Clinical Characteristics and Outcomes of Intravenous Inotropic Therapy in Advanced Heart Failure

Hashim et al: Inotropes in Heart Failure

Taimoor Hashim, MD1; Kumar Sanam, MD1; Marina Revilla-Martinez, MD2; Charity J. Morgan, PhD3; Jose A. Tallaj, MD1; Salpy V. Pamboukian, MD, MSPH1; Renzo Y. Loyaga-Rendon, MD, PhD1; James F. George, PhD4; Deepak Acharya, MD, MSPH1

1Division of Cardiovascular Diseases, University of Alabama at Birmingham, Birmingham, AL
2Division of Cardiovascular Disease, University Hospital at Valladolid, Spain
3Department of Biostatistics, University of Alabama at Birmingham School of Public Health, Birmingham, AL
4Division of Cardiovascular Surgery, University of Alabama at Birmingham, Birmingham, AL

Correspondence to
Deepak Acharya MD, MSPH
THT 321, 1900 University Boulevard
University of Alabama at Birmingham
Birmingham, AL 35294
Fax: 205-975-9320
Phone: 205-934-3438
Email: dacharya@uab.edu

DOI: 10.1161/CIRCHEARTFAILURE.114.001778

Journal Subject Codes: Heart failure:[11] Other heart failure, Heart failure:[110] Congestive
Abstract

Background—Inotrope use in heart failure was associated with improved symptoms, but worse survival in clinical trials. However, these studies predated use of modern heart failure therapies. This study evaluates contemporary outcomes on long-term inotropes.

Methods and Results—We collected baseline and post-inotrope data on 197 patients discharged on inotropes between January 2007 and March 2013. Baseline characteristics, hemodynamic and clinical changes on inotropes, and survival were evaluated. Patients initiated on inotropes had refractory heart failure, with median baseline NYHA Class IV, cardiac index 1.7 L/min/m², PCWP 25.6 mmHg, and LVEF 18.7%. Inotropes were used in patients listed for transplant or scheduled for LVAD (60 patients), in patients being evaluated for LVAD/transplant (20 patients), for stabilization pending CRT/PCI (4 patients), in patients who were offered LVAD but chose inotropes (15 patients), and for palliation (98 patients). Milrinone was used in 84.8% and dobutamine in 15.2%. At the end of the study, 68 patients had died, 24 were weaned off inotropes, 23 were transplanted, 32 received LVADs, and 50 remained on inotropes. Patients who received inotropes for palliation or those who preferred inotropes over LVAD had median survival of 9.0 months (IQR 3.1, 37.1 months), actuarial 1-year survival of 47.6%, and 2-year survival of 38.4%. Of 60 patients who were placed on inotropes as a bridge to transplant/LVAD, 55 were successfully maintained on inotropes until transplant/LVAD.

Conclusions—Survival on inotropes for patients who are not candidates for transplant/LVAD is modestly better than previously reported, but remains poor. Inotropes are effective as a bridge to transplant/LVAD.

Key Words: congestive heart failure, inotropes, survival, arrhythmia
Approximately 6 million adults currently have heart failure (HF) in the United States, and this is expected to increase to 8.4 million by 2030. The number of patients with advanced HF who have refractory symptoms despite medical therapy is also expected to increase. Options for the majority of these patients with end-stage heart disease are limited. Both heart transplantation and mechanical circulatory support improve survival and quality of life, but due to limited donor supply and medical comorbidities, most patients are not candidates for these lifesaving therapies. The 1-year survival in the medical management group of the REMATCH trial, which studied such patients, was dismal, at 25%. Inotropes are sometimes used in these patients, but despite evidence that they improve hemodynamics, continuous outpatient inotrope use has not been shown to improve survival, and in some cases has worsened survival, with studies reporting a 6-month mortality between 40 and 74%. However, many inotrope trials predated the use of modern heart failure therapies, including Implantable cardioverter defibrillators (ICD), cardiac resynchronization therapy (CRT), aldosterone antagonists, and even beta-blockers in some cases. These therapies may have altered the prognosis of patients on chronic inotropes. The purpose of this study is to evaluate outcomes of patients with Stage D HF on chronic outpatient support with inotropic therapy in a contemporary patient population.

Methods

Study Design and Patients

This study was a retrospective review of all adult patients with advanced HF discharged from a single institution on continuous milrinone or dobutamine from January 2007 to March 2013. Patients on an inotrope were identified by several means: review of our patient records for that period for three of five home infusion companies providing inotropes; query of hospital and
clinic electronic medical records for all patients prescribed dobutamine or milrinone; review of heart failure clinic charts; and review of the list of transplant and left ventricular assist device (LVAD) recipients for that period. Patients less than 18 years old, those who had no follow-up data, patients on inotropes post LVAD for right ventricular (RV) dysfunction or for congenital heart disease or pulmonary arterial hypertension with RV dysfunction, and those receiving inotropes solely in the hospital were excluded. Patients included in the study had stage D HF and were deemed inotrope dependent by a heart failure specialist. Inotrope dependence was defined as worsening end-organ function, deteriorating hemodynamics, exacerbation of HF symptoms, or significant hypotension upon attempted inotrope wean, or poor hemodynamics even on inotropes where immediate weaning was not felt to be safe. Patients were followed in clinic by heart failure/transplant cardiologists, and managed over the phone by dedicated heart failure nurses. Local home health agencies provided inotropes and dressing supplies. Inotropes were administered through peripherally inserted central catheters (PICC). In cases of recurrent infection or dislodgements, patients had tunneled PICC or port placement. Palliative care services were available for inotrope dependent patients who were not candidates for advanced therapies. Each chart was abstracted by one of three investigators (TH, KS, MRM) and primary outcomes were independently verified (DA). Study data were collected and managed using REDCap electronic data capture tools. The study was approved by the Institutional Review Board.

Clinical data and Outcomes

The primary outcome measure was all-cause mortality. Data was collected on participants until they died, received a LVAD or transplant, were weaned off inotropes, or remained on inotropes
at the end of the data collection period. For patients who were weaned off inotropes, survival was assessed one year later. Vital status was ascertained using review of hospital data, clinic charts, infusion company records and the Social Security Death Index. Functional status, physical exam, catheterization, echocardiographic and laboratory data were collected prior to initiation of inotropes and at the time of the first clinic and/or catheterization visit after being on inotropes. ICD interrogation and hospitalization data was collected throughout the follow-up period.

**Statistical Analysis**

Continuous variables are presented as mean ± SD. Pre and post-inotrope clinical echocardiographic, laboratory and hemodynamic data were compared using paired T-tests for continuous data, and Chi-square tests for categorical data. The Kaplan-Meier method was used to evaluate survival. Patients were censored at the time of transplant, LVAD, on the date that they were completely weaned off inotropes, or at the end of the study if they remained on inotropes. Statistical analysis was performed using Statistical Analysis Software (SAS) 9.3.

**Results**

**Baseline Characteristics**

We identified 197 consecutive patients who were discharged on continuous inotropes between January 2007 and March 2013. The median baseline New York Heart Association (NYHA) class was IV, mean age was 54.4 years (±14.6 years), 40% had ischemic cardiomyopathy, and 25.8% were female. Sixty-two percent of patients had two or more hospitalizations for heart failure in the year prior to inotrope initiation. Milrinone was used in 84.8 % of patients at a mean discharge
dose of 0.296 (± 0.092) mcg/kg/min, and dobutamine was used in 15.2 % at a mean dose of 4.38
(±1.78) mcg/kg/min. The baseline mean arterial pressure was 79.2 mmHg in the milrinone group
and 74.7 mmHg in the dobutamine group (p 0.07). Over 90% of patients had ICD/CRT-D or a
Lifevest (Table 1). Patients were placed on inotropes for several reasons—as a bridge in patients
listed for transplant or scheduled for LVAD (60 patients), for patients being evaluated for
VAD/transplant (20 patients), for acute stabilization pending CRT or high risk PCI (4 patients),
in patients who were offered LVAD evaluation but refused and preferred inotropes (15 patients),
and for palliation (98 patients).

Clinical and Laboratory Data Pre- and Post-Inotrope

Baseline studies showed poor hemodynamics, with mean right atrial pressure 14.8  (±7.0)
mmHg, pulmonary capillary wedge pressure (PCWP) 25.6  (±8.1) mmHg, and assumed Fick
cardiac index  (CI) 1.7 (±0.4) L/min/m². The baseline left ventricular ejection fraction (LVEF)
was 18.7 (±8.1) %. After initiation of inotropes and discharge from the hospital, most patients
were seen in clinic within 4-6 weeks (Table 2). At the time of the first post-inotrope outpatient
measurement, there was improvement in mean CI to 2.2 (+0.5) L/min/m², decrease in PCWP to
21.1 (+9.0) mmHg, and improvement in LVEF to 21.1 (±10.1)%. Mean Blood Urea Nitrogen
(BUN) level decreased from 31.1 (±20.2) to 26.6 (±19.9) mg/dL, and mean serum creatinine
improved from 1.6 (±0.8) to 1.5 (+0.7) mg/dL. There was also improvement in congestion as
measured by weight and serum BNP levels (Table 3). The median NYHA class improved from
IV to III. Patients who died and those who remained on inotropes had more hospitalizations than
those who were weaned, transplanted, or underwent LVAD placement (Table 2). Oral HF
medications were maintained during inotrope therapy in a substantial proportion of patients (Table 4).

All patients who were candidates for LVAD/transplant had ICDs or Lifevest active until LVAD/transplant. Among the 113 patients who were not candidates for LVAD/transplant, 11 were discharged home on inotropes without ICD or Lifevest. Nineteen additional patients had ICDs deactivated at our institution at a median of 190 days (IQR 23, 479) after inotrope initiation. Some patients may have had their ICDs deactivated at home by their hospice physicians, and this information was not available. During follow-up, 33 patients (16.7%) had ICD shocks. These patients had a mean of 2.09 (+/- 1.8) episodes of shocks and 3.3 (+/- 3.0) total ICD shocks.

Outcomes and Survival
Sixty-eight patients died, 24 were weaned off inotropes, 23 were transplanted, 32 received a LVAD, and 50 remained on inotropes at the end of the study. The subset of patients who were placed on inotropes for palliation or those who were offered LVAD but chose inotropes had median survival of 9.0 months (IQR 3.1, 37.1 months) (Figure 1). The 1-year actuarial survival for this group was 47.6%, and the 2-year actuarial survival was 38.4%.

Fifty-five of the 60 patients (92%) who were placed on inotropes pending LVAD or transplant were successfully supported on inotropes until LVAD or transplant. Among all patients placed on inotropes, 24 were successfully weaned off, of who 19 were alive, three had died, and two were lost to follow-up one year later. Clinical characteristics of patients weaned off inotropes are listed in Table 5. Among all patients placed on inotropes, those on milrinone had a better survival than those on dobutamine (log rank p value 0.01) (Figure 2).
**Discussion**

The management of patients with advanced heart failure can be challenging. They are often already on maximally tolerated oral therapy, hypotension precludes aggressive afterload reduction, and intensive diuretic therapy often worsens cardiorenal syndrome. Those who are not candidates for LVAD or transplant have poor outcomes.

Inotropes are often used for acute hemodynamic stabilization or until resolution of the condition that precipitated the acute decompensation or shock, but their role in chronic management is more complex. Studies of chronic inotrope use from the late 1980s to early 2000s showed poor outcomes, with 6-month mortality in excess of 50%. However, these prior studies differed considerably from modern practice in regards to patient selection and management. There are no recent trials on chronic inotrope use, and given the clinical uncertainty and controversy over their utility, there is wide variation in inotrope use among institutions.

The two largest and most influential studies to examine inotrope therapy with currently available inotropes are PROMISE and OPTIME-CHF. PROMISE enrolled 1088 patients with NYHA III or IV HF between 1989 and 1990, and randomized them to placebo or oral milrinone. Patients did not have defibrillators, and those requiring beta-blockers were excluded. The milrinone group had 28% higher mortality at 6.1 months. OPTIME-CHF evaluated in-hospital inotrope use in 958 patients with HF exacerbation between 1997 and 1999. The primary end-point was the number of days hospitalized for cardiovascular causes within 60 days. Patients were excluded if “the treating physician judged that intravenous inotropic therapy was essential”. There was more hypotension and atrial arrhythmias in the milrinone group, and no difference in the primary outcome or survival.
Neither of these populations reflects current patients with advanced heart failure who are being considered for long-term inotropes. OPTIME-CHF did not evaluate home inotrope use and specifically excluded patients with low output states and evidence of end-organ hypoperfusion, precisely the population that in current practice may be “inotrope-dependent”. PROMISE was performed in an era without contemporary HF therapy including beta-blockers, aldosterone antagonists, defibrillators, or cardiac resynchronization, and used oral rather than intravenous milrinone. Moreover, neither study evaluated hemodynamics at enrollment or with therapy in detail.

Many other studies on inotropes have been performed, with mixed results. Vesnarinone, ibopamine, and xamoterol are not used due to higher mortality in trials, and enoximone was safe but did not meet efficacy endpoints. Secondary analysis of OPTIME-CHF revealed a neutral to beneficial effect of milrinone on 60-day cardiovascular hospitalizations, and the composite of death and readmission in nonischemic cardiomyopathy but harmful effect in ischemic cardiomyopathy. For heart transplant candidates, home inotropes are useful and cost-effective compared to hospitalization. For some patients with end-stage HF, quality of life may be more important than quantity of life, and inotropes can be used for palliative care.

In light of the existing evidence, the 2013 guidelines from ACC/AHA recommend temporary intravenous inotropes for patients with cardiogenic shock until definite therapy or resolution of the precipitating problem (Class I, LOE C), as a bridge to transplant or LVAD in candidates with refractory symptoms on oral and device therapy (Class IIa, LOE C), and state that inotropes can be considered for palliative therapy or in hospitalized patients with low output state (Class IIb, LOE B).
In our study, with contemporary HF management, patients who had inotrope-dependent advanced heart failure but were not candidates for heart transplant or LVAD had a median survival of 9 months. This survival is modestly better than reported in prior studies, and this may be related to advances in medical therapy and high utilization of electrophysiologic devices that can treat VT/VF. However, despite contemporary medical and device therapy, survival is still suboptimal, similar to that in patients with stage IIIb non-small cell lung cancer or stage III pancreatic cancer. Conversely, inotropes were very effective in bridging patients who were candidates for advanced therapies, with 92% of patients successfully supported until LVAD or transplant. Patients on inotropes had early symptomatic benefit, accompanied by improvement in hemodynamic parameters. Interestingly, 12% of patients who presented with a low output state were stabilized with inotropes, which were subsequently weaned off as an outpatient after optimization of contemporary oral and device therapy. At least 79% of patients weaned off inotropes were alive one year later.

In our study, a significant proportion of patients on inotropes were also maintained on oral heart failure therapy, including beta-blockers. There is limited evidence on how the addition of beta-blockers to inotrope therapy affects symptoms and survival. The effects of dobutamine are attenuated in the presence of beta-blockers, but phosphodiesterase inhibitors continue to have hemodynamic effects in the presence of beta-blockade. Several small studies of beta blockers in combination with milrinone have shown that this combination is well tolerated, may improve hemodynamics compared to milrinone alone, and that it is feasible to use inotropes initially in patients presenting with severe heart failure, then initiate beta-blockers and other oral heart failure therapies with subsequent wean of inotropes. In a post-hoc analysis of the OPTIME study, in patients who were continued on beta-blockers on admission, there was no
difference in the primary endpoint regardless of assignment to milrinone or placebo. Patients whose beta-blockers were withdrawn upon randomization to milrinone had worse outcomes.\textsuperscript{35} It has been our practice to use milrinone preferentially, attempt low dose beta-blockers in patients on milrinone, and assess the feasibility of weaning inotropes in clinic visits.

Previous studies have not shown a consistent difference in survival between patients receiving milrinone and those receiving dobutamine.\textsuperscript{7, 24, 36, 24, 37, 38} In this study, patients on milrinone had higher survival than those on dobutamine. However, given the small number of patients on dobutamine and potential differences in patient selection and characteristics that could have influenced outcomes, we are unable to make a robust claim about the independent effect of milrinone vs. dobutamine on survival. We also used lower doses of milrinone than were reported in previous studies, which may have mitigated some of the arrhythmic and ischemic risks of milrinone.

Limitations of this study include the single center nature of the study, which may reflect local practice patterns. Nevertheless, patients had objective clinical and hemodynamic evidence of advanced heart failure, with the severity of echocardiographic and hemodynamic abnormalities similar to that reported in other inotrope and LVAD studies, and were clinically inotrope dependent.\textsuperscript{10, 3, 39, 40} There was incomplete clinical and hemodynamic data, but the primary outcome information was available on all patients. Identification of eligible patients may have been incomplete due to stepwise EMR rollout during the study period and lack of access to records from two infusion companies. However, electronic record rollout and assignments of patients to infusion companies were done without regard to medical condition and would not be expected to create systematic bias. There was also no comparison group, and thus this study does not directly address whether inotropes improve or worsen survival. Such a
group would be difficult to create given current practice: many patients who present in shock or low output states acutely benefit from inotropes, have symptomatic and hemodynamic deterioration with inotrope wean, and may not survive hospital discharge without inotropes.\textsuperscript{5, 6, 41} This role of inotropes in stabilizing end-organ function is illustrated by the inclusion of inotropes in the heart transplant listing process.\textsuperscript{42} In this setting, it would be unusual to have a comparable non-inotrope group in routine clinical practice.

In summary, inotropic agents provide symptomatic benefit in advanced HF. Survival, although still suboptimal, is somewhat better than reported in prior studies. Inotropes may be used for rescue or as a short- and intermediate-term strategy to improve hemodynamics and maintain end-organ function until LVAD or transplant. Despite their risks, inotropes continue to have a role in a selected population of patients with end-stage heart failure.

**Sources of Funding**

Division of Cardiovascular Diseases, University of Alabama at Birmingham.

**Disclosures**

None.

**References**


### Table 1. Demographic and Baseline Data

<table>
<thead>
<tr>
<th>Sex</th>
<th>Female</th>
<th>51 (25.8%)</th>
<th>Male</th>
<th>146 (74.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Hospitalizations in Year Prior to Inotrope Initiation</td>
<td>0</td>
<td>17 (9.3%)</td>
<td>1</td>
<td>51 (27.9%)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>51 (27.9%)</td>
<td>2</td>
<td>45 (24.6%)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>19 (10.4%)</td>
<td>4</td>
<td>18 (9.8%)</td>
</tr>
<tr>
<td></td>
<td>Greater than 4</td>
<td>33 (18.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrophysiology Device</td>
<td>None</td>
<td>14 (7.4%)</td>
<td>Pacemaker only</td>
<td>3 (1.6%)</td>
</tr>
<tr>
<td></td>
<td>ICD</td>
<td>84 (44.2%)</td>
<td>BIV-ICD</td>
<td>82 (43.2%)</td>
</tr>
<tr>
<td></td>
<td>Lifevest</td>
<td>7 (3.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Dobutamine</td>
<td>30 (15.2%)</td>
<td>Milrinone</td>
<td>167 (84.8%)</td>
</tr>
<tr>
<td>History of Cardiac Arrest</td>
<td>No</td>
<td>182 (92.9%)</td>
<td>Yes</td>
<td>14 (7.1%)</td>
</tr>
<tr>
<td>Etiology</td>
<td>Ischemic</td>
<td>79 (40.1%)</td>
<td>Nonischemic</td>
<td>118 (59.9%)</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>No</td>
<td>133 (67.5%)</td>
<td>Yes</td>
<td>64 (32.5%)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>No</td>
<td>152 (77.2%)</td>
<td>Yes</td>
<td>45 (22.8%)</td>
</tr>
<tr>
<td>Ventricular Tachycardia</td>
<td>No</td>
<td>138 (70.1%)</td>
<td>Yes</td>
<td>59 (30.0%)</td>
</tr>
<tr>
<td></td>
<td>Death (N = 68)</td>
<td>Weaned (N = 24)</td>
<td>Remained on Inotropes (N = 50)</td>
<td>Transplant (N = 23)</td>
</tr>
<tr>
<td>--------------------------</td>
<td>---------------</td>
<td>-----------------</td>
<td>-------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Time between initiation of inotropes and initial clinic visit (days) Median (IQR)</td>
<td>26 (3, 188) [n = 52]</td>
<td>38 (3, 233) [n = 23]</td>
<td>34 (5, 214) [n = 46]</td>
<td>19 (5, 758) [n = 21]</td>
</tr>
<tr>
<td>Number of Hospitalizations on inotrope</td>
<td>1.8 (2.1)</td>
<td>1.2 (1.5)</td>
<td>1.9 (1.9)</td>
<td>0.7 (1.4)</td>
</tr>
<tr>
<td>Follow up time on inotrope</td>
<td>6.5 (7.6)</td>
<td>10.2 (9.0)</td>
<td>12.2 (11.5)</td>
<td>3.6 (4.3)</td>
</tr>
</tbody>
</table>

Values for number of hospitalization are N(SD). Values for follow up time are months (SD).
Table 3. Clinical and Laboratory Data Pre- and Post-Inotrope.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Pre-Inotrope</th>
<th>Post-Inotrope</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>158</td>
<td>105.6 (17.0)</td>
<td>108.0 (18.5)</td>
<td>0.08</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>158</td>
<td>65.5 (11.4)</td>
<td>67.5 (10.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>157</td>
<td>85.3 (15.8)</td>
<td>83.6 (16.2)</td>
<td>0.26</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>141</td>
<td>90.4 (25.3)</td>
<td>86.5 (24.4)</td>
<td>0.00</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>160</td>
<td>135.2 (4.7)</td>
<td>134.9 (11.3)</td>
<td>0.78</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>160</td>
<td>31.1 (20.2)</td>
<td>26.6 (19.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>159</td>
<td>1.6 (0.8)</td>
<td>1.5 (0.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>BNP (pg/ml)</td>
<td>96</td>
<td>1239.2 (1135.1)</td>
<td>711.4 (717.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>139</td>
<td>3.5 (0.5)</td>
<td>3.5 (0.5)</td>
<td>0.16</td>
</tr>
<tr>
<td>Left Ventricular Ejection Fraction (%)</td>
<td>131</td>
<td>18.7 (8.1)</td>
<td>21.1 (10.1)</td>
<td>0.00</td>
</tr>
<tr>
<td>RHC Right Arterial Pressure (mmHg)</td>
<td>106</td>
<td>14.8 (7.0)</td>
<td>10.5 (6.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RHC Pulmonary Capillary Wedge Pressure (mmHg)</td>
<td>107</td>
<td>25.6 (8.1)</td>
<td>21.1 (9.0)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RHC Fick Cardiac Index (L/min/m²)</td>
<td>103</td>
<td>1.7 (0.4)</td>
<td>2.2 (0.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RHC Thermal Cardiac Index (L/min/m²)</td>
<td>82</td>
<td>2.0 (0.5)</td>
<td>2.4 (0.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RHC Systemic Vascular Resistance (dynes/s/cm⁵)</td>
<td>76</td>
<td>1603.1 (536.6)</td>
<td>1295.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RHC Pulmonary Vascular Resistance (dynes/s/cm⁵)</td>
<td>88</td>
<td>350.7 (268.3)</td>
<td>244.4 (157.9)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

* Only subjects who had both pre- and post-inotrope measurements represented in this table.
** p-value from a paired t-test.
Table 4. Neurohormonal antagonist use before and during inotrope use

<table>
<thead>
<tr>
<th></th>
<th>Pre-Inotrope</th>
<th>Post-Inotrope</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta Blocker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>159 (80.7%)</td>
<td>142 (72.1%)</td>
</tr>
<tr>
<td>No</td>
<td>32 (16.2%)</td>
<td>42 (21.3%)</td>
</tr>
<tr>
<td>Missing</td>
<td>6 (3.0%)</td>
<td>13 (6.6%)</td>
</tr>
<tr>
<td>ACE Inhibitor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>103 (52.3%)</td>
<td>98 (49.7%)</td>
</tr>
<tr>
<td>No</td>
<td>85 (43.1%)</td>
<td>85 (43.1%)</td>
</tr>
<tr>
<td>Missing</td>
<td>9 (4.6%)</td>
<td>14 (7.1%)</td>
</tr>
<tr>
<td>ARB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24 (12.2%)</td>
<td>25 (12.7%)</td>
</tr>
<tr>
<td>No</td>
<td>164 (83.2%)</td>
<td>157 (79.7%)</td>
</tr>
<tr>
<td>Missing</td>
<td>9 (4.6%)</td>
<td>15 (7.6%)</td>
</tr>
<tr>
<td>Aldosterone Antagonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>105 (53.3%)</td>
<td>116 (58.9)</td>
</tr>
<tr>
<td>No</td>
<td>85 (43.1%)</td>
<td>65 (33.0%)</td>
</tr>
<tr>
<td>Missing</td>
<td>7 (3.6%)</td>
<td>16 (8.1%)</td>
</tr>
</tbody>
</table>
Table 5. Demographic and baseline data for subjects that were weaned from inotropes.

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>9 (37.5%)</td>
<td>15 (62.5%)</td>
</tr>
<tr>
<td>Number of Hospitalizations in Year Prior to Inotrope Initiation</td>
<td>(unknown)</td>
<td>5 (20.8%)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>2 (8.3%)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>7 (29.2%)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>6 (25.0%)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4 (16.7%)</td>
</tr>
<tr>
<td>Electrophysiology Device</td>
<td>None</td>
<td>2 (8.3%)</td>
</tr>
<tr>
<td></td>
<td>ICD</td>
<td>10 (41.7%)</td>
</tr>
<tr>
<td></td>
<td>BIV-ICD</td>
<td>12 (50.0%)</td>
</tr>
<tr>
<td>Drug</td>
<td>Dobutamine</td>
<td>6 (25.0%)</td>
</tr>
<tr>
<td></td>
<td>Milrinone</td>
<td>18 (75.0%)</td>
</tr>
<tr>
<td>History of Cardiac Arrest</td>
<td>No</td>
<td>22 (91.7%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>2 (8.3%)</td>
</tr>
<tr>
<td>Etiology</td>
<td>Ischemic</td>
<td>8 (33.3%)</td>
</tr>
<tr>
<td></td>
<td>Nonischemic</td>
<td>16 (66.7%)</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>No</td>
<td>15 (62.5%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>9 (37.5%)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>No</td>
<td>16 (66.7%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>8 (33.3%)</td>
</tr>
<tr>
<td>Ventricular Tachycardia</td>
<td>No</td>
<td>19 (79.2%)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>5 (20.8%)</td>
</tr>
</tbody>
</table>
Figure Legends

**Figure 1.** Kaplan-Meier Survival Curve for Patients on inotrope who were not candidates for transplant or left ventricular assist device.

**Figure 2.** Kaplan-Meier Survival curves for patients on dobutamine vs. milrinone. Log rank p-value 0.01.
Circulation: Heart Failure
Clinical Characteristics and Outcomes of Intravenous Inotropic Therapy in Advanced Heart Failure
Taimoor Hashim, Kumar Sanam, Marina Revilla-Martinez, Charity J. Morgan, Jose A. Tallaj, Salpy V. Pamboukian, Renzo Y. Loyaga-Rendon, James F. George and Deepak Acharya

_Circ Heart Fail_. published online July 15, 2015;
_Circulation: Heart Failure_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circheartfailure.ahajournals.org/content/early/2015/07/15/CIRCHEARTFAILURE.114.001778

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Heart Failure_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Heart Failure_ is online at:
http://circheartfailure.ahajournals.org/subscriptions/