New Strategies in the Management of Acute and Advanced Heart Failure

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Professor of Medicine (adj.) Duke University
Editor in Chief, JACC: Heart Failure
President, Heart Failure Society of America
Disclosures

- Research Support: Merck, Roche, Resmed, NHLBI

- Consultant: Resmed, Merck, FDA

- Equity: BisCardia
Why Do We Care: Quantity of Life?

The Next Generation

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER
Quality of Life

Charlie going to UNC formal

Duke BB Lovefest
Heart Failure therapy

Goals of Therapy

1) Relieve symptoms
2) Stabilize condition and lower risk for rehospitalization and death
3) Initiate treatments that will slow disease progression and improve long-term survival
4) Limit significant adverse effects (arrhythmia, renal failure)
Dobutamine and Increased Mortality


Follow-up in years

Fraction Survived

No Dobutamine

Dobutamine

The OPTIME Trial: First Large Trial

Short-term Intravenous Milrinone for Acute Exacerbation of Chronic Heart Failure
A Randomized Controlled Trial

Michael S. Cuffe, MD
Robert M. Califf, MD
Kirkwood F. Adams, Jr, MD
Raymond Benza, MD
Robert Bourge, MD
Wilson S. Colucci, MD
Barry M. Massie, MD
Christopher M. O’Connor, MD
Ileana Pina, MD
Rebecca Quigg, MD
Marc A. Silver, MD
Mihai Gheorghiade, MD

for the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) Investigators

Context Little randomized evidence is available to guide the in-hospital management of patients with an acute exacerbation of chronic heart failure. Although intravenous inotropic therapy usually produces beneficial hemodynamic effects and is labeled for use in the care of such patients, the effect of such therapy on intermediate-term clinical outcomes is uncertain.

Objective To prospectively test whether a strategy that includes short-term use of milrinone in addition to standard therapy can improve clinical outcomes of patients hospitalized with an exacerbation of chronic heart failure.

Design Prospective, randomized, double-blind, placebo-controlled trial conducted from July 1997 through November 1999.

Setting Seventy-eight community and tertiary care hospitals in the United States.

Participants A total of 951 patients admitted with an exacerbation of systolic heart failure not requiring intravenous inotropic support (mean age, 65 years; 92% with baseline New York Heart Association class III or IV; mean left ventricular ejection fraction, 23%).

Intervention Patients were randomly assigned to receive a 48-hour infusion of either milrinone, 0.5 μg/kg per minute initially (n = 477), or saline placebo (n = 472).

Main Outcome Measure Cumulative days of hospitalization for cardiovascular cause within 60 days following randomization.

Results The median number of days hospitalized for cardiovascular causes within 60 days after randomization did not differ significantly between patients given milrinone (6 days) compared with placebo (7 days; P = .71). Sustained hypotension requiring intervention (10.7% vs 3.2%; P < .001) and new atrial arrhythmias (4.6% vs 1.5%; P = .004) occurred more frequently in patients who received milrinone. The milrinone and placebo groups did not differ significantly in in-hospital mortality (3.8% vs 2.3%; P = .19), 60-day mortality (10.3% vs 8.9%; P = .41), or the composite incidence of death or readmission (35.0% vs 35.3%; P = .92).

Conclusion These results do not support the routine use of intravenous milrinone as an adjunct to standard therapy in the treatment of patients hospitalized for an exacerbation of chronic heart failure.

JAMA. 2002;287:1541-1547

www.jama.com
History of Drug Development in Acute HF

Milrinone
Tezosentan
Rolofylline
Levosimendan
Nesiritide
Diuretic Strategies in Patients with Acute Decompensated Heart Failure

G. Michael Felker, M.D., M.H.S., Kerry L. Lee, Ph.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Lynne W. Stevenson, M.D., Steven R. Goldsmith, M.D., Martin M. LeWinter, M.D., Anita Deswal, M.D., M.P.H., Jean L. Rouleau, M.D., Elizabeth O. Ofili, M.D., M.P.H., Kevin J. Anstrom, Ph.D., Adrian F. Hernandez, M.D., Steven E. McNulty, M.S., Eric J. Velazquez, M.D., Abdallah G. Kfoury, M.D., Horng H. Chen, M.B., B.Ch., Michael M. Givertz, M.D., Marc J. Semigran, M.D., Bradley A. Bart, M.D., Alice M. Mascette, M.D., Eugene Braunwald, M.D., and Christopher M. O’Connor, M.D., for the NHLBI Heart Failure Clinical Research Network*
Patient Global Assessment VAS AUC: Low vs. High Intensification

Low VAS AUC, mean (SD) = 4171 (1436)
High VAS AUC, mean (SD) = 4430 (1401)
P = 0.06
## Secondary Endpoints: Low vs. High Intensification

<table>
<thead>
<tr>
<th>Metric</th>
<th>Low</th>
<th>High</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea VAS AUC at 72 hours</td>
<td>4478</td>
<td>4668</td>
<td>0.041</td>
</tr>
<tr>
<td>% free from congestion at 72 hrs</td>
<td>11%</td>
<td>18%</td>
<td>0.091</td>
</tr>
<tr>
<td>Change in weight at 72 hrs</td>
<td>-6.1 lbs</td>
<td>-8.7 lbs</td>
<td>0.011</td>
</tr>
<tr>
<td>Net volume loss at 72 hrs</td>
<td>3575 mL</td>
<td>4899 mL</td>
<td>0.001</td>
</tr>
<tr>
<td>Change in NTproBNP at 72 hrs (pg/mL)</td>
<td>-1194</td>
<td>-1882</td>
<td>0.06</td>
</tr>
<tr>
<td>% Treatment failure</td>
<td>37%</td>
<td>40%</td>
<td>0.56</td>
</tr>
<tr>
<td>% with Cr increase &gt; 0.3 mg/dL within 72 hrs</td>
<td>14%</td>
<td>23%</td>
<td>0.041</td>
</tr>
<tr>
<td>Length of stay, days (median)</td>
<td>6</td>
<td>5</td>
<td>0.55</td>
</tr>
</tbody>
</table>
Effect of Nesiritide in Patients with Acute Decompensated Heart Failure


Study design and drug procedures

Acute HF < 24 hrs from IV RX

Nesiritide

24–168 hrs Rx

Placebo

Co-primary endpoint:
Dyspnea relief at 6 and 24 hrs

Co-primary endpoint:
30-day death or HF rehosp

All-cause mortality at 180 days
Study design and drug procedures

- Double – blind placebo controlled
- IV bolus (loading dose) of 2 µg/kg nesiritide or placebo
  - Investigator’s discretion for bolus
  - Followed by continuous IV infusion of nesiritide 0.01 µg/kg/min or placebo for up to 7 days
- Usual care per investigators including diuretics and/or other therapies as needed
- Duration of treatment per investigator based on clinical improvement

Nesiritide

Placebo

Co-primary endpoint: Dyspnea relief at 6 and 24 hrs

Co-primary endpoint: 30-day death or HF rehosp

All-cause mortality at 180 days

Acute HF < 24 hrs from IV RX

24–168 hrs Rx
ASCEND RESULTS

Minimal Improvement in Dyspnea and no difference in HF hosp. or Death
Co-Primary outcome: 30-day all-cause mortality or HF rehospitalization

Hazard Ratio 0.93 (95% CI: 0.8, 1.08)

Risk Diff (95% CI)
- 30-day Death/HF Rehospitalization: -0.7 (-2.1; 0.7)
- 30-day Death: -0.4 (-1.3; 0.5)
- HF Rehospitalization: -0.1 (-1.2; 1.0)

P = 0.31
### 30-day all-cause death or hospitalization (Nesiritide efficacy)

<table>
<thead>
<tr>
<th>Income Level</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High, &gt;$11,455</td>
<td>1.04 (0.89-1.23)</td>
</tr>
<tr>
<td>Upper-Middle, $3,706-$11,455</td>
<td>0.68 (0.49-0.94)</td>
</tr>
<tr>
<td>Lower-Middle, $936-$3,705</td>
<td>0.77 (0.53-1.12)</td>
</tr>
</tbody>
</table>
EDITOR’S PAGE

Why Negative Trials Are Positive for Heart Failure Patients

Christopher M. O’Connor, MD, FACC, Editor-in-Chief, JACC: Heart Failure
Relaxin

- Insulin-like protein
- Naturally-occurring peptide
- Found in men and women
- Normal hormone of pregnancy
- In humans, contributes to maternal hemodynamic adaptations to pregnancy
- Women “exposed” for 9 months to increased plasma concentrations: 0.8–1.6 ng/mL pregnancy\(^1,2\)
- Benign safety profile

Serelaxin 30 µg/kg/day

Study design

Primary endpoint:
CV mortality through Day 180

Serelaxin: 285/3274 (8.7%)
Placebo: 290/3271 (8.9%)
Hazard ratio (95% CI): 0.98 (0.83, 1.15)
p-value (log-rank): 0.3857
Primary endpoint: WHF through Day 5

Serelaxin: 227/3274 (6.9%)
Placebo: 252/3271 (7.7%)
Hazard ratio (95% CI): 0.89 (0.75, 1.07)
p-value (Gehan’s generalized Wilcoxon test): 0.0968

- WHF includes in-hospital WHF, adjudicated rehospitalization due to HF and death through Day 5
Urodilatin is synthesized in the distal tubulus cells
↓
is luminally secreted
↓
binds downstream in inner medullar-collecting duct to NPR-A and acts via cGMP
↓
and inhibits Na-reabsorption

Physiology of Urodilatin (INN: Ularitide)
Effect of Ularitide on In-Hospital Heart Failure Events During First 120 Hours

<table>
<thead>
<tr>
<th>Study drug infusion</th>
<th>Placebo</th>
<th>Ularitide</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>48 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>72 hr</td>
<td></td>
<td></td>
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<tr>
<td>120 hr</td>
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</table>

Number of In-Hospital Worsening Heart Failure Events

P = 0.005
TRUE-AHF: Cardiovascular Mortality

Placebo
225 deaths

Ularitide
236 deaths

HR = 1.03
(96% CI: 0.85-1.25)
P = 0.75

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>Ularitide</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months</td>
<td>Number</td>
<td>Number</td>
</tr>
<tr>
<td>0</td>
<td>1088</td>
<td>1069</td>
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<tr>
<td>6</td>
<td>988</td>
<td>987</td>
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<td>12</td>
<td>942</td>
<td>934</td>
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<td>18</td>
<td>789</td>
<td>786</td>
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<td>24</td>
<td>669</td>
<td>668</td>
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<td>30</td>
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<td>36</td>
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<td>0</td>
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<td>6</td>
<td>234</td>
<td>219</td>
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<td>12</td>
<td>106</td>
<td>104</td>
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<td>18</td>
<td>26</td>
<td>19</td>
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<tr>
<td>24</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
TRUE-AHF: Clinical Composite

P=0.82

% Patients

Improved

Unchanged

Worse
“Why can’t you conduct a positive HF trial?”
Designer Drugs vs. Lasix
Efficacy of Intravenous Furosemide Versus a Novel, pH-Neutral Furosemide Formulation Administered Subcutaneously in Outpatients With Worsening Heart Failure

Nisha A. Gilotra, MD, Oluseyi Princewill, MD, Bonnie Marino, RN, Ike S. Okwuosa, MD, Jessica Chasler, PharmD, Johana Almansa, DNP, Abby Cummings, CRNP, Parker Rhodes, MS, Julianne Chambers, RN, Kimberly Cuomo, CRNP, Stuart D. Russell, MD
METHODS Outpatients presenting with decompensated HF were randomized to receive a single SC or IV dose of furosemide. Primary outcome was 6-h urine output, and secondary outcomes were weight change, natriuresis, and adverse events.

RESULTS Forty-one patients were randomized: 19 were treated with IV (mean dose: 123 ± 47 mg) and 21 with SC furosemide (fixed dose of 80 mg over 5 h). The 6-h urine output in the IV group was not significantly different from that in the SC furosemide group (median IV: 1,425 ml; interquartile range [IQR]: 1,075 to 1,950 ml; vs. median SC: 1,350 ml; IQR: 900 to 1,900 ml; p = 0.84). Additionally, mean weight loss was not significantly different (−1.5 ± 1.1 kg in the IV group vs. −1.5 ± 1.2 kg in the SC group; p = 0.95). Hourly urine output was significantly higher in the IV group at hour 2 (425 ml in the IV group vs. 250 ml in the SC group; p = 0.02) and higher in the SC group at hour 6 (125 ml, IV group vs. 325 ml, SC group; p = 0.005). Natriuresis was higher in the SC group (IV: 7.3 ± 35.3 mEq/l vs. SC: 32.8 ± 43.6 mEq/l; p = 0.05). There was no worsening renal function, ototoxicity, or skin irritation with either formulation. Thirty-day hospitalization rates were similar.
EDITORIAL COMMENT

Furosemide Reimagined

Novel Subcutaneous Formulation for a 50-Year-Old Loop Diuretic Agent for the Treatment of Acute Decompensated Heart Failure*

Gary S. Francis, MD, Tamas Alexy, MD, PhD
State of the Art ADHF Therapy

- Diuretics
- Vasodilators
- Oxygen
- Consider inotropic therapy


Fonarow, GC et al. AHJ 2007, 16
Cardiac Transplantation: 50 Years

GUEST EDITORS' PAGE

Happy 50th Birthday, Cardiac Transplantation

Happy 5th Birthday, JACC: Heart Failure

Joseph G. Rogers, MD, JoAnn Lindenfeld, MD

INOVA HEART AND VASCULAR INSTITUTE
US Adult and Pediatric Heart Transplants

Number of transplants

Adult Heart Transplants
Kaplan-Meier Survival by Era
(Transplants: January 1982 – June 2013)

Median survival (years):
## The Evolution of MCS Devices

<table>
<thead>
<tr>
<th>Position</th>
<th>External</th>
<th>Internal</th>
<th>Internal</th>
<th>Internal</th>
<th>Internal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Large</td>
<td>Large</td>
<td>Small</td>
<td>Smaller</td>
<td>Smallest</td>
</tr>
<tr>
<td>Power</td>
<td>Pneumatic</td>
<td>Electric</td>
<td>Electric</td>
<td>Electric</td>
<td>Electric</td>
</tr>
<tr>
<td>Flow</td>
<td>Pulsatile</td>
<td>Pulsatile</td>
<td>Continuous</td>
<td>Continuous</td>
<td>Continuous</td>
</tr>
<tr>
<td>Mechanics</td>
<td>Complex</td>
<td>Complex</td>
<td>Simplified</td>
<td>Simplified</td>
<td>Simplified</td>
</tr>
</tbody>
</table>

-INOVÀ HEART AND VASCULAR INSTITUTE-
The Evolution of Mechanically Assisted Circulation

Data Source: INTERMACS website, May 2017
Chronic Mechanical Circulatory Support for Inotrope-Dependent Heart Failure Patients Who Are Not Transplant Candidates

Results of the INTrEPID Trial

Joseph G. Rogers, MD, FACC,* Javed Butler, MD, FACC;† Steven L. Lansman, MD, PhD;‡ Alan Gass, MD, FACC;§ Peer M. Portner, PhD, FACC;¶ Michael K. Pasque, MD;# Richard N. Pierson III, MD, FACC,** for the INTrEPID Investigators

Durham, North Carolina; Atlanta, Georgia; Valhalla and New York, New York; Palo Alto, California; St. Louis, Missouri; and Baltimore, Maryland
Contemporary LVAD Survival Outcomes

Original Article

Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device

Mark S. Slaughter, M.D., Joseph G. Rogers, M.D., Carmelo A. Milano, M.D., Stuart D. Russell, M.D., John V. Conte, M.D., David Feldman, M.D., Ph.D., Benjamin Sun, M.D., Antone J. Tatrooles, M.D., Reynolds M. Delgado, III, M.D., James W. Long, M.D., Ph.D., Thomas C. Wozniak, M.D., Waqas Ghumman, M.D., David J. Farrar, Ph.D., and O. Howard Frazier, M.D., for the HeartMate II Investigators

Intrapericardial Left Ventricular Assist Device for Advanced Heart Failure


Event-free Survival Rate (%)


N Engl J Med 2017; 376:451-60
Continuous Flow Left Ventricular Assist Device Improves Functional Capacity and Quality of Life of Advanced Heart Failure Patients

Joseph G. Rogers, MD,* Keith D. Aaronson, MD;† Andrew J. Boyle, MD;‡ Stuart D. Russell, MD;§ Carmelo A. Milano, MD,* Francis D. Pagani, MD;† Brooks S. Edwards, MD;|| Soon Park, MD;|| Ranjit John, MD;¶ John V. Conte, MD;§ David J. Farrar, PhD;¶ Mark S. Slaughter, MD;# for the HeartMate II Investigators

6 Minute Walk Distance

Kansas City Cardiomyopathy

* p<0.05 vs. baseline

J Am Coll Cardiol 2010;55:1826-34
Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients

Results From the ROADMAP Study

Jerry D. Estep, MD,* Randall C. Starling, MD, MPH,‖ Douglas A. Horstmannhof, MD,‖ Carmelo A. Milano, MD,§
Craig H. Selzman, MD,‖ Keyur B. Shah, MD,¶ Matthias Loewe, MD, PhD,* Nader Moazami, MD,‖
James W. Long, MD, PhD,‖ Josef Stehlik, MD, MPH,‖ Vigneshwar Kasirajan, MD,§ Donald C. Haus, MD,‡
John B. O’Connell, MD,** Andrew J. Boyle, MD,‖‖ David J. Farrar, PhD,** Joseph G. Rogers, MD,§
for the ROADMAP Study Investigators

- Non-randomized
- Current indication for DT VAD but not on inotropes
- 6MWD < 300 m
- Primary endpoint: survival + 6MWD at 12 months
- Secondary
Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients

Results From the ROADMAP Study

Jerry D. Estep, MD,* Randall C. Starling, MD, MPH,|| Douglas A. Horstmannhof, MD,‖ Carmelo A. Milano, MD,‡Craig H. Selzman, MD,‖ Keyur B. Shah, MD,§ Matthias Loebae, MD, PhD,* Nader Moazami, MD,‖James W. Long, MD, PhD,‡ Josef Stehlik, MD, MPH,|| Vigneshwar Kasirajan, MD,¶ Donald C. Haas, MD,#John B. O’Connell, MD,** Andrew J. Boyle, MD,†† David J. Farrar, PhD,** Joseph G. Rogers, MD,‡ for the ROADMAP Study Investigators

<table>
<thead>
<tr>
<th>Alive at 12 months on original therapy with increase in 6MWD by 75 m</th>
<th>OMM (n = 82)*</th>
<th>LVAD (n = 85)+</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First event that prevented success:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death within 1 yr</td>
<td>18 (22)</td>
<td>17 (20)</td>
<td></td>
</tr>
<tr>
<td>Delayed LVAD</td>
<td>18 (22)‡</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Delta 6MWD &lt;75 m</td>
<td>29 (35)</td>
<td>33 (39)</td>
<td></td>
</tr>
<tr>
<td>Urgent transplant</td>
<td>0</td>
<td>2 (2)</td>
<td></td>
</tr>
</tbody>
</table>

Values are n (%). Odds ratio is calculated (95% confidence interval) as LVAD versus OMM. *Excluded OMM patients: 9 withdrawn, 12 missing 6MWD. †Excluded LVAD patients: 3 withdrawn, 8 missing 6MWD, 1 elective heart transplant. ‡Including 1 total artificial heart.
Facilitated Myocardial Recovery: Mesenchymal Precursor Cells
Comorbidities and Complications

- Bleeding
- Thrombosis
- Infection
- Stroke
Adverse Events: INTERMACS

*Major Event: First occurrence of infection, bleeding, device malfunction, stroke or death

Patients 5436, Events = 3611

<table>
<thead>
<tr>
<th>Months</th>
<th>% Freedom</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>59%</td>
</tr>
<tr>
<td>3</td>
<td>48%</td>
</tr>
<tr>
<td>6</td>
<td>40%</td>
</tr>
<tr>
<td>12</td>
<td>30%</td>
</tr>
<tr>
<td>24</td>
<td>19%</td>
</tr>
<tr>
<td>36</td>
<td>14%</td>
</tr>
</tbody>
</table>
ENDURANCE: Hemocompatibility Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>HVAD (n=296)</th>
<th>HMII (n=149)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>No. of Events</td>
<td>No. of Patients</td>
</tr>
<tr>
<td>Bleeding</td>
<td>176 (59.5%)</td>
<td>400</td>
<td>90 (60.4%)</td>
</tr>
<tr>
<td>GI Bleed</td>
<td>103 (34.8%)</td>
<td>225</td>
<td>51 (34.2%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>85 (28.7%)</td>
<td>110</td>
<td>18 (12.1%)</td>
</tr>
<tr>
<td>Ischemic CVA</td>
<td>50 (16.9%)</td>
<td>65</td>
<td>13 (8.7%)</td>
</tr>
<tr>
<td>Hemorrhagic CVA</td>
<td>42 (14.2%)</td>
<td>45</td>
<td>6 (4.0%)</td>
</tr>
<tr>
<td>TIA</td>
<td>24 (8.1%)</td>
<td>27</td>
<td>7 (4.7%)</td>
</tr>
<tr>
<td>Pump Exchange</td>
<td>23 (7.8%)</td>
<td>27</td>
<td>20 (13.4%)</td>
</tr>
</tbody>
</table>

Adapted from N Engl J Med 2017;376:451-460
Non-Surgical Bleeding in LVAD Patients

- 37 CF VAD patients
- High molecular weight vWF (0=normal, 3=severe loss)
- 100% of patients demonstrated loss of HMW vWF
- 10/37 patients had bleeding complications
Unexpected Abrupt Increase in Left Ventricular Assist Device Thrombosis

Randall C. Starling, M.D., M.P.H., Nader Moazami, M.D., Scott C. Silvestry, M.D., Gregory Ewald, M.D., Joseph G. Rogers, M.D., Carmelo A. Milano, M.D., J. Eduardo Rame, M.D., Michael A. Acker, M.D., Eugene H. Blackstone, M.D., John Ehrlinger, Ph.D., Lucy Thuita, M.S., Maria M. Mountis, D.O., Edward G. Sotlesz, M.D., M.P.H., Bruce W. Llyle, M.D., and Nicholas G. Smedira, M.D.
Trial Design

- Prospective, single-center, randomized, controlled clinical trial in patients (n=200) at high risk of 6-month re-hospitalization or death comparing:
  - GDMT
  - GDMT + multidisciplinary palliative care intervention

- Co-primary endpoint
  - KCCQ overall summary score
  - FACIT-PAL

- Secondary endpoints
  - FACIT - Spiritual Well-Being
  - HADS - Depression
  - Composite of death, hospitalization, QoL
  - Resource utilization
Baseline Characteristics

<table>
<thead>
<tr>
<th>TABLE 1 Baseline Characteristics</th>
<th>UC + PML (n = 75)</th>
<th>UC Alone (n = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>71.9 ± 12.4</td>
<td>69.8 ± 13.4</td>
</tr>
<tr>
<td>Female</td>
<td>33 (44.0)</td>
<td>38 (50.7)</td>
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<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>36 (48.0)</td>
<td>26 (34.7)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (1.3)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>White</td>
<td>38 (50.7)</td>
<td>48 (6.4.0)</td>
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<tr>
<td>Other</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>History of coronary artery disease</td>
<td>38 (50.7)</td>
<td>47 (63.2)</td>
</tr>
<tr>
<td>History of stroke</td>
<td>18 (24.0)</td>
<td>10 (13.3)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>61 (81.3)</td>
<td>52 (69.3)</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>42 (56.0)</td>
<td>38 (50.7)</td>
</tr>
<tr>
<td>NYHA functional class III</td>
<td>54 (72.0)</td>
<td>58 (77.3)</td>
</tr>
<tr>
<td>NYHA functional class IV</td>
<td>15 (20.0)</td>
<td>5 (6.7)</td>
</tr>
<tr>
<td>Ischemic heart failure</td>
<td>34 (45.3)</td>
<td>38 (50.7)</td>
</tr>
<tr>
<td>Level of impairment of most recent ejection fraction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (&gt;55%)</td>
<td>21 (28.0)</td>
<td>14 (18.7)</td>
</tr>
<tr>
<td>Mildly impaired (40%-55%)</td>
<td>14 (18.7)</td>
<td>19 (25.3)</td>
</tr>
<tr>
<td>Moderately impaired (25%-40%)</td>
<td>17 (22.7)</td>
<td>14 (18.7)</td>
</tr>
<tr>
<td>Severely impaired (&lt;25%)</td>
<td>23 (30.7)</td>
<td>28 (37.3)</td>
</tr>
<tr>
<td>Prior ICD/pacemaker implantation</td>
<td>35 (46.7)</td>
<td>34 (45.3)</td>
</tr>
<tr>
<td>ICD only</td>
<td>8 (10.7)</td>
<td>12 (16.0)</td>
</tr>
<tr>
<td>Pacing only</td>
<td>9 (12.0)</td>
<td>7 (9.3)</td>
</tr>
<tr>
<td>Biventricular pace only</td>
<td>1 (1.3)</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Biventricular pace and ICD</td>
<td>17 (22.7)</td>
<td>13 (17.3)</td>
</tr>
<tr>
<td>NT-proBNP, pg/mL</td>
<td>10,040.2 ± 9,434.2</td>
<td>13,212.4 ± 14,698.2</td>
</tr>
<tr>
<td>Duration of HF, months</td>
<td>64.7 ± 70.0</td>
<td>69.1 ± 76.5</td>
</tr>
<tr>
<td>Importance of religious/spirituality</td>
<td>15 (20.0)</td>
<td>13 (17.3)</td>
</tr>
<tr>
<td>Faith</td>
<td>54 (72.0)</td>
<td>49 (65.3)</td>
</tr>
<tr>
<td>Deeply</td>
<td>35 (46.7)</td>
<td>34 (45.3)</td>
</tr>
<tr>
<td>Time spent in bed/chair in past month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than one-half</td>
<td>16 (21.3)</td>
<td>20 (26.7)</td>
</tr>
<tr>
<td>Almost all</td>
<td>26 (35.3)</td>
<td>29 (38.7)</td>
</tr>
<tr>
<td>Depression treated with medications</td>
<td>12 (16.0)</td>
<td>13 (17.3)</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>6 (8.0)</td>
<td>8 (10.7)</td>
</tr>
<tr>
<td>Drug abuse</td>
<td>5 (6.7)</td>
<td>5 (6.7)</td>
</tr>
<tr>
<td>Cardiovascular model</td>
<td>1 (1.3)</td>
<td>1 (1.3)</td>
</tr>
</tbody>
</table>

ACE inhibitor: 17 (22.7%); 16 (21.3%)
ARB: 4 (5.3%); 7 (9.3%)
Aldosterone antagonist: 30 (40.0%); 22 (29.3%)
Aspirin: 54 (72.0%); 46 (61.3%)
Beta-blocker: 51 (68.0%); 48 (64.0%)
Diuretics
- Bumetanide: 1 (1.3%); 1 (1.3%)
- Furosemide: 39 (52.0%); 49 (65.3%)
- Torasemide: 27 (36.0%); 14 (18.7%)
- Statin: 43 (57.3%); 41 (54.7%)

J Am Coll Cardiol. 2017;70:331-41
• RCT of palliative care intervention in patients with advanced HF and high mortality risk
• Focus on advance care planning, symptom reduction
• Inpatient and outpatient intervention by palliative care NP and MD
Impact of Palliative Care Intervention on Spirituality, Depression, and Anxiety

FACIT-SP

HADS-Depression

HADS-Anxiety

J Am Coll Cardiol. 2017;70:331-41
Summary

- Acute Heart Failure starts the negative cascade towards increase morbidity and mortality without any breakthroughs of new therapies.
- Advanced heart failure remains a condition accompanied by high residual morbidity and mortality.
- Transplant improves survival but is limited by the number of donors.
- LVADs have been shown to improve survival, quality of life and submaximal functional capacity.
- The PAL-HF trial was the first randomized, controlled clinical trial to test a longitudinal palliative care intervention in a heart failure population resulting in improved quality of life.
- More research is needed for advanced heart failure; acute heart failure research deserves a pause.