Management of the RV in cardiogenic shock

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No disclosures/conflicts of interest
Cardiogenic shock
ICU mortality

- MOF
- Haem-onc
- RVI revasc
- Sepsis
- SARF
- ARF
- RVI no revasc

Lupi-Herrera et al., World J Cardiol, 2014
Cardiogenic shock management

- Revascularisation
- Structural
- Device therapy

Cardiogenic shock/AHF

Medical treatment?

- Oral antiplatelets
- Heparin
- GP IIb/IIIa inhibitors
- Bivalirudin
- Beta blockers & -ve inotropes
- Inotropes & pressors
- Intubation & ventilation
- Electrolytes
  - Volume
  - Nutrition
  - Endocrine
  - Care bundles

Multi-organ failure

Death

Improved survival with good QoL

Revascularisation

cardiology >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>> critical care
Guidelines, 2016

Statement

Contemporary management of acute right ventricular failure: a statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology

Veli-Pekka Harjola, Alexandre Mebazaa, Jelena Čelutkienė,
Dominique Bettex, Hector Bueno, Ovidiu Chioncel, Maria G. Crespo-Leiro,
Volmar Falk, Gerasimos Filippatos, Simon Gibbs, Adelino Leite-Moreira,
Johan Lassus, Josep Masip, Christian Mueller, Wilfried Mullens, Robert Naeije,
Anton Vonk Nordegraaf, John Parissis, Jillian P. Riley, Arsen Ristic,
Giuseppe Rosano, Alain Rudiger, Frank Ruschitzka, Petar Seferovic,
Benjamin Sztrymf, Antoine Vieillard-Baron, Mehmet Birhan Yilmaz,
Stavros Konstantinides

First published: 15 March 2016  Full publication history
Complex, management requires understanding of anatomy and mechanics,
Identification
Treat underlying causes
Support

Uncertainties remain
www.escardio.org/ACCA
Step 1: Assess severity:
- Clinical evaluation (arterial pressure, mental status, diuresis)
- Biochemical evaluation (lactate, liver markers, renal function, BNP, troponins)
- Imaging (echocardiography, CT scan)
- Invasive evaluation (central venous or pulmonary artery catheter)

Step 2: Identify and treat triggering factor(s):
- Sepsis, arrhythmias, drug withdrawal

Ensure cause-specific management:
- PCI for RV infarction, reperfusion for acute high-risk PE

Step 3: Optimize fluid status:
- IV diuretics if volume overload
- RRT if situation insufficiently managed with diuretics
- Cautious fluid filling if low CVP; avoid overfilling

Step 4: Maintain arterial pressure:
- Norepinephrine

Step 5: Consider inotropes reducing cardiac filling pressures:
- Levosimendan
- Dobutamine
- Phosphodiesterase III inhibitors

Step 6: Further measures for afterload reduction:
- Inhaled NO
- Inhaled prostacyclins

Consider transfer to hospital with possibility for ECMO/mechanical circulatory support
Volume?

CVP: +ve predictive value 47%

PCWP: +ve predictive value 54%
RV preload optimisation

- **Initial studies:**
  - Normal saline infusion, maintaining RAP <10mmHg

- **Later clinical studies**
  - Variable response reported
  - Aim target PCWP 18-24 mmHg

- **Berisha et al.,** 41 patients, electrocardiographic and haemodynamic criteria for RV infarction
  - maximal RV SWI with filling pressure 10-14mmHg
  - mean RAP >14mmHg associated with RV distension
  - haemodynamic response variable - optimal PCWP (corresponding to maximum LVSWI) 16mmHg
RV preload optimisation

Smaller studies: Change in PCWP and CI
Wide variation in response
No linear association with higher mRAP target

**Practically:**
Aim transmural pressure 8-12mmHg

Measure CO and ScvO$_2$/systemic organ perfusion
(not well-studied in acute RV failure)
1. Preload evaluation

IPPV:
Increases ITP

Hypovolaemia:
Sepsis/SIRS
Vascular permeability
Insensible loss

$P_{syst}$ reduced by analgesia & sedatives

2. Pressure-volume

3. RV afterload evaluation

PVR normal: need increased RVEDP

PVR elevated: increase in RVEDP will shift septum

4. Septal involvement

5. The pericardium
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Haemodynamic monitoring and support (ICU or Intermediate Care Unit)

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Vasoconstriction

**Dopamine**
- If >15mcg/kg/min is α-agonist
- Positive inotrope
- Elevation in PCWP

**Noradrenaline**
- Constrictor
- Antithrombotic
- Positive inotrope

1678 patients with circulatory shock – 280 cardiogenic
## Systemic arterial pressure optimisation

Vasoactive drugs for management of acute right ventricular failure and their mechanism of action

<table>
<thead>
<tr>
<th>Agent</th>
<th>α1</th>
<th>β1</th>
<th>β2</th>
<th>D</th>
<th>V1</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>++</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>Improves PA/RV coupling in animals (73–75)</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increases PVR (71, 74, 77); may induce reflex bradycardia</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td></td>
<td></td>
<td>(79)</td>
</tr>
<tr>
<td>Vasopressin</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>Dose dependent pulmonary vasodilatation (0.01–0.03 U/min) and vasoconstriction (24, 82, 83)</td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Risk of arrhythmias</td>
</tr>
<tr>
<td>Low (&lt;5 µg/kg/min)</td>
<td></td>
<td>+</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium (&gt;10 µg/kg/min)</td>
<td>+</td>
<td>++</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High (&gt;10 µg/kg/min)</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dobutamine</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td>β2-mediated drop in SVR (31); risk of arrhythmias</td>
<td></td>
</tr>
<tr>
<td>Milrinone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phosphodiesterase-3 inhibitor; inotropy and pulmonary vasodilatation; drop in LVEDP and SVR (72, 84, 89); risk of arrhythmias</td>
</tr>
</tbody>
</table>

**Definition of abbreviations:** D = dopaminergic receptor; LVEDP = left ventricular end-diastolic pressure; PA = pulmonary artery; PVR = pulmonary vascular resistance; RV = right ventricle; SVR = systemic vascular resistance; V1 = vasopressin receptor 1. + = low to moderate affinity, ++ = moderate to high affinity.
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Haemodynamic monitoring and support (ICU or Intermediate Care Unit)

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Positive inotropic agents

- Diverse collection of pluripotent molecules
- Differing pharmacological properties
- Some shared activities – only one of which is positive inotropy
  - Will increase $dP/dt$ with variable effects on cardiac output/index
  - Alteration in myocardial oxygen demand
  - Arrhythmia

Inotropes and vasopressors: more than haemodynamics!

Hendrik Bracht, Enrico Calzia, Michael Georgieff, Joel Singer, Peter Radermacher, and James A Russell

- Alteration in bacterial metabolism and translocation
- Alteration in inflammatory markers and ROS
- Immune-modulatory effects
- Coagulation
- Differential effects on macrocirculation & microcirculation
Conventional Hemodynamic Resuscitation May Fail to Optimize Tissue Perfusion: An Observational Study on the Effects of Dobutamine, Enoximone, and Norepinephrine in Patients with Acute Myocardial Infarction Complicated by Cardiogenic Shock


<table>
<thead>
<tr>
<th></th>
<th>Dobutamine (n = 14)</th>
<th>Enoximone (n = 10)</th>
<th>Norepinephrine (n = 9)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔHR, bpm</td>
<td>+9 [0; +16]**</td>
<td>+4 [−11; +9]</td>
<td>+1 [−15; +4]</td>
<td>NS</td>
</tr>
<tr>
<td>ΔMAP, mmHg</td>
<td>+6 [−5; +21]</td>
<td>+8 [+1; +14]</td>
<td>+17 [+13; +32]**</td>
<td>NS</td>
</tr>
<tr>
<td>ΔCVP, mmHg</td>
<td>−1 [−3; +1]</td>
<td>−2 [−3; −1]*</td>
<td>+2 [−4; +4]</td>
<td>NS</td>
</tr>
<tr>
<td>ΔPCWP, mmHg</td>
<td>−2 [−4; −1]*</td>
<td>−2 [−3; −1]**</td>
<td>+5 [−1; +7]</td>
<td>NS</td>
</tr>
<tr>
<td>ΔMPAP, mmHg</td>
<td>0 [−3; +3]</td>
<td>−1 [−9; 0]</td>
<td>+4 [−1; +7]</td>
<td>NS</td>
</tr>
<tr>
<td>ΔCI, L.min⁻¹.m⁻²</td>
<td>+0.8 [+0.3; +1.4]**</td>
<td>+0.6 [−0.1; +1.5]</td>
<td>0.0 [−0.5; +0.1]</td>
<td>0.006</td>
</tr>
<tr>
<td>ΔSVR, dynes.sec.cm⁻⁵</td>
<td>−201 [−623; +220]</td>
<td>−119 [−491; +175]</td>
<td>+390 [+237; +505]*</td>
<td>0.03</td>
</tr>
<tr>
<td>ΔSvO₂, %</td>
<td>+6 [+2; +12]**</td>
<td>0 [−3; +4]</td>
<td>0 [−3; +6]</td>
<td>0.04</td>
</tr>
<tr>
<td>ΔLactate, mmol.L⁻¹</td>
<td>−0.4 [−2.5; −0.1]*</td>
<td>0.0 [−0.6; +0.2]</td>
<td>0.0 [−0.2; +0.5]</td>
<td>NS</td>
</tr>
<tr>
<td>ΔDelta-T, °C</td>
<td>−0.4 [−0.8; 0]</td>
<td>−1.1 [−1.9; +0.6]</td>
<td>0.0 [−2.2; +0.6]</td>
<td>NS</td>
</tr>
<tr>
<td>ΔPCD, mm.mm⁻²</td>
<td>+0.6 [−0.9; +2.3]</td>
<td>+2.0 [+0.5; +3.4]*</td>
<td>−0.4 [−3.3; 0.0]</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Abbreviations: HR, heart rate; MAP, mean arterial pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; MPAP, mean pulmonary artery pressure; CI, cardiac index; SVR, systemic vascular resistance; SvO₂, mixed-venous oxygen saturation; delta-T, central-peripheral temperature gradient; PCD, perfused capillary density.

Values represent median [interquartile range]. The p-value in the last column represents differences among groups. Asterisks indicate statistical significance versus baseline:

*, p < 0.05
**, p < 0.01

P-values > 0.05 (NS, non-significant) are not shown.

A pulmonary artery catheter was present in 27/33 (82%) of the measurements.

doi:10.1371/journal.pone.0103978.t003
Cardiac output: global vs regional perfusion?

Regional resistance:
- neurohumoral factors related to inflammation and the sympathetic nervous system
- local factors related to autoregulation

Key (neglected) organs:
- GIT (gastric tonometry, splanchnic/hepatic saturations, indocyanine green)
- Brain
Each inotropic agent: efficacy vs toxicity

- Each inotropic agent
- Each organ system
  - Cardiac
  - Renal
  - Hepatic
  - Cerebral
  - GIT
  - Microcirculation
- Each pathological situation:
  - Sepsis
  - AMI+CS
  - DCM+CS
  - Haemorrhagic shock
- In context of different ICU interventions
Which inotrope?

- No real evidence to support one over another
Afterload reduction

- Critical illness frequently associated with increased PVR
- HPV – alveolar, pulmonary arterial/bronchial arterial hypoxaemia, worsened with acidemia
- **Focus on:**
  - Reducing pulmonary vascular tone
  - Judicious use of pulmonary vasodilators
  - Awareness of the effects of positive pressure ventilation

Aim: normoxia, normocarbia
Lung volumes near FRC
pH normal

Ventetuolo & Klinger, Ann Am Thorac Soc 2014
Potentially injurious effects of ventilation

Tavazzi G, ESICM 2014
Characterization of Right Ventricular Diastolic Performance After Complete Repair of Tetralogy of Fallot

Restrictive Physiology Predicts Slow Postoperative Recovery

Seamus Cullen; Darryl Shore; Andrew Redington

From the Royal Brompton Hospital and The National Heart and Lung Institute, London, UK.

Correspondence to Dr Andrew Redington, Royal Brompton Hospital and The National Heart and Lung Institute, Sydney Street, London SW3 6NP, UK.
Effects of IPPV in RV restrictive physiology

- Inspiration increases E/A ratio
- Abolishes PA diastolic wave
- Relative contribution of “restrictive” antegrade a wave to forward flow:
  - Inspiration: 7 ±8%
  - Expiration: 22 ±10%
- 43% patients with SARF
- Inducible by IPPV

Cullen, Circulation. 1995 Mar;91(6):1782
Pulmonary vasodilators

- None approved for treatment of RV failure in critically ill
- All have systemic & pulmonary effects
- Systemic administration may alter V/Q mismatch, and worsen hypoxaemia

Currently available pulmonary vasodilator medications

<table>
<thead>
<tr>
<th>Name</th>
<th>Drug Class</th>
<th>Action</th>
<th>Route of Administration</th>
<th>Terminal Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambrisant</td>
<td>Endothelin receptor antagonist</td>
<td>Blocks endothelin receptor A</td>
<td>Oral</td>
<td>15 h</td>
</tr>
<tr>
<td>Bosentan</td>
<td>Endothelin receptor antagonist</td>
<td>Blocks endothelin receptor A and B</td>
<td>Oral</td>
<td>5.4 h</td>
</tr>
<tr>
<td>Macitentan</td>
<td>Endothelin receptor antagonist</td>
<td>Blocks endothelin receptor A</td>
<td>Oral</td>
<td>14–18 h</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>Phosphodiesterase type-5 inhibitor</td>
<td>Slows metabolism of intracellular cGMP</td>
<td>Oral or intravenous</td>
<td>4 h orally</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>Phosphodiesterase type-5 inhibitor</td>
<td>Slows metabolism of intracellular cGMP</td>
<td>Oral</td>
<td>17.5 h</td>
</tr>
<tr>
<td>Epoprostenol</td>
<td>Prostacyclin</td>
<td>Increases intracellular cAMP</td>
<td>Intravenous or inhaled*</td>
<td>&lt;6 min</td>
</tr>
<tr>
<td>Treprostinil</td>
<td>Prostacyclin derivative</td>
<td>Increases intracellular cAMP</td>
<td>Intravenous, subcutaneous, inhaled, or oral</td>
<td>4 h</td>
</tr>
<tr>
<td>Iloprost</td>
<td>Prostacyclin derivative</td>
<td>Increases intracellular cAMP</td>
<td>Inhaled</td>
<td>20–30 min</td>
</tr>
<tr>
<td>Nitric oxide</td>
<td>Soluble guanylate cyclase stimulator</td>
<td>Increases intracellular cGMP</td>
<td>Inhaled</td>
<td>Seconds</td>
</tr>
<tr>
<td>Riociguat</td>
<td>Soluble guanylate cyclase stimulator</td>
<td>Increases intracellular cGMP</td>
<td>Oral</td>
<td>7–12 h</td>
</tr>
</tbody>
</table>

*Harjola et al., Eur J Heart Failure 2016
Right heart afterload

Maximal pulmonary vasodilatation
- iNO
- Levosimendan
- Nebulised prostacyclin
- Low dose vasopressin
- Nebulised milrinone
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Haemodynamic monitoring and support
(ICU or Intermediate Care Unit)

Consider transfer to hospital with possibility for ECMO/mechanical circulatory support
Peripheral VA-ECMO

Cardiac (or cardiopulmonary) support
Percutaneous, rapid access
Awake or ventilated

**Up to 8L/min – high, stable flow, 2-4 weeks**
Better kit – transportation and monitoring
Cheaper than Tandem Heart and Impella
Expanding indications

23Fr venous, 19-21Fr arterial
(Legmo: 10-12Fr)
Guidelines?

2014 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

IABP insertion should be considered in patients with haemodynamic instability/cardiogenic shock due to mechanical complications.

Patients with mechanical complication after acute myocardial infarction require immediate discussion by the Heart Team.

Short-term mechanical circulatory support in ACS patients with cardiogenic shock may be considered.

90-Day Survival

Days

Myocarditis
Pulmonary Embolism
Others
Acute Coronary Syndrome
??RV failure

www.escardio.org/ACCA
Transfemoral insertion

3D shaped cannula

22Fr motor housing
Pump on 1Fr catheter

4L/min @33,00rpm

ACT160-180

COHORT B: 58.3% survival (cohort predicted survival 40%)

Anderson MB¹, Goldstein J², Milano C³, Morris LD⁴, Kormos RL⁵, Bhama J⁶, Kapur NK⁶, Bansal A⁷, Garcia J⁸, Baker JN⁸, Silvestry S⁹, Holman WL¹⁰, Douglas PS¹¹, O'Neill W¹².

Anderson MB¹, Goldstein J², Milano C³, Morris LD⁴, Kormos RL⁵, Bhama J⁵, Kapur NK⁶, Bansal A⁷, Garcia J⁸, Baker JN⁸, Silvestry S⁹, Holman WL¹⁰, Douglas PS¹¹, O'Neill W¹².

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Primary Endpoint
Survival to 30 Day, Discharge or Next Therapy
(N=30)

Benchmark Reference:
Survival Rates observed in the Surgical
HDE approved RVAD device*

Anderson MB\textsuperscript{1}, Goldstein J\textsuperscript{2}, Milano C\textsuperscript{3}, Morris LD\textsuperscript{4}, Kormos RL\textsuperscript{5}, Bhama J\textsuperscript{5}, Kapur NK\textsuperscript{6}, Bansal A\textsuperscript{7}, Garcia J\textsuperscript{8}, Baker JN\textsuperscript{8}, Silvestry S\textsuperscript{9}, Holman WL\textsuperscript{10}, Douglas PS\textsuperscript{11}, O'Neill W\textsuperscript{12}.
Statement from ESC

Contemporary management of acute right ventricular failure: a statement from the Heart Failure Association and the Working Group on Pulmonary Circulation and Right Ventricular Function of the European Society of Cardiology


First published: 15 March 2016  Full publication history

Conclusions

Acute RV failure is a complex clinical scenario and its appropriate management requires an understanding of RV anatomy and mechanics, rapid identification and treatment of underlying causes, and knowledge of supportive treatment measures. Many uncertainties remain, and there is a need for randomized trials to investigate the efficacy and safety of pharmacological and mechanical interventions for the treatment of acute RV failure.
Many interventions seem physiologically/intuitively sensible – but that doesn’t mean they are right

Sir Iain Chalmers, co-founder Cochrane collaboration, BBC Radio 4, 2013