Recognition & Treatment of Right Ventricular Failure

Robert L Kormos MD, FRCS(C), FACS, FAHA
Deputy Director McGowan Institute for Regenerative Medicine
Brack G Hattler Chair of Cardiothoracic Transplantation University of Pittsburgh
Disclosures

• Medtronic HeartWare:
  – Medical advisory panel
Surgeries Commonly Associated With Postoperative Right Ventricular Failure

Transplantation
- Heart: follows chronic heart failure associated with fixed pulmonary artery hypertension
- Bleeding Primary Graft Dysfunction

Cardiac Surgery
- **Valve repair/replacement**
  - Mitral most common
  - Robotic surgery
  - Aortic
- **Surgery for Acute Ischemia**
  - CABG +/- acute Myocardial Infarction
  - Acute VSD
- **Congenital heart surgery**
  - Congenital intra-cardiac shunts (ventricular septal defect)
- **Left-ventricular-assist devices**

Thrombo-endarterectomy
- Chronic thromboembolic pulmonary hypertension
The RV and its Challenges

- Incidence of RH failure in post-cardiotomy failure = 0.04% to 0.1%.
- Seen in 20-30% in pts with LVAD’s
- Accounts for 50% of all cardiac complications post-hrt trx and 20% of deaths early post-trx.
RV Dysfunction is Time Related (1)

• **Preoperative burden:**
  – Native Biventricular dysfunction
  – Anatomic and structural determinants
  – Inflammatory overload

• **Intra-operative “Black Box”**
  – Management of LVAD performance
  – Management of total pulmonary resistance
  – Protecting lung (avoid bleeding)
  – Inotropic agents
  – Tricuspid insufficiency
  – Control of LV afterload
RV Dysfunction is Time Related (2)

- **Postoperative management:**
  - Focal Tamponade
  - Arrhythmias (Atrial and Ventricular)
  - Volume management
  - Pulmonary resistance

- **Late Post Discharge Events**
  - Cardio-renal syndrome
  - Aortic insufficiency
  - Device malfunction
RV Response to Afterload and Preload

Relates to ischemia and altered inter-ventricular balance.
RV developed pressure is determined by RV free wall function, LV function and inter-ventricular septal position and function.
RV can do pressure work or volume work, but not both simultaneously.

Right Ventricular Failure
HeartMate II BTT Clinical Trial (n=484)

<table>
<thead>
<tr>
<th>Category</th>
<th>Patients (n=484)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No RV Failure</td>
<td>386 (80%)</td>
</tr>
<tr>
<td>RV Failure</td>
<td></td>
</tr>
<tr>
<td>RVAD</td>
<td>30 (6%)</td>
</tr>
<tr>
<td>Inotropes – Early</td>
<td>35 (7%)</td>
</tr>
<tr>
<td>Inotropes – Late</td>
<td>33 (7%)</td>
</tr>
<tr>
<td>Total</td>
<td>98 (20%)</td>
</tr>
</tbody>
</table>

Kormos, Teuteberg, Pagani et al J Thorac Cardiovasc Surg 2010;139:1316-24
### The Right Ventricular Failure Risk Score

A Pre-Operative Tool for Assessing the Risk of Right Ventricular Failure in Left Ventricular Assist Device Candidates

Jennifer Cowger Matthews, MD,* Todd M. Koelling, MD,* Francis D. Pagani, MD, PhD,† Keith D. Aaronson, MD, MS*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasopressor requirement</td>
<td>3.9</td>
<td>1.5 - 9.8</td>
<td>4</td>
</tr>
<tr>
<td>AST ≥ 80 IU/l</td>
<td>2.1</td>
<td>0.96 - 4.5</td>
<td>2</td>
</tr>
<tr>
<td>Total bilirubin ≥ 2.0 mg/dl</td>
<td>2.4</td>
<td>1.1 - 5.2</td>
<td>2.5</td>
</tr>
<tr>
<td>Creatinine ≥ 2.3 mg/dl</td>
<td>2.9</td>
<td>1.1 - 7.7</td>
<td>3</td>
</tr>
</tbody>
</table>

*MICHIGAN*
### Table 7. Results of Multivariate Logistic Regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac index ≤ 2.2</td>
<td>5.7</td>
<td>1.3–24.4</td>
<td>0.0192</td>
</tr>
<tr>
<td>liters/min/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVSWI ≤ 0.25</td>
<td>5.1</td>
<td>2.1–12.2</td>
<td>0.0002</td>
</tr>
<tr>
<td>mm Hg · liter/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe pre-VAD RV dysfunction</td>
<td>5.0</td>
<td>2.0–12.5</td>
<td>0.0006</td>
</tr>
<tr>
<td>Creatinine ≥ 1.9 mg/dl</td>
<td>4.8</td>
<td>1.9–12.0</td>
<td>0.0010</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>4.5</td>
<td>1.7–11.8</td>
<td>0.0023</td>
</tr>
<tr>
<td>SBP ≤ 96 mm Hg</td>
<td>2.9</td>
<td>1.2–6.9</td>
<td>0.0162</td>
</tr>
</tbody>
</table>
CVP >15 mmHg (OR 2.0, “C”), severe RV dysfunction (OR 3.7, “R”), preoperative intubation (OR 4.3, “I”), severe tricuspid regurgitation (OR 4.1, “T”), heart rate >100 (OR 2.0, Tachycardia - “T”) -CRITT as the major criteria predictive of the need for biventricular support

Thus, 93% of patients with a score of 1 or less underwent successful isolated LVAD therapy. 80% of patients with a score of 4 or higher required biventricular assistance

Right ventricular function was measured by echo by evaluation of regional myocardial contractility, tricuspid valve competence, and TAPSE. Severe RV dysfunction was defined by echo parameters, taking into account RV contractility, tricuspid regurgitation, and TAPSE
## Risk Factors Predictive of Right Ventricular Failure After Left Ventricular Assist Device Implantation

Stavros G. Drakos, MD\textsuperscript{a,c}, Lindsay Janicki, MS\textsuperscript{a,b}, Benjamin D. Horne, PhD\textsuperscript{a}, Abdullah G. Kfouri, MD\textsuperscript{a,b}, Bruce B. Reid, MD\textsuperscript{a,b}, Stephen Clayson, MD\textsuperscript{a}, Kenneth Horton, RCS\textsuperscript{a}, Francois Haddad, MD\textsuperscript{a}, Dean Y. Li, MD, PhD\textsuperscript{a}, Dale G. Replund, MD\textsuperscript{a,b}, and Patrick W. Fisher, DO, PhD\textsuperscript{a,c,o}

### Multivariate predictors for right ventricular failure (RVF)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full model</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Destination therapy</td>
<td>3.31</td>
<td>0.005</td>
</tr>
<tr>
<td>Inotrope dependency</td>
<td>2.47</td>
<td>0.08</td>
</tr>
<tr>
<td>Obesity (body mass index $\geq 30$ kg/m\textsuperscript{2})</td>
<td>1.99</td>
<td>0.08</td>
</tr>
<tr>
<td>Intra-aortic balloon counterpulsation</td>
<td>3.88</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Pulmonary vascular resistance</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq 1.7$ Wood unit</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>1.8–2.7 Wood unit</td>
<td>1.95</td>
<td>0.22</td>
</tr>
<tr>
<td>2.8–4.2 Wood unit</td>
<td>3.01</td>
<td>0.045</td>
</tr>
<tr>
<td>$\geq 4.3$ Wood unit</td>
<td>4.14</td>
<td>0.012</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker</td>
<td>0.49</td>
<td>0.054</td>
</tr>
<tr>
<td>$\beta$ Blocker</td>
<td>1.60</td>
<td>0.258</td>
</tr>
</tbody>
</table>

© 2010 Elsevier Inc. All rights reserved. (Am J Cardiol 2010;105:1030–1035)
Need for an RVAD

Use of pulmonary vasodilators for >48 hours

Multi-organ failure due to RVF

Inotrope use for >7 days after implantation

Or re-institution of inotropes after 7 days with concomitant venous pressure > 18 mmHg with cardiac index < 2.0 liters/min/m² with PCWP <18 mmHg) or renal or hepatic dysfunction
Early Right Ventricular Assist Device Use in Patients Undergoing Continuous-Flow Left Ventricular Assist Device Implantation (14 Days = 3.9%)
Incidence and Risk Factors From the Interagency Registry for Mechanically Assisted Circulatory Support

Michael S. Kiernan, MD, MS E. Wilson Grandin, MD Marshall Brinkley Jr, MD, Navin K. Kapur, MD Duc Thinh Pham, MD, Robin Ruthazer, MS J, Eduardo Rame, MD, Pavan Atluri, MD, Edo Y. Birati, MD, Guilherme H. Oliveira, MD, Francis D. Pagani, MD, PhD, James K. Kirklin, MD, David Naftel, MD, Robert L. Kormos, MD, Jeffrey J. Teuteberg, MD, David DeNofrio, MD

Table 2. Multivariable Predictive Risk Model for Early Right Ventricular Assist Device

<table>
<thead>
<tr>
<th>Term</th>
<th>OR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept*</td>
<td>0.04</td>
<td>(0.01-0.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prior CABG/valve surgery</td>
<td>1.70</td>
<td>(1.34-2.14)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>INTERMACS profile 1*</td>
<td>2.79</td>
<td>(2.00-3.89)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>INTERMACS profile 2*</td>
<td>1.98</td>
<td>(1.49-2.64)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ECMO within 48 h</td>
<td>2.71</td>
<td>(1.82-4.05)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hemodialysis or UF within 48 h</td>
<td>1.67</td>
<td>(1.08-2.57)</td>
<td>0.02</td>
</tr>
<tr>
<td>Creatinine (per 1-mg/dL increase)</td>
<td>1.25</td>
<td>(1.02-1.46)</td>
<td>0.005</td>
</tr>
<tr>
<td>INR (per unit increase)</td>
<td>1.50</td>
<td>(1.02-2.22)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total bilirubin (per 1-mg/dL increase)</td>
<td>1.13</td>
<td>(1.04-1.23)</td>
<td>0.003</td>
</tr>
<tr>
<td>WBC (per x10^9/L increase)</td>
<td>1.04</td>
<td>(1.01-1.07)</td>
<td>0.008</td>
</tr>
<tr>
<td>RA pressure (per 1-mmHg increase)</td>
<td>1.05</td>
<td>(1.03-1.08)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Stroke volume ×100 (per unit increase)</td>
<td>0.89</td>
<td>(0.80-0.99)</td>
<td>0.03</td>
</tr>
<tr>
<td>PA pressure (per 1-mmHg increase)</td>
<td>0.96</td>
<td>(0.94-0.98)</td>
<td>0.0002</td>
</tr>
<tr>
<td>LVEDD (per 1-cm increase)</td>
<td>0.80</td>
<td>(0.67-0.95)</td>
<td>0.01</td>
</tr>
<tr>
<td>Tricuspid regurgitation (severe)</td>
<td>1.61</td>
<td>(1.18-2.19)</td>
<td>0.002</td>
</tr>
<tr>
<td>Other concomitant procedure</td>
<td>1.47</td>
<td>(1.14-1.88)</td>
<td>0.003</td>
</tr>
<tr>
<td>Concomitant TV repair*</td>
<td>1.06</td>
<td>(0.78-1.45)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

AUC = 0.78

Case Examples
Patterns of RV Regional Dysfunction

- Normal RV Systolic Function
- Global RV systolic dysfunction
- RV free wall hypokinesis
- RV basal hypokinesis
- RV apical hypokinesis
- RV apical dyskinesis
Clusters of Adverse Events Accompanying a Primary Adverse Event
<table>
<thead>
<tr>
<th>Subsequent AE</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Failure</td>
<td>3.94</td>
<td>(1.78, 8.66)</td>
<td>0.0007</td>
<td>76%</td>
</tr>
<tr>
<td>Respiratory Failure</td>
<td>2.88</td>
<td>(1.54, 5.38)</td>
<td>0.0009</td>
<td>82%</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.57</td>
<td>(1.10, 6.02)</td>
<td>0.029</td>
<td>71%</td>
</tr>
<tr>
<td>Infection</td>
<td>2.30</td>
<td>(1.04, 5.10)</td>
<td>0.040</td>
<td>76%</td>
</tr>
</tbody>
</table>

A patient who requires an early RVAD is 3.9 times more likely to have renal failure. 76% of those needing an RVAD had renal failure.
Basic Principles of Managing Postoperative RV Failure (1)

**Optimize cardiac output**
- Use inotropic agents to maintain cardiac index 2 L/min/m2

**Attempt to reduce right-ventricular afterload**
- Moderate systemic vasodilators
- Use pulmonary vasodilators: inhaled vasodilators are less likely to have adverse effects on systemic blood pressure or oxygenation. Nitric Oxide/ Prostacyclin/ Sildenafil/ Flolan Remodulin

**Treat respiratory failure**
- Lung-protective ventilation strategy (tidal volume 6 mL/kg, plateau. Minimize PEEP/ peak pressure 30 cm H2O and reduce CO₂ < 40 cm
- Low ventilation rate during CPB
- Optimize oxygenation
- Avoid Bleeding
- Ensure airway clear, clear pleural spaces of blood or air
Optimize fluid balance
Avoid excessive fluid in patient with distended inferior vena cava and right ventricle. May need to ultra-filtrate during surgery

Optimize metabolic state
Correct acidosis, hypoxemia, anemia

Maintain systemic perfusion pressure and avoid vasodilatation
Inotropic support
(Milrinone/Epinephrine/Levosamendin/Isuprel)
Pressors (Norepinephrine/Vasopressin/Phenylephrine)

Maintain A-V synchrony and sinus rhythm

Treat Etiology: Pulmonary Embolism, Acute RV MI, Left heart failure, CHD, Valve Disease

Ensure that there is not a component of LV failure
Points to consider before choosing the RVAD

• Is RV failure accompanied by LV failure?
  – Is Biventricular support or ECMO the pathway?
• Is the RV failure going to require long-term or durable support?
• Is the end-game transplantation or recovery?
• Is there a component of pulmonary failure or lung damage where an RVAD can be fatal?

Direct Left Atrial Pressure assessment may help differentiate strategy
Biventricular Support With Intracorporeal, Continuous Flow, Centrifugal Ventricular Assist Devices

Francisco A. Arabía, MD, MBA, Carmelo A. Milano, MD, Claudius Mahr, DO, Edwin C. McGee, Jr, MD, Nahush A. Mokadam, MD, J. Eduardo Rame, MD, Jaime D. Moriguichi, MD, Danny Ramzy, MD, PhD, David C. Naftel, PhD, Susan L. Myers, BBA QMIS, and James K. Kirklin, MD
Results: Implant Hospitalization Mortality
Patient Profiles Associated With Futility

Overall Cohort
N=14,101
IHM=1,035
(7.3%)

LVAD Only
N=13,660
IHM=898
(6.6%)

RVAD at time of LVAD
N=441
IHM=137
(31%)

No Pre-Op Dialysis/Ultrafilt
N=13,329
IHM=824
(6.1%)

Pre-Op Dialysis/Ultrafilt
N=331
IHM=74
(22%)

Age < 53
N=183
IHM=31
(17%)

Age > 53
N=258
IHM=106
(41%)

No Pre-Op Dialysis/Ultrafilt
N=162
IHM=21
(13%)

Pre-Op Dialysis/Ultrafilt
N=21
IHM=10
(48%)

Age < 66
N=266
IHM=47
(18%)

Age > 66
N=65
IHM=27
(42%)
INTERMACS RHF = Condition*

**Step 1: Diagnose RHF**

**Hemodynamics (≥1)**
- CVP > 16
- Dilated IVC
- Elevated JVP

**Manifestations (≥1)**
- ≥ 2+ edema
- Ascites
- ✈ Cr to > 2.0 mg/dL
- ✈ Bili to > 2.0 mg/dL

= RHF Present

**Step 2: Grade RHF Severity**

- 1. Mild if < 7 days
- 2. Moderate if 7 – 14 days
- 3. Severe if > 14 days
- 4. Severe Acute

**Therapy/Outcome**
- Inotropes
- INH/IV PA Vasodilators
- RVAD at any time
- Death due to RHF

*Started June 2014*
Duration of Inotropic Support and Survival

- Inotropes < 1 Week
- Inotropes 1 – 2 Weeks
- Inotropes 2- 4 Weeks
- Inotropes >4 Wks/Ongoing
- Early RVAD

% Survival vs. Months Since LVAD Implant

- 5694 3240 1173 887 423 158 <1 Week
- 3761 2161 1115 522 230 85 1-2 Weeks
- 1178 621 332 169 79 30 2-4 Weeks
- 547 224 106 56 23 8 >4 Weeks/Ongoing
- 485 202 103 62 41 26 Early RVAD
An Analysis of Early Versus Late Right Heart Failure with an Intrapericardial Continuous-Flow LVAD

J. Eduardo Rame,1 Jeffrey J. Teuteberg,2 Emma Birks,3 Joseph Rogers,4 Michael Acker,1 Edo Birati,1 Mark S. Slaughter,3 Keith Aaronson,5 Katrin Leadley,6 Francis Pagani,5 and Robert Kormos2

1Hospital of the University of Pennsylvania, Philadelphia, PA, 2University of Pittsburgh Medical Center, Pittsburgh, PA, 3University of Louisville, Louisville, KY, 4Duke University Medical Center, Durham, NC, 5University of Michigan, Ann Arbor, MI, 6HeartWare Inc., Framingham, MA.

BTT + CAP, N=382

ISHLT April 17, 2015
Late Right Heart Failure (N=28): Categories from Adjudication

<table>
<thead>
<tr>
<th>Category</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute RHF associated with systemic illness</td>
<td>10 (28.6%)</td>
</tr>
<tr>
<td>Infection, sepsis, MSOF, renal failure, v-tach</td>
<td></td>
</tr>
<tr>
<td>Clinical RHF</td>
<td>16 (57.1%)</td>
</tr>
<tr>
<td>25.0% confirmed by right-heart catheterization</td>
<td></td>
</tr>
<tr>
<td>Uncertain etiology</td>
<td>4 (14.3%)</td>
</tr>
</tbody>
</table>

* This category is in overlap with acute RHF.

Mean time to late RHF = 274.6 days
(median = 199 days)
Survival by Right Heart Failure Severity at 3 months post implant
For patients alive on device at 3 months post implant, n=6587*

- No RHF at 3 months N=5524, deaths=679
- Mild RHF at 3 months n=326, deaths=69
- Moderate RHF at 3 months n=276, deaths=102

<table>
<thead>
<tr>
<th>RHF Severity</th>
<th>% Survival at At 3 mths post</th>
<th>6mth</th>
<th>12 mth</th>
</tr>
</thead>
<tbody>
<tr>
<td>No RHF</td>
<td>98%</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>Mild RHF</td>
<td>92%</td>
<td>82%</td>
<td></td>
</tr>
<tr>
<td>Mod RHF</td>
<td>80%</td>
<td>68%</td>
<td></td>
</tr>
</tbody>
</table>
Case Example
Pre- and Post- LVAD

Pre-LVAD

1y Post-LVAD
Overall Summary

• RHF after an intrapericardial LVAD is clinically significant with implications for mortality and morbidity

• At baseline -- Patients with late RHF demonstrated increased RV load and decreased RV function — even more so than early RHF
  — Higher pre-implant CVP and PA systolic and mean PAP
  — More-severe reduction in RV function
  — More moderate to severe tricuspid regurgitation

• Patients with late RHF experienced significantly more GI bleeding, sepsis events, respiratory dysfunction and renal dysfunction

• A significant difference in baseline Pulmonary Artery Compliance (PAC) suggests a potential signal to explore mechanisms of late RHF in chronic heart failure assisted with left –sided mechanical support
Conclusions

• RV Failure presents after LVAD implant acutely related to clinical presentation and late stage of CHF.
• Future work may focus on composite risk scores based upon imaging techniques and inflammatory state.
• Perioperative RV dysfunction may be less concerning than late RV dysfunction
• New percutaneous techniques for support may help alleviate the acute scenario.
• Chronic RVAD’s are still a dream