Management of right ventricular failure

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The clinical condition associated with any structural or functional process that restricts the ability of the RV to fill with blood and/or to eject blood into the pulmonary vasculature.
Main causes of RV failure

1. LV failure (biventricular failure, most common)
2. Severe pulmonary embolism
3. ARDS (acute lung injury)
4. Sepsis induced RV dysfunction
5. Idiopathic or secondary forms of pulmonary hypertension
6. Right ventricle infarction or ischemia
7. Pericardial diseases (constrictive pericarditis, tamponade)
8. RV failure after cardiac surgery (e.g. cardiac transplant or LVAD implantation)
9. Congenital heart disease (e.g. Ebstein’s anomaly)
10. Valvulopathies (e.g. pulmonary valve stenosis, TR)
11. Rare cardiomyopathies (e.g. Arrhythmogenic RV dysplasia)
12. Arrhythmias
13. Hematologic disorders (e.g. Acute chest syndrome in sicle cell disease)
EHS HF II vs ALARM-HF clinical classification according to ESC AHF Guidelines

EHS HF II: 3,580 patients, ALARM-HF: 4,953 patients (1911 AdHF, 1820 p-oed, 581 C-shock, 365 Hyp AHF, 222 RV AHF, 54 High cardiac output)

ALARM-HF: mortality across classification

Sample = EHS HF II (3.580), All ALARM-HF patients (4.953)

Follath F, Yilmaz B, Delgado J, Parissis J, Mebazaa A. Intens Care Med 2011
Effects of Right Ventricular Ejection Fraction on Outcomes in Chronic Systolic Heart Failure
*Circulation* published online Jan 4, 2010;
Prognostic Value of Tissue Doppler Right Ventricular Systolic and Diastolic Function Indexes Combined With Plasma B-Type Natriuretic Peptide in Patients With Advanced Heart Failure

V Bistola, JT. Parissis, ... , E. Iliodromitis, D. Kremastinos. Am J Cardiol 2010;105:249–254
Pathophysiology of RV failure. *The time course (acute or chronic) and time of onset of the disease process (newborn, pediatric, or adult years) also influence RV adaptation to disease.

Pathophysiology of failing RV

- RV infarction
- Right-sided cardiomyopathy
- Perioperative RV injury
- Severe sepsis
- Post-cardiac transplantation
- Pulmonary embolism
- Left-sided cardiomyopathy
- Pulmonic stenosis
- Pericardial disease
- Positive pressure ventilation
- Left-sided valvular disease
- Pulmonary hypertension
- ARDS

Ventricular interdependence

- During systole, LV protrudes in RV
- Surrounding pericardium with limited distensibility
- Compliance of one ventricle can modify the other = Diastolic ventricular interaction
Right to left shunting

- Increase in RA pressure due to RVF
- Reopening of patent foramen ovale
- Right to left shunting
- Secondary hypoxemia
- Can be improved by improving RV function
- Hypoxemia usually not improved by mechanical ventilation in case of RVF due to pulmonary hypertension due to pulmonary vascular disease (PAH, CTEPH)
Vicious cycle of auto-aggravation

1. RV pressure overload
2. Reduced cardiac output
3. Systemic hypotension
4. Reduced RV tissue perfusion
5. RV free wall ischemia
6. Reduced RV free wall contractility
Clinical and biological signs of acute RV failure

**CLINICAL**
- Signs of systemic congestion
  Jugular venous distension, hepatojugular reflex, peripheral oedema, pleural effusions, congestive liver/hepatomegaly, ascites, anasarca
- Signs of RV dysfunction
  Third heart sound, systolic murmur of TR regurgitation, hepatic pulse, signs of concomitant LV dysfunction
- Signs of low cardiac output state
  Hypotension, tachycardia, cool extremities, central nervous system abnormalities, oliguria

**BIOLOGICAL**
- Hypoxemia, hyper- or hypocapnia, increased lactate, elevated natriuretic peptides and/or Hs-troponins and/or d-dimers, abnormal liver biochemistry (elevated ALP, GGT, bilirubin, INR, transaminases), abnormal renal function (urine output, BUN, creatinine), increased inflammatory markers (e.g. CRP)
Management

- Control of trigerring factors

- Supportive treatment:
  - Optimization of preload
  - Improving contractility
  - Pulmonary vasodilators

- Specific therapies addressing the cause of RVF
Treatment of triggering factors (acute on chronic)

- Arrhythmias
- Infections
- Pulmonary embolism
- Thyroid dysfunction
Optimization of preload

Frank-Starling relationship between preload and stroke volume: preload dependence (A) and preload independence (B)
### Fluid therapy

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>FL 250</th>
<th>FL 500</th>
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<tbody>
<tr>
<td>CI (L/min/m²)</td>
<td>1.6 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>2.0 ± 0.1&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>91 ± 5</td>
<td>92 ± 5</td>
<td>91 ± 4</td>
</tr>
<tr>
<td>SVI (mL/m²)</td>
<td>19 ± 2</td>
<td>19 ± 2</td>
<td>23 ± 2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>RAP (mm Hg)</td>
<td>9 ± 1</td>
<td>14 ± 1&lt;sup&gt;c&lt;/sup&gt;</td>
<td>17 ± 1&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>MPAP (mm Hg)</td>
<td>31 ± 2</td>
<td>34 ± 2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>35 ± 2&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>MBP (mm Hg)</td>
<td>101 ± 4</td>
<td>103 ± 4</td>
<td>103 ± 4</td>
</tr>
<tr>
<td>TPRI (dyne·sec/cm⁵·m²)</td>
<td>1689 ± 187</td>
<td>1752 ± 211</td>
<td>1492 ± 166</td>
</tr>
<tr>
<td>RVEDVI (mL/m²) (n = 8)</td>
<td>123 ± 14</td>
<td>135 ± 13</td>
<td>150 ± 11&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>RVEF (%) (n = 8)</td>
<td>15 ± 3</td>
<td>15 ± 3</td>
<td>16 ± 3</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>96 ± 1</td>
<td>96 ± 1</td>
<td>97 ± 1</td>
</tr>
<tr>
<td>SvO₂ (%)</td>
<td>59 ± 2</td>
<td>59 ± 2</td>
<td>57 ± 3</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>13.5 ± 0.3</td>
<td>12.1 ± 0.3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11.3 ± 0.3&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Do₂ (mL/min/m²)</td>
<td>268 ± 24</td>
<td>255 ± 23</td>
<td>296 ± 23</td>
</tr>
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</table>

CI, cardiac index; HR, heart rate; SVI, stroke volume index; RAP, right atrial pressure; MPAP, mean pulmonary artery pressure; MBP, mean blood pressure; TPRI, total pulmonary resistance index; RVEDVI, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; SpO₂, pulse oxymeter arterial oxygen saturation; SvO₂, mixed venous oxygen saturation; Hb, hemoglobin; Do₂, oxygen delivery.

<sup>a</sup>Different from baseline (p < .05);  <sup>b</sup>different from FL 250 (p < .05).
Diuretics

- Frequent volume overload
- At a point of Frank-Starling curve where there is no more reserve on contractility
- Ventricular interdependence
- Diuretics to be considered
- Sometimes with continuous high dose infusion
- (plus high dose of MRAs and/or metolazone especially in biventricular failure)
- If fails, consider CVVHF
Figure 1. Mean pulmonary wedge pressure (PWP), mean right atrial pressure (RAP), cardiac output (CO) and stroke volume (SV) before, during and after extracorporeal ultrafiltration (UF). *p < 0.01 vs. before ultrafiltration.
Dobutamine

- \( \beta_1 \) adrenergic stimulation
- \( \uparrow \text{CI} \downarrow \text{PVR} \) at 5 \( \mu \text{g/kg/mn} \)
- At higher dose \( \uparrow \text{HR} \) without subsequent \( \downarrow \) in PVR
- Experimental models Dobutamine \( > \) Norepinephrine to improve right-ventricular – pulmonary artery coupling
- Improves CI, PVR and \( \text{PaO}_2/\text{FiO}_2 \) in combination with Inhaled nitric oxyde
Norepinephrine

- $\alpha_1$ and $\beta_1$ adrenergic stimulation
- Increases mPAP and PVR
- But marked improvement in CO
- Useful in combination with Dobutamine for hypotensive patients
- Causes less tachycardia than other inotropes
- Second choice after Dobutamine in normotensive patients
Levosimendan

• Calcium sentitizer: increases the sensitivity of troponin C for Ca\textsuperscript{2+} within cardiac myocyte
• Dilatation of pulmonary vasculature by activation of adenosin tri-phosphate potassium channel
• Animal studies and pilot studies support its efficacy in right ventricle failure associated with pulmonary hypertension
Levosimendan and Right Ventricle in Advanced Heart Failure

• 35 ICU patients with ARDS and sepsis randomized to receive placebo or levosimendan 0.2μg/kg/mn

• Mean arterial pressure 80 to 90 mmHg (sustained by norepinephrine infusion)

• Improvement of right ventricle performance:
  – CI (from 3.8 ±1.1 to 4.2 ±1.0 L/min/m2)
  – PAPm (from 29 ± 3 to 25 ± 3 mm Hg)
  – ↓RVESV, ↑RVEF, ↑SvO2
Randomised, double-blind placebo-controlled parallel-group trial in patients with pulmonary hypertension

28 patients with pulmonary hypertension in four centres in Germany, one in Sweden

Dosing:
- initial: 12 mcg/kg/10 min bolus + 0.1 mcg/kg/min for 50 min + 0.2 mcg/kg/min up to 24 h
- repeated doses: 0.2 mcg/kg/min for 6 h, in total 4 times with 2-week interval

PEP: Change in pulmonary vascular resistance (PVR)

Change in mPAP (mean ± SEM)

Addressing the cause of the RV failure, if possible

- Treatment of Pulmonary Arterial Hypertension
- Pericardiotomy/drainage
- Thrombolysis/embolectomy
- Thrombolysis/angioplasty
- Thromboendarterectomy
- Atrial septostomy
- ECMO, BiVAD, Transplantation
Pulmonary vasodilators
Inhaled nitric oxyde

• Dilate pulmonary vessels in ventilated units of the lung
• Reverses hypoxic pulmonary vasoconstriction
• In acutely decompensated RV improves PVR, increase CO improve PaO2/FiO2
• Beware of methemoglobinemia (high concentration, prolonged use)
Effect of abrupt discontinuation of NO
Prostanoids

- Intravenous Epoprostenol
- Effect on survival in stable patients with PAH
- Reduces mPAP and improves CO
- Systemic side effects
- Worsening PaO2/FiO2
- Systemic effects (hypotension)
- Inhaled prostacyclin / nebulized iloprost: case series
Sildenafil

- Phosphodiesterase-5 inhibitor
- Approved for treatment of PAH (stable patients)
- May be useful for weaning from inhaled nitric oxide
- Effect start 15mn after administration, peak effects within 30-60mn
- Systemic hypotension
Effects of mechanical ventilation

- Increased RV afterload due to positive pressure ventilation
- Hemodynamic failure frequently refractory in PAH patient put on MV
- In ARDS increase in mPAP while increasing tidal volume and PEEP
- Permissive hypercapnia is deleterious (increase in mPAP)
Effects of PEEP on RV performance

![Graph showing the relationship between PEEP (cm H₂O) and PVR (dynes sec cm⁻⁵). There is a gradual increase in PVR with increasing PEEP, indicated by asterisks.]
Effect of high PEEP on RV
Risk factors for RHF

Relative Risk Ratios

Vent Support
RVSWI < 300
CVP/PCWP > 0.63
HCT < 31
WBC > 10.42
CVP > 15
AST > 49
BUN > 39
PAPs < 52
PAPm < 36
Creatinine > 1.7
BSA < 1.8
Female

Univariate

Risk Ratio

Vent Support
CVP/PCWP > 0.63
BUN > 39

Multivariate

Predictors of RHF in the recent VAD era

CRITT Score

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p Value</th>
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<tbody>
<tr>
<td>Severe right ventricular dysfunction</td>
<td>3.7</td>
<td>1.7 - 8.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Severe tricuspid regurgitation</td>
<td>4.1</td>
<td>1.4 - 12.4</td>
<td>0.011</td>
</tr>
<tr>
<td>Preoperative mechanical ventilation</td>
<td>4.3</td>
<td>1.9 - 9.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Central venous pressure &gt;15 mm Hg</td>
<td>2.0</td>
<td>0.9 - 4.2</td>
<td>0.089</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats/min</td>
<td>2.0</td>
<td>0.9 - 4.3</td>
<td>0.086</td>
</tr>
<tr>
<td>Constant</td>
<td>0.04</td>
<td></td>
<td></td>
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</tbody>
</table>

SCORE 0-1: LVAD ONLY
SCORE 4-5: BiVAD
SCORE 2-3: LVAD + pharmacologic therapy for RHF OR temporary BiVAD
Management of Acute RV failure

Lung protective mechanical ventilation: $P_{plat} \leq 30 \text{ mmHg}$, consider $V_t$, 4-6 ml/kg/PBW, minimize PEEP, avoid acidosis, hypoxemia, hypercarbia and/or auto-PEEP (4, 7, 9)

Treat underlying disease

Pulmonary hypertension: ±diuresis, inhaled NO, intravenous/inhaled prostacyclins (avoid subcutaneous route in severe RHF), PDE5 inhibitors, ET-1 receptor antagonists (1, 3, 5, 7, 10)

Pulmonary embolus: anticoagulation, thrombolytics, thrombectomy (surgical or catheter-directed) (5, 7, 11)

CTEPH: thrombendarterectomy (5, 11)

RV infarction: PCI, thrombolitics (8)

LV dysfunction: afterload reduction, diuresis, inotropes, nesiritide, IABP, LVAD (2)

CHD/VHD: surgical or percutaneous correction (2, 3, 7, 8)

Sepsis/acute lung injury: volume resuscitation, broad spectrum antibiotics, activated protein C, lung protective ventilation strategy (1, 2, 3, 4, 5, 6, 9, 10)

Post cardiothoracic surgery: inhaled NO, inhaled/intravenous prostacyclins, milrinone, PDE5 inhibitors (1, 2, 3, 4, 7, 8)

Acute right heart failure

Volume optimization

Rhythm stabilization: cardioversion, antiarrhythmics, pacemaker, resynchronization (1, 2, 8)

Hemodynamic support

Volume overload

Salt restriction, daily weights (3)

Diuretics (3) • Goal: net loss of 500 – 1000 ml/day • Consider continuous infusion of loop diuretics or combination of diuretics if nonresponsive to moderate doses of intermittently given diuretics

Hypovolemia

Continuous or intermittent RRT (3)

RV infarct

Acute PE

Hypotension/Shock

Volume challenge (1, 3) (500 – 1000 ml; no further volume challenge if no effect)

Vasopressors/inotropes/inodilators: dobutamine, milrinone, levosimendan, norepinephrine, low-dose vasopressin? (1, 2, 8)

Avoid: dopamine, phenylephrine

Consider combination therapy with inhaled NO or inhaled/intravenous prostacyclins

Rescue therapies: atrial septostomy, RVAD, ECMO, transplantation

JACC 2010;56:1435
Workshop on Acute Right Ventricular Failure

Coordinators: Veli-Pekka Harjola (FI), Stavros Constantinides (DE)
Date: 26-27th of March, 2015
Location: Brussels ESC European heart Agency

Day 1

Lunch (11:15 – 12:00)

12:00-12:15 Opening words: aim, working plan V-P Harjola (FI), S Constantinides (DE)

12:15 – Session 1 - Background
12:15-12:30 Anatomy, physiopathology and epidemiology A. Mebazaa (FR)
12:30-12:45 Venous congestion and organ dysfunction W. Mullens (BE)
12:45-13:00 Discussion

13:00 – Session 2 - Clinical assessment of patient with acute RV failure
13:00-13:15 Clinical & biological signs of acute RV failure J. Parissis (GR)
13:15-13:25 Discussion
13:25-13:40 Echo S. Martins (PT)
13:40-13:55 Discussion
13:55-14:10 Biomarkers C. Mueller (CH)
14:10-14:25 Discussion

14:25 – Session 3 - Etiology and common clinical scenarios
14:25-14:35 Pulmonary embolism: epidemiology and pathophysiology A. Vonk Nordegraaf (NL)
14:35-14:50 Clinical assessment (how to diagnose and to assess severity) of pulmonary embolism S. Gibbs (UK)
14:50-15:05 Discussion
15:05-15:20 Right ventricular infarction H. Bueno (ES)
15:20-15:35 Discussion

Coffee break (15:35 – 15:50)

15:50-16:05 Valvular causes (tricuspid regurgitation; endocarditis etc) D. Chioncel (RO)
16:05-16:20 Discussion
16:20-16:40 Left ventricular failure – Biventricular failure P. Seferovic (RS)
16:40-16:55 Discussion
16:55-17:15 ICU setting (sepsis, pulmonary disease, mechanical ventilation) A. Vieillard-Baron (FR)
17:15-17:30 Discussion

To improve quality of life and longevity, through better prevention, diagnosis and treatment of heart failure, including the establishment of networks for its management, education and research.
Assessment of severity:
- Clinical (mental status, diuresis, arterial pressure
- Biochemical evaluation (lactate, liver markers, BUN, creatinine, BNP, troponins, )
- Echocardiography, right heart catheterization, MRI

Identification and treatment of a triggering factor
- Sepsis, drug withdrawal, arrhythmias
Cause specific management
- PPCI for RV infarction, reperfusion for acute PE

Preload balance
- IV diuretics in case of volume overload
- RRT if situation insufficiently managed with diuretics
- Cautious fluid filling if low CVP; avoid overfilling

Arterial pressure support:
- Norepinephrine

Inotropic support in case of estimated low cardiac output
- Levosimendan
- Dobutamine
- Phosphodiesterase III inhibitors

Afterload reduction In acute conditions
- Inhaled NO
- Inhaled prostacyclins

Mechanical circulatory support
First-in-Human Transcatheter Tricuspid Valve Repair in a Patient With Severely Regurgitant Tricuspid Valve

A dedicated plication lock device was used to bring the 2 pledgeted sutures together, plicating the annulus and effectively bicuspidizing the tricuspid valve. (A) Illustration of the sutures placed in the postero-anterior commissure and the septo-posterior commissure (yellow arrows). (B) Illustration of the 2 sutures after plication. Patient’s 3-dimensional transesophageal echocardiographic images are shown before plication (C) and after plication (D). Ant = anterior leaflet; Post = posterior leaflet; Sept = septal leaflet.

(J Am Coll Cardiol 2015;65:1190-5)
TAKE HOME MESSAGES

- Patients with RV failure have an increased risk for major CV outcomes

-- Identification of underlying cause and pathophysiology is essential for the optimal management

-- Treat the underlying cause supporting also central hemodynamics and optimizing volume status

-- Biventricular failure needs therapeutic approaches of advanced HF (inotropic support, mechanical support, ultrafiltration)

-- Isolated RV failure may need specific treatment with pulmonary vascular bed vasodilators