantation

Critical care management of pulmonary hypertension

Treat precipitating factors
- Arrhythmia, saponis
- Anaemia, thrombus

Optimize RV preload
- Diuretics
- Fluids

Improve RV contractility
- Intropes
- Inotilators

Reduce RV afterload
- Prostanoid
- No pathway
- Inotilators

Maintain perfusion pressures
- Pressor agents

Am J Respir Crit Care Med Vol 184. pp 1114-1124, 2011

Inotropic support

• Dobutamine is the most common b1 agonist used. Dobutamine dosing is often limited by tachycardia and systemic hypotension.

• The phosphodiesterase-3 inhibitor milrinone has positive inotropic effects combined with the capacity to reduce RV afterload (‘inodilators’) without significant chronotropic effect, but can be associated with significant systemic hypotension.

• Levosimendan is a calcium-sensitizing agent, which also has inodilating properties but may result in less systemic hypotension.
Vasopressors

• Vasopressor agents are often required in combination with inotropes to augment systemic vascular resistance and maintain systemic blood pressure.

• Norepinephrine is a potent α1 agonist and so there is a concern of increasing pulmonary (in addition to systemic) vascular resistance. However, norepinephrine also has inotropic properties owing to β1 effects and appears to improve coupling between RV function and afterload.

• Vasopressin may have pulmonary vasodilatory effects in addition to a systemic vasoconstrictive effect.
RV afterload increase → Loss of RV-PA Coupling → RV dilatation → Increased RV wall stress → Reduced right coronary perfusion → RV ischaemia → Reduced RV output → Diastolic VV interaction (pericardium and IVS) → Ongoing RV ischaemia → Reduced in overall CO → Ongoing RV ischaemia → Low aortic root pressure → RCA perfusion limited to systole → Compensatory tachycardia → Normal cardiac output

1. RV volume overload
2. Tricuspid regurgitation
3. High right-sided filling pressures
4. Oedema; Organ congestion
5. Adaptive RV hypertrophy
6. Normal cardiac output

ECMO

Arterio-venous

⇒ Overtake of lung and heart function

- From Vena Femoralis into Arteria Femoralis
- From Vena Jugularis into Arteria Femoralis
- From Vena Femoralis into Aorta ascendens
- From Right Atrium into Aorta ascendens
- From Right Atrium into Arteria Femoralis

Veno – Venous

⇒ Overtake of lung function

- From Vena femoralis into Vena jugularis
- From Vena femoralis right into Vena femoralis left
- From Right Atrium into Vena femoralis
- From Vena Femoralis into Vena subclavia
ECMO – Implantationen an der MHH

![Bar Chart](image-url)
Organ donation during the financial crisis in Greece

*Demetrios Moris, Georgios Zavos, Georgia Menoudakou, Antreas Karampinis, John Boletis

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Lung TX

• Comparing lung transplants performed from 1990 to 1997 to a second cohort from 1998 to 2004, and then to a third cohort from 2005 to 2012, the median survival has improved from 4.1 to 5.7 and 6.1 years, respectively.
Lung TX in PAH

• Survival after lung transplantation for PAH is reduced in the first 3 months after transplantation, when compared to other etiologies of respiratory failure.
• But, for those who survive this early postoperative period, their survival curve plateaus while the survival curves of those with other underlying diagnoses continue to deteriorate.
• In fact, patients with idiopathic pulmonary arterial hypertension have a 50% survival improvement at 9 years compared to 5 years.
Survival of PAH vs Non-PAH patients

### Number of cases

<table>
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<tr>
<th>Year</th>
<th>PAH</th>
<th>LHD-PH</th>
<th>Lung-PH</th>
<th>CTEPH</th>
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<td>528</td>
<td>733</td>
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### Survival after diagnosis

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<td>65.5%</td>
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<td>74.4%</td>
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</table>
Does all this apply to non-PAH PH?

Delcroix, ERJ, submitted
In the past it was not unusual to see patients being admitted to the intensive care unit (ICU) with RV failure due to undiagnosed and untreated PAH.

Fortunately, with increased awareness of the condition, this scenario has become increasingly rare.

Today, the majority of patients with PH and RV failure admitted to the ICU have exhausted their medical treatment options, which renders their management particularly challenging and, at times, frustrating.

Hoeper, AJRCCM, 2011
In conclusion

• Despite advances in medical therapy, PAH remains a lethal condition for many patients.
• ICU admission carries dismal prognosis.
• Treatment decisions are based on biological plausibility and clinical experience.
• Transfer critically ill patients with PAH to a large-volume PAH center is advisable.