HEART FAILURE IN CORONARY DISEASE.
SYNCHRONIZING THE OPTIMAL MEDICAL & SURGICAL TREATMENT FOR THE BEST OUTCOME

JANUARY 20, 2018

Thessaloniki, 2016
PULMONARY HYPERTENSION IN CORONARY ARTERY DISEASE: FOCUS ON THE PERIOPERATIVE PERIOD

Dr Nandor Marczin

Imperial College Royal Brompton Harefield NHS Trust
Pathophysiologicaal Mechanisms of and Treatment Options for End-Stage Heart Failure
Central tenet: Backward/forward biventricular-pulmonary circulation interactions

- Development of CHF results of maladaptation of the pulmonary circulation with PH
- PH contributes to advanced stages of HF
  - Symptoms
  - Progression
- Surgical implications
- Perioperative therapeutic opportunities
Clinical Classification of Pulmonary Hypertension

1. Pulmonary arterial hypertension
2. Pulmonary hypertension due to left heart disease
3. Pulmonary hypertension due to lung diseases and/or hypoxia
4. Chronic thromboembolic pulmonary hypertension (CTEPH)
5. Pulmonary hypertension with unclear multifactorial mechanisms

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)
# PH Classification

<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, PAWP ≤15 mmHg | 1. Pulmonary arterial hypertension  
                              |                  | 3. PH due to lung diseases       |
|                                  |                  | 4. Chronic thromboembolic PH     |
|                                  |                  | 5. PH with unclear and/or multifactorial mechanisms |
| Post-capillary PH                | PAPm ≥25 mmHg, PAWP >15 mmHg | 2. PH due to left heart disease |
| isolated post-capillary PH (Ipc-PH) | DPG <7 mmHg and/or PVR ≤3 WUc | 5. PH with unclear and/or multifactorial mechanisms |
| combined post-capillary and pre-capillary PH (Cpc-PH) | DPG ≥7 mmHg and/or PVR >3 WUc | 5. PH with unclear and/or multifactorial mechanisms |
## Classification of Group 2 PH in LHD

<table>
<thead>
<tr>
<th>2. Pulmonary hypertension due to left heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Left ventricular systolic dysfunction</td>
</tr>
<tr>
<td>2.2 Left ventricular diastolic dysfunction</td>
</tr>
<tr>
<td>2.3 Valvular disease</td>
</tr>
<tr>
<td>2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies</td>
</tr>
<tr>
<td>2.5 Congenital/acquired pulmonary veins stenosis</td>
</tr>
</tbody>
</table>
Basic principles of PH due to Left Heart Disease

PULMONARY CIRCULATION

Superimposed components:
- Vasoconstriction
- NO availability
- Desensitisation to NP-induced vasodilation
- Arteriolar remodeling
- Venous congestion
- Metabolic factors
- Inflammatory cells

Pulmonary vascular disease (i.e. remodeling)

Passive backward transmission of left-sided filling pressures

RIGHT HEART

Loss of LA compliance
(exercise increased)
Mitral regurgitation
Systolic/diastolic LV dysfunction

LEFT HEART

RV failure

EHJ, 37: 12, 21 March 2016, pp 942–954
Backward transmission of LHD pathology

EHJ, 37: 12, 21 March 2016, pp 942–954
Backward transmission of LA pressures

Rev Esp Cardiol. 2010;63(3):334-45
Biopathology of PVD in LHD

- Left ventricular dysfunction
  - ↑ LVEDP
  - ↑ Neurohormones (local/systemic)
  - ↑ Cytokines

  Endothelial dysfunction (↑ET/↓NO)

  Remodeling and vasoconstriction

  Pulmonary hypertension

  Right ventricular dysfunction

Rev Esp Cardiol. 2010;63(3):334-45
Biopathology of PVD in LHD
Biopathology of PVD in LHD
Biopathology of PVD in LHD

[Images of micrographs showing various cellular and tissue structures labeled with annotations such as EC, A, C, Pn, P, BLM, etc.]

PROGRESS IN CARDIOVASCULAR DISEASES 59 (2016) 11–21
Biopathology of PVD in LHD

Figure 3. Marked medial hypertrophy of a muscular pulmonary artery in a patient with chronic heart failure (left, arrow indicates the medial thickness), compared to another of similar size with minimal medial thickening (right) in a patient with heart failure but not pulmonary hypertension (van Gieson stain, ×100).

Rev Esp Cardiol. 2010;63(3):334-45
RV anatomical considerations

- Triangular and crescent shape; anatomical inflow and outflow tract pattern and timing of peristaltic contraction
- Thin wall > volume compliance, pressure limitation

RV afterload sensitivity

![Graph showing RV and LV afterload sensitivity](image)
Impact of PVD on RV function

RA Dilatation

Functional TR

RV Dysfunction

PA Compliance

PVR↑

PA / RV Uncoupling

EHJ, 37: 12, 21 March 2016, pp 942–954
Backward transmission of LA pressures

JACC Vol. 37, No. 1, 2001 pp 183-188
Relationship between mPAP and RV function in HF

JACC Vol. 37, No. 1, 2001 pp 183-188
Survival according to RV-PAP coupling

Group 1 normal PAP/preserved RVEF
Group 2 5 normal PAP/low RVEF
Group 3 high PAP/preserved RVEF
Group 4 high PAP/low RVEF
Optimisation of pulmonary hypertension in left heart disease?

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimization of the treatment of the underlying condition is recommended before considering assessment of PH-LHD (i.e. treating structural heart disease)</td>
<td>I</td>
<td>B</td>
<td>[396]</td>
</tr>
<tr>
<td>It is recommended to identify other causes of PH (i.e. COPD, sleep apnoea syndrome, PE, CTEPH) and to treat them when appropriate before considering assessment of PH-LHD</td>
<td>I</td>
<td>C</td>
<td>[344]</td>
</tr>
<tr>
<td>It is recommended to perform invasive assessment of PH in patients on optimized volume status</td>
<td>I</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>
Surgical implications
PH as preoperative risk factor

- Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients

Does the Society of Thoracic Surgeons risk score accurately predict operative mortality for patients with pulmonary hypertension?

Jamie L. W. Kennedy, MD, a Damien J. LaPar, MD, MSc, b John A. Kem, MD, b Irving L. Kron, MD, b James D. Bergin, MD, a Sandeep Kamath, MD, a and Gorav Ailawadi, MD b

❖ Single centre
❖ All cardiac surgery with CABG subgroup
❖ 1994-2010
❖ N= 3343 patient with PAP and STS PROM data (67% CABG)
❖ PAP by SG cath prior to incision
Predicted vs. Observed mortalities

- Observed mortality levels increase with MPAP:
  - <25: 0.67%
  - 25-34: 0.91%
  - 35-44: 1.57%
  - >44: 2.46%

- Predicted mortality levels:
  - <25: 0.67%
  - 25-34: 0.91%
  - 35-44: 1.57%
  - >44: 2.46%

- Statistical significance: *p=0.04
### TABLE 3. Multivariate analysis demonstrating significant association between pulmonary hypertension and mortality and major complications

<table>
<thead>
<tr>
<th></th>
<th>Mortality</th>
<th>Major complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Entire cohort</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (&lt;25)</td>
<td>1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mild (25-34)</td>
<td>1.74 (0.95-3.18)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Moderate (35-44)</td>
<td>7.17 (3.91-6.68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Severe (&gt;44)</td>
<td>13.7 (6.68-26.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Isolated CABG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (&lt;25)</td>
<td>1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mild (25-34)</td>
<td>1.99 (0.88-4.52)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Moderate (35-44)</td>
<td>11.5 (4.97-26.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Severe (&gt;44)</td>
<td>38.9 (13.9-109)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure

Mandeep R. Mehra, M.D., Yoshifumi Naka, M.D., Nir Uriel, M.D.,
Daniel J. Goldstein, M.D., Joseph C. Cleveland, Jr., M.D., Paolo C. Colombo, M.D.,
Mary N. Walsh, M.D., Carmelo A. Milano, M.D., Chetan B. Patel, M.D.,
Ulrich P. Jorde, M.D., Francis D. Pagani, M.D., Keith D. Aaronson, M.D.,
David A. Dean, M.D., Kelly McCants, M.D., Akinobu Itoh, M.D.,
Gregory A. Ewald, M.D., Douglas Horstmanshof, M.D., James W. Long, M.D.,
and Christopher Salerno, M.D., for the MOMENTUM 3 Investigators*
<table>
<thead>
<tr>
<th>Condition</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>p-Value 1</th>
<th>p-Value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>14 (9.3)</td>
<td>19 (9.3)</td>
<td>9 (6.5)</td>
<td>10 (6.5)</td>
<td>1.42 (0.64–3.18)</td>
<td>0.39</td>
</tr>
<tr>
<td>LVAS drive-line infection</td>
<td>18 (11.9)</td>
<td>21 (11.9)</td>
<td>9 (6.5)</td>
<td>11 (6.5)</td>
<td>1.83 (0.85–3.93)</td>
<td>0.12</td>
</tr>
<tr>
<td>Local infection not associated with LVAS</td>
<td>46 (30.5)</td>
<td>57 (30.5)</td>
<td>36 (26.1)</td>
<td>58 (35.1)</td>
<td>1.17 (0.81–1.69)</td>
<td>0.41</td>
</tr>
<tr>
<td>Right heart failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any right heart failure</td>
<td>45 (29.8)</td>
<td>49 (29.8)</td>
<td>34 (24.6)</td>
<td>36 (23.9)</td>
<td>1.21 (0.83–1.77)</td>
<td>0.33</td>
</tr>
<tr>
<td>Right heart failure managed with RVAS</td>
<td>4 (2.6)</td>
<td>4 (2.6)</td>
<td>8 (5.8)</td>
<td>8 (5.8)</td>
<td>0.46 (0.14–1.48)</td>
<td>0.18</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any cardiac arrhythmia</td>
<td>47 (31.1)</td>
<td>61 (34.3)</td>
<td>52 (37.7)</td>
<td>68 (43.9)</td>
<td>0.83 (0.60–1.14)</td>
<td>0.24</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>27 (17.9)</td>
<td>33 (18.9)</td>
<td>27 (19.6)</td>
<td>37 (23.9)</td>
<td>0.91 (0.57–1.48)</td>
<td>0.71</td>
</tr>
<tr>
<td>Supraventricular arrhythmia</td>
<td>23 (15.2)</td>
<td>27 (15.2)</td>
<td>30 (21.7)</td>
<td>31 (20.0)</td>
<td>0.70 (0.43–1.15)</td>
<td>0.15</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>33 (21.9)</td>
<td>44 (25.3)</td>
<td>24 (17.4)</td>
<td>27 (17.1)</td>
<td>1.26 (0.78–2.02)</td>
<td>0.34</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>17 (11.3)</td>
<td>18 (11.3)</td>
<td>12 (8.7)</td>
<td>12 (7.9)</td>
<td>1.29 (0.64–2.61)</td>
<td>0.47</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>7 (4.6)</td>
<td>7 (4.6)</td>
<td>3 (2.2)</td>
<td>3 (2.0)</td>
<td>2.13 (0.56–8.08)</td>
<td>0.34</td>
</tr>
<tr>
<td>Hemolysis not associated with pump thrombosis</td>
<td>1 (0.7)</td>
<td>1 (0.7)</td>
<td>2 (1.4)</td>
<td>2 (1.2)</td>
<td>0.46 (0.04–4.98)</td>
<td>0.61</td>
</tr>
</tbody>
</table>
Continuous Flow LVAD/BiVAD Implants: 2008 – 2016, n=17633*

* CFLVAD entered in 2006 – removed for this analysis

Era 1: LVAD 2008 – 2012
N=6675, deaths=2693

n=10340, Deaths=2401

Era 1: BiVAD 2008 – 2012
n=231, Deaths=133

Era 2: BiVAD 2013 – 2016
n=387, deaths=171

Event: Death (censored at transplant and device cessation)

P(overall) < .0001

% Survival

Months post implant
A Bayesian model to predict RV Failure

JACC Heart Fail. 2016 Sep; 4(9): 711–721.
Adult Heart Transplants
Kaplan-Meier Survival by PVR
(Transplants: January 2003 – June 2011)

1-<3 vs. 3-<5: p = 0.0006
No other pair-wise comparisons were significant at p < 0.05

Survival (%)

1-<3 Wood units (N = 8,495)
3-<5 Wood units (N = 2,758)
5+ Wood units (N = 889)

Years

0 1 2 3 4 5 6 7

100 90 80 70 60 50
Adult Heart Transplants (2010-6/2015)
Risk Factors For 1 Year Mortality with 95% Confidence Limits

PA systolic pressure

Hazard Ratio for 1 Year Mortality

PA systolic pressure (mm/Hg)

\( p = 0.0155 \)

(N = 21,614)
Patient Prognosis with PH and LHD?
Intraoperative aspects of PH/RV dysfunction

Risks and optimisation
PH as intraoperative risk factor

- Intraoperative hemodynamic abnormalities including
  - pulmonary hypertension,
  - hypotension during cardiopulmonary bypass,
  - and post cardiopulmonary bypass pulmonary diastolic hypertension
were independently associated with
- mortality, stroke, and perioperative myocardial infarction
over and above the effects of other preoperative risk factors.

RV overload
RV MANAGEMENT

PRELOAD OPTIMISATION!!!
RV MANAGEMENT

PERFUSION PRESSURE!!!!!
RV MANAGEMENT

PVR !!!!!
PHARMACOLOGIC APPROACHES

❖ Inotropic agents
  – Catecholamines
  – Phosphodiesterase inhibitors
  – Levosimendan
  – Digoxin, calcium, T₃

❖ Pulmonary vasodilators
  – Systemic vasodilators
  – Phosphodiesterase inhibitors
  – Inhaled nitric oxide and Prostaglandins
MILRINONE EFFECTS ON LVEDP AND DP/DT

INHALED NO and vasodilators
iNO: the master
“reperfusion anaesthetic”

- ↓PVR, PAP, RV failure
- Improved hemodynamics
- ↓Capillary filtration
- ↓Pulmonary oedema
- Ventilation/perfusion Matching, ↓shunt
- Improved gas exchange

- ↓PMN responses
  (adhesion molecule expression, Free radical release)

- ↓Cytokine expression
  ↓Activation of NF-kB)

- ↓Immune response, activation
INOmax®
(nitric oxide) FOR INHALATION

Turn it on. Sooner.
Inhaled nitric oxide therapy in adults:
European expert recommendations
Inhaled nitric oxide after left ventricular assist device implantation: A prospective, randomized, double-blind, multicenter, placebo-controlled trial

Evgenij Potapov, MD, PhD, Dan Meyer, MD, Madhav Swaminathan, MD, Michael Ramsay, MD, Aly El Banayosy, MD, Christoph Diehl, MD, Bryan Veynovich, DO, Igor D. Gregoric, MD, Marian Kukucka, MD, Tom W. Gromann, MD, Nandor Marcin, MD, PhD, Kanti Chittuluru, MD, James S. Baldassarre, MD, Mark J. Zucker, MD, and Roland Hetzer, MD, PhD
# Use of iNO After LVAD

<table>
<thead>
<tr>
<th></th>
<th>Inhaled NO (iNO) Group</th>
<th>Placebo Group</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Meeting RVD Criteria in 48 Hours, ( n/N )(%)</td>
<td>7/73 (9.6)</td>
<td>12/77 (15.6)</td>
<td>0.330</td>
</tr>
<tr>
<td>Days on Mechanical Ventilation*</td>
<td>5.4 (7.7)</td>
<td>11.1 (24.8)</td>
<td>0.077</td>
</tr>
<tr>
<td>Mean (SD) Median (range)</td>
<td>2 (1−30)</td>
<td>3 (0−160)</td>
<td></td>
</tr>
<tr>
<td>ICU Hospital Days† Mean (SD)</td>
<td>20.5 (32.3)</td>
<td>19.9 (24.4)</td>
<td>0.630</td>
</tr>
<tr>
<td>Median (range)</td>
<td>11 (3−194)</td>
<td>9 (3−115)</td>
<td></td>
</tr>
<tr>
<td>Total Hospital Days‡ Mean (SD)</td>
<td>40.6 (32.2)</td>
<td>40.8 (29.4)</td>
<td>0.979</td>
</tr>
<tr>
<td>Median (range)</td>
<td>32 (11−194)</td>
<td>32 (10−156)</td>
<td></td>
</tr>
<tr>
<td>Quantity of Blood Products Used</td>
<td>4232 (4675)</td>
<td>4885 (7760)</td>
<td>0.220</td>
</tr>
<tr>
<td>Mean mL, (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients Requiring Renal Replacement Therapy ( n/N )(%)</td>
<td>10/71 (14.1)</td>
<td>8/70 (11.4)</td>
<td>0.637</td>
</tr>
<tr>
<td>Non-Survival at 28 Days ( n/N )(%)</td>
<td>8/71 (11.2)</td>
<td>8/70 (11.4)</td>
<td>0.924</td>
</tr>
<tr>
<td>Patients Requiring Right Ventricular Assist Device by Day 28 ( n/N )(%)</td>
<td>4/71 (5.6)</td>
<td>7/70 (10.0)</td>
<td>0.468</td>
</tr>
</tbody>
</table>
Inhaled nitric oxide in cardiac surgery: Evidence or tradition?

Maria Benedetto a, c, 1, Rosalba Romano a, b, 1, Georgiana Baca a, Despoina Saridou a, b, Andreas Fischer a, Andre Simon a, Nandor Marcin a, b, d, *
Possibilities for “extended” iNO therapy

1. Antioxidants (NAC, SOD)

2. PDE Inhibitors

3. sGC sensitisers

4. PGI

NO → GMP → PDE

iNO → O2^-

sGC

GTP

ATP

cGMP

AC

cAMP

PDE
New trials on approved PAH treatments?

Expansion of promising new therapies?

New trials on iNO?

New registry on inhaled vasodilators in cardiac surgery?
Acute Hemodynamic Effects of Riociguat in Patients With Pulmonary Hypertension Associated With Diastolic Heart Failure (DILATE-1)
A Randomized, Double-Blind, Placebo-Controlled, Single-Dose Study

Diana Bonderman, MD; Ingrid Pretsch, MD; Regina Steringer-Mascherbauer, MD; Pavel Jansa, MD; Stephan Rosenkranz, MD; Caroline Tufaro, MS; Andja Bojic, MD; Carolyn S. P. Lam, MD; Reiner Frey, MD; Michael Ochan Kilama, MD; Sigrun Unger, MSc; Lothar Roessig, MD; and Irene M. Lang, MD
Sodium Nitrite Improves Exercise Hemodynamics and Ventricular Performance in Heart Failure With Preserved Ejection Fraction
Echocardiographic probability of PH in symptomatic patients with a suspicion of PH

<table>
<thead>
<tr>
<th>A: The ventricles&lt;sup&gt;a&lt;/sup&gt;</th>
<th>B: Pulmonary artery&lt;sup&gt;a&lt;/sup&gt;</th>
<th>C: Inferior vena cava and right atrium&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ventricle/left ventricle basal diameter ratio &gt;1.0</td>
<td>Right ventricular outflow Doppler acceleration time &lt;105 msec and/or midsystolic notching</td>
<td>Inferior cava diameter &gt;21 mm with decreased inspiratory collapse (&lt;50% with a sniff or &lt;20% with quiet inspiration)</td>
</tr>
<tr>
<td>Flattening of the interventricular septum (left ventricular eccentricity index &gt;1.1 in systole and/or diastole)</td>
<td>Early diastolic pulmonary regurgitation velocity &gt;2.2 m/sec</td>
<td>Right atrial area (end-systole) &gt;18 cm²</td>
</tr>
<tr>
<td>PA diameter &gt;25 mm.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Echocardiographic probability of PH in symptomatic patients with a suspicion of PH

<table>
<thead>
<tr>
<th>Peak tricuspid regurgitation velocity (m/s)</th>
<th>Presence of other echo 'PH signs'a</th>
<th>Echocardiographic probability of pulmonary hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2.8 or not measurable</td>
<td>No</td>
<td>Low</td>
</tr>
<tr>
<td>≤2.8 or not measurable</td>
<td>Yes</td>
<td>Intermediate</td>
</tr>
<tr>
<td>2.9–3.4</td>
<td>No</td>
<td>High</td>
</tr>
<tr>
<td>2.9–3.4</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>&gt;3.4</td>
<td>Not required</td>
<td></td>
</tr>
</tbody>
</table>
Diagnostic workup

**Confirm PH**

mean PAP $\geq 25$ mmHg

**Complete hemodynamic profile**

(PAPs, PAPm, PAPd, PAWP, RVP, RAP, CO, SvO$_2$, TPG, DPD, PVR)

**Characterize: PAWP / LVEDP**

(pre-capillary: $\leq 15$ mmHg; post-capillary: $>15$ mmHg)

be aware of limitations and uncertainties*

*EHJ, 37: 12, 21 March 2016, pp 942–954
Diagnostic workup

Measurement consistent with suspected diagnosis?

YES

WORKING DIAGNOSIS

NO

reconsider non-invasive measures

consider:
- exercise testing
- volume challenge

PH-LHD
(Nice group 2)

PAH
(Nice group 1)

consider other causes of PH:
- recurrent PE
- left sided valvular disease
- chronic lung disease
- systemic-to-pulmonary shunt
- Sleep apnoea

DPG <7 mmHg and/or PVR ≤3 WU

Ipc-PH

Cpc-PH

DPG ≥7 mmHg and/or PVR > 3 WU

PAWP >15 mmHg

HFpEF

HFrEF

consider additional hemodynamic variables:
- PVR
- CO
- TPG
- DPG
- PA compliance

EHJ, 37: 12, 21 March 2016, pp 942–954
Efficacy of iNO in post CPB pulmonary hypertension

- **Effective as preventive modality**
  - iNO (20-40ppm) during and after CPB reduced PVR
    

- **Effective as therapeutic modality in developed PHT**
  - iNO lowered PVR and increased RVEF in 17 adult patients

- **Superior to standard dose of milrinone**
  
  - increased RV EF
  - Decrease PVR, increased RV EF
  - Less systemic vasodilation and requirement for vasopressors
Consensus on iNO and Post CPB pulmonary hypertension

- There are no randomised placebo-controlled clinical trials that conclusively show that iNO improves clinical outcomes.

- There is substantial clinical experience suggesting that in patients with confirmed acute RV dysfunction and elevated pulmonary vascular resistance, use of iNO may result in haemodynamic improvement.
Efficacy of iNO in HTx

- Effective in reducing PVR post transplantation
  

- Superior to PGE1 in terms of selectivity and efficacy in HTx
  
  *Rajek et al. Anesth Analg 200: 90; 522-30*

- Increased survival after HTx
  
  *Ardehali et al. Transplantation 2001 Transplantation 72(4) p638*
Several institutions with extensive experience in cardiac transplantation
  – use and recommend iNO
  – as part of standard therapy
  – for all cardiac transplant procedures associated with increased PVR
Consensus on iNO and LVAD

- iNO therapy is effective in providing favourable pulmonary haemodynamics
  - leading to improved RV and LVAD assisted cardiac output
  - in patients with PH and inadequate LVAD flow refractory to conventional manoeuvres.

- The expert panel recommends that it is reasonable to consider the use of iNO in this clinical situation.
Use of iNO After LVAD

❖ iNO was safe and well tolerated
❖ iNO reduced the incidence of RV failure
❖ iNO reduced duration of mechanical ventilation

❖ Results are clinically meaningful considering the cross-over design.

❖ The use of iNO after LVAD placement may improve clinical outcomes
NM Personal views

- Current status quo is not sustainable
- We are risking loosing this promising therapy from our daily practice
- International cooperation to conduct definite studies to determine the place of iNO therapy in
  - lung transplantation and
  - high risk mitral surgery.
- multi-institutional experience from large retrospective and matched studies
- Prospective data from a new international registry
Thank you!