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Hemodynamic Predictors of Heart Failure Morbidity and Mortality: Fluid or Flow?

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Abstract

Background—Patients with advanced heart failure may persist for prolonged times with persistent hemodynamic abnormalities; intermediate and long-term outcomes of these patients are unknown.

Methods and Results—We used ESCAPE trial data to examine characteristics and outcomes of patients with invasive hemodynamic monitoring during an acute heart failure hospitalization. Patients were stratified by *final* measurement of cardiac index (CI; L/min/m2) and pulmonary capillary wedge pressure (PCWP; mmHg) before catheter removal. The study groups were CI ≥ 2/PCWP <20 (n = 74), CI ≥ 2/PCWP ≥ 20 (n = 37), CI < 2/PCWP < 20 (n = 23), and CI < 2/PCWP ≥ 20 (n = 17). Final CI was not associated with the combined risk of death, cardiovascular hospitalization, and transplantation (HR:1.03, 95% CI:0.96–1.11 per 0.2 L/min/m^2 decrease, p=0.39), but final PCWP ≥ 20mmHg was associated with increased risk of these events (HR:2.03, 95% CI:1.31–3.15, p<0.01), as was higher final right atrial pressure (RAP; HR:1.09, 95% CI: 1.06–1.12 per mmHg increase, p<0.01).

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Conclusion—Final PCWP and final RAP were stronger predictors of post-discharge outcomes than CI in patients with advanced heart failure. The ability to lower filling pressures appears to be more prognostically important than improving CI in the management of patients with advanced heart failure.

ClinicalTrials.gov Identifier—NCT00000619

Keywords

heart failure; edema; cardiogenic shock

Introduction

In the United States, heart failure affects over 5 million people and results in over 1 million hospitalizations per year.[1] In patients age 65 and older, there are more hospitalizations for a primary diagnosis of heart failure than any other condition.[2] While many patients have evidence of poor perfusion on admission,[3] volume overload is the most common reason for hospitalization for heart failure.[4–6] Even with in-patient treatment, many patients are discharged with signs and symptoms of persistent congestion.[4] Despite optimal therapy for heart failure, morbidity and mortality following hospitalization remain high.[6, 7]

Invasive hemodynamic measurements of cardiac index (CI) and left ventricular filling pressure are commonly used to characterize the clinical phenotype of patients with advanced heart failure. Patients with heart failure may remain in a hemodynamic state consistent with cardiogenic shock and congestion for prolonged periods of time. However, data on the impact of persistent hemodynamic abnormalities are limited. The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial enrolled patients hospitalized for acute heart failure, with at least one sign and one symptoms of congestion, and collected information from invasive hemodynamic assessments. The ESCAPE data provides an ideal population from which to assess associations between hemodynamic measurements and outcomes. Therefore, we examined morbidity and mortality outcomes of patients with advanced heart failure based upon hemodynamic variables obtained during an acute heart failure hospitalization.

Methods

ESCAPE Trial

The ESCAPE trial was a multicenter randomized controlled trial evaluating the effectiveness of pulmonary artery catheter (PAC) in the management of patients hospitalized with severe symptomatic heart failure with reduced ejection fraction. The trial was conducted at 26 sites from 2000 to 2003. Patients were eligible for the study if they had three months of symptoms despite treatment with an ACE inhibitor and diuretics and had at least one sign and one symptom of congestion. Patients were required to have a left ventricular ejection fraction ≤ 30% and systolic blood pressure ≤ 125mmHg. Exclusion criteria included creatinine level ≥ 3.5mg/dL, prior use of dobutamine or dopamine ≥3μg/kg/min, or prior use of milrinone during hospitalization. Four hundred thirty-three patients from 26 centers were randomized to receive therapy guided by clinical assessment alone or clinical assessment

and data from a PAC. Of the 215 patients randomized to PAC, 141 (65.6%) had complete hemodynamic and follow-up data at 6 months, and were included in this analysis. Ten patients who were not randomized to PAC had hemodynamic data and were included in this analysis. Hemodynamic measurements from the PAC were recorded at baseline and serially at least twice daily until the catheter was removed (median 48 hours). All hemodynamic measurements were performed at rest. Follow-up occurred after hospital discharge at 1–2 weeks, then at 1, 2, 3, and 6 months. The primary endpoint was days to death, cardiac transplantation, or cardiac hospitalization in the 6 months following randomization. Results of the ESCAPE trial have been published previously.[8]

Classification and Definitions

For the present study, we included patients with complete hemodynamic data and follow up (N=151). Treatment goals in the PAC group included resolution of signs and symptoms of congestion, pulmonary capillary wedge pressure (PCWP) ≤ 15mmHg, and right atrial pressure ≤ 8mmHg. Final measurements were defined as the last recorded measurements prior to PAC removal. Patients were stratified by final measurements of CI (CI < 2, CI ≥ 2 L/min/m2) and pulmonary capillary wedge pressure (PCWP < 20, PCWP ≥ 20 mmHg). The cutoffs for CI and PCWP were chosen to reflect the severity of poor perfusion and congestion in this patient population, and have been used previously to define shock or the need for invasive hemodynamic monitoring.[9, 10]

Statistics

Demographics, physical and laboratory findings, medical history, and therapies were summarized as frequencies and percentages for categorical variables and by the medians with 25th and 75th percentiles for continuous variables. Baseline characteristics were compared using the Kruskal-Wallis test for continuous variables, and chi-square or Fisher's exact tests for categorical variables. Event rate curves for the primary endpoint in the four hemodynamic groups were shown using unadjusted Kaplan-Meier estimates and compared with log-rank tests. Relationships between baseline characteristics or hemodynamic measurements and 6-month mortality, cardiovascular hospitalization, or transplant were tested with univariable Cox proportional hazards regression models. Hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) are presented for baseline and final hemodynamic measures as well as significant baseline patient characteristics. Statistical significance was assessed using 2-sided P values. A P value <0.05 was considered statistically significant. All statistical computations were generated using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

Results

Table 1 shows the baseline characteristics of the study population. Of 151 patients, 74 (49.0%) had final CI ≥ 2/PCWP <20 (warm and dry), 37 (24.5%) had final CI ≥ 2/PCWP ≥ 20 (warm and wet), 23 (15.2%) had final CI < 2/PCWP < 20 (cold and dry), and 17 (11.3%) had final CI < 2/PCWP ≥ 20 (cold and wet). Patients with the most abnormal final hemodynamic measurements (low CI and high PCWP) were more likely to have ischemic etiology and other comorbidities including peripheral vascular disease, cerebrovascular

disease, and diabetes. They also had the shortest baseline 6 minute walk distance compared with the other groups. Those with a persistently reduced CI were older, and there was a higher percentage of female patients with persistently reduced CI than with a normal final CI. Patients with a final PCWP <20mmHg were more likely to be female, non-white, and have higher baseline blood pressure and lower baseline creatinine.

Patients with a low CI and high PCWP at the end of the study had the highest right atrial pressure, pulmonary artery pressure, and PCWP at baseline. Conversely, patients with the most favorable final hemodynamic measurements (higher CI and lower PCWP) were most likely to have a lower right atrial pressure, pulmonary artery pressure, and PCWP at baseline. (Figure 1, Table 2) Patients with an elevated final PCWP had higher baseline right atrial pressure, pulmonary artery pressure, and PCWP compared to patients with a lower final PCWP. Patients with residual low CI had a higher baseline right atrial pressure and PCWP, and lower baseline CI, regardless of final PCWP.

Supplemental Tables 1 and 2 show pairwise comparisons between those with CI < 2 and CI ≥ 2 and those with PCWP < 20 and PCWP ≥ 20 for baseline characteristics and hemodynamic measurements, and medication use, respectively. Supplemental Table 3 presents medication use in the patient groups stratified by hemodynamic profiles. The hemodynamic profile was not significantly associated with baseline medications, drugs used during the hospitalization, or discharge medications.

Supplemental Table 4 presents in-hospital complications and procedures. Few patients experienced in-hospital complications or underwent cardiac procedures. While patients with a high PCWP and normal CI were more likely to have ventricular tachyarrhythmias and receive cardiopulmonary resuscitation and cardioversion, those with a high PCWP and low CI were most likely to have ischemia or angina and receive mechanical circulatory support with intra-aortic balloon pump or left ventricular assist device.

In follow-up, 34 patients died, 60 were rehospitalized, and 9 underwent cardiac transplantation (Table 3). Variables associated with increased risk of mortality, cardiovascular hospitalization, or cardiac transplant included abnormal baseline and final right- and left-sided filling pressures, abnormal renal function, and COPD, while variables associated with decreased risk of adverse events included higher baseline sodium, higher baseline blood pressure, and ACE inhibitor use (Figure 2). Final CI was not associated with the combined risk of death, cardiovascular hospitalization, or cardiac transplantation (HR 1.03, 95% CI 0.96–1.11 per 0.2 L/min/m2 decrease, p=0.39). Conversely, final PCWP ≥ 20 mmHg was univariably associated with increased morbidity and mortality (HR 2.03, 95% CI 1.31–3.15, p<0.01), as was final right atrial pressure (HR 1.09, 95% CI 1.06–1.12 per mmHg increase, p<0.01). Figure 3 presents the unadjusted association between final hemodynamic measurements and the combined outcomes of death, cardiac hospitalization, and cardiac transplantation.

Discussion

The role of hemodynamic perturbation is central to our understanding of heart failure physiology. Reduced contractility leads to reduced stroke volume, which in turn leads to increased heart rate, increased filling pressures, and increased vasoconstriction. These compensatory mechanisms become maladaptive and ultimately lead to increased myocardial oxygen demand and worsening cardiac function.[11] In its most advanced stages, heart failure is characterized by elevated intracardiac filling pressures, peripheral vasoconstriction, and decreased cardiac output. These hemodynamic alterations indirectly form the basis of targeted pharmacotherapy. While hemodynamic abnormalities in heart failure may persist despite optimal medical treatment, data on the impact of persistent hemodynamic abnormalities on intermediate-term morbidity and mortality outcomes are limited.[5, 12, 13] We demonstrate that baseline hemodynamics tend to predict the hemodynamic profile following medical therapy. More importantly, persistently elevated right- and left-sided filling pressures in patients with heart failure during a heart failure hospitalization is predictive of the combined risk of death, cardiovascular hospitalization, and heart transplantation whereas resting CI has less prognostic utility.

In this study the combined primary endpoint was driven by rehospitalizations, which accounted for more than half of the events. Furthermore, the mortality rate for those with persistent congestion was more than double that of patients who achieved adequate congestion. Persistent congestion and symptoms may have been the basis for the rehospitalizations, given that most patients hospitalized with heart failure present with dyspnea.[7] Taken in the context of prior studies that have shown that hospitalizations are associated with increased mortality in the heart failure population and that the risk of death increases with repeated hospitalizations, these findings highlight the importance assessing for and managing congestion in patients with acute heart failure.[14–16]

Prior studies that have shown that the presence of congestion is associated with adverse outcomes, including heart failure hospitalization and death.[3, 10, 17–20] It is also recognized that a significant proportion of patients hospitalized for volume overload are inadequately decongested at the time of discharge, and persistent congestion is associated with worse outcomes.[12, 21] In addition, prior work has shown that a change in cardiac index with treatment is not predictive of poor outcomes.[10, 13] Our findings confirm these prior findings using invasive hemodynamic data. Furthermore, by categorizing patients by both PCWP and CI, we extend the prior findings by showing that congestion is associated with worse outcomes independent of CI.

While we found that resting CI is not associated with outcomes, prior work has shown that using resting CI in conjunction with exercise testing is predictive of outcomes.[22–24] In our study, it appears that congestion is the driver of adverse outcomes in this patient population; however, low CI likely contributes in that it may be more difficult to achieve adequate diuresis in patients with a low CI. Notably, patients with persistent congestion had lower blood pressure and worse renal function at baseline. Poor perfusion may lead to impaired renal function which limits the bioavailability of diuretics; furthermore, hypoperfusion

resulting from low blood pressure often reduces the tolerability of decongestion and vasodilator strategies.

The downstream effects of congestion on other organs may be another mechanism by which persistently congested patients have worse outcomes. Several studies have shown interactions between renal function and congestion. Prior work from Metra and colleagues showed persistent congestion in the setting of worsening renal function in acute heart failure was associated with worse outcomes compared to worsening renal function alone.[25] Additionally, in a prior analysis from ESCAPE, renal insufficiency at baseline and discharge were associated with increased risk of death and rehospitalization. The results could not be explained by low cardiac output; however, a correlation between right atrial pressure and renal function was noted, suggesting that elevated filling pressures may have played a role.[26]

Despite the differences, patients with low final PCWP and high final PCWP were treated similarly with regard to baseline, in-hospital, and discharge medications. Relatively few patients experienced inhospital complications or underwent cardiac procedures to treat low CI or elevated intracardiac filling pressures. This may reflect the lack of supportive treatments that result in sustained improvements in CI during the time period the ESCAPE study was conducted. While inotropes can temporarily augment cardiac output, they provide no long term positive effects on cardiac recovery or remodeling, and are associated with increased mortality.[27–29] And while temporary mechanical circulatory support (MCS) can help sustain a patient in the short-term, the benefits do not persist once the device is removed.[30, 31] Furthermore, availability of durable MCS as a long term therapy did not develop until after completion of ESCAPE.[32–35] While there is a paucity of short-term treatment strategies to improve long-term CI, it appears, based on this study, that the driver of outcomes is not in the ability to improve CI, but to improve filling pressures.

Initiation of inotropic support and referral for consideration of advanced heart failure therapies is often driven by low CI and advanced therapies may be withheld in the setting of preserved CI. However, congestion, regardless of CI, may be an additional target for agents that increase contractility or devices that directly unload the left ventricle to lower PCWP.

Clinical Implications

Results of this analysis confirm that many patients have persistent hemodynamic abnormalities despite treatment aimed at reversing these abnormalities. While persistently low CI and persistently high PCWP or high right atrial pressure are all associated with poor outcomes, it appears that persistent volume overload is a stronger predictor of worse outcomes in a heart failure population compared with CI.

Importantly, though invasive hemodynamic testing was used to determine hemodynamic profiles in this study, clinician assessments of hemodynamics based on history and physical exam findings have also been shown to predict outcomes.[3, 17, 36] Therefore, these results may be able to be extended to patients without invasive hemodynamic measurements.

In the care of patients with advanced heart failure, choosing when to abort temporary measures, such as inotropes or temporary mechanical support, for more permanent solutions, like durable LVADs or transplantation, can be a difficult decision. This study suggests that the inability to effectively achieve a more normal intravascular volume status may be a harbinger of poor outcomes; therefore persistent congestion may represent an important clinical sign that in addition to other clinical characteristics may help to inform the decision on when to move forward with advanced heart failure therapies.

Limitations

There are several limitations of this study. First, this study was a retrospective analysis. Second, only 151 patients in the ESCAPE trial had complete hemodynamic data and thorough follow-up, limiting the sample size for the study. Given the overall limited sample size, the number of patients in each group was small. Furthermore, due to the small sample size and few number of events, a multivariable analysis could not be done. Third, while most patients hospitalized for heart failure have congestion, the entry criteria for this trial required it, so patients were only included in this study if they had one sign and one symptom of congestion, potentially influencing the importance of congestion for prognosis in this cohort. Furthermore, patients with worse final hemodyanmics may have been more likely to be referred to transplant or had a lower threshould for rehospitalization given that it was known that they were sicker. Fourth, the ESCAPE trial was designed to evaluate an acute heart failure population in which there was clinical equipoise with regard to PAC use. Therefore, patients deemed “too sick” or “too well” were not included. It is possible that persistent hemodynamic derangements have different effects on outcomes for those patients not captured in the trial. Also, treatment strategies were not specified in the trial. While all centers participating in the ESCAPE trial were experienced in the management of advanced heart failure, patients may have received different treatments for similar hemodynamic profiles. Finally, treatment options for the advanced heart failure population has changed in the time period between the ESCAPE trial and this analysis, specifically with the increased use of durable MCS devices.

Conclusion

Time to death, cardiovascular hospitalization, or transplant was not influenced by CI whereas elevated right- and left-sided filling pressures were associated with this endpoint. PCWP was a stronger predictor of worse outcomes than CI in patients with advanced heart failure within six months of hospitalization. Our study suggests the ability to lower filling pressures appears to be more prognostically important than improving CI in the management of patients with advanced heart failure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

We performed an analysis using ESCAPE data of patients with invasive hemodynamic data.

We examined outcomes of HF patients with persistent hemodynamic abnormalities.

Final PCWP was associated with adverse outcomes, but final CI was not.

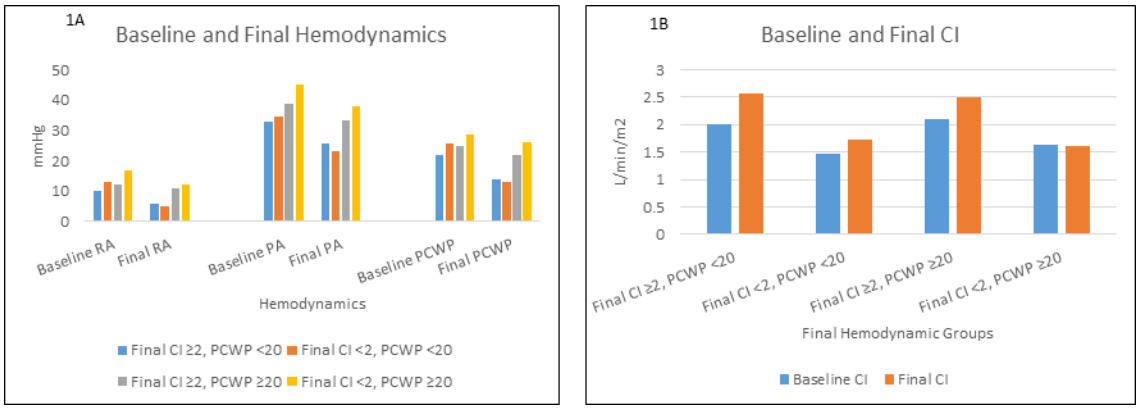

Figure 1.

Bar Graph of Baseline and Final Median Hemodynamic Pressure and Cardiac Index Measurements by Group

Panel A shows the median baseline and final hemodyamic pressure measurements for patients stratified by final hemodynamic measurements.

Panel B shows the median baseline and final cardiac index measurements for patients stratified by final hemodynamic measurements.

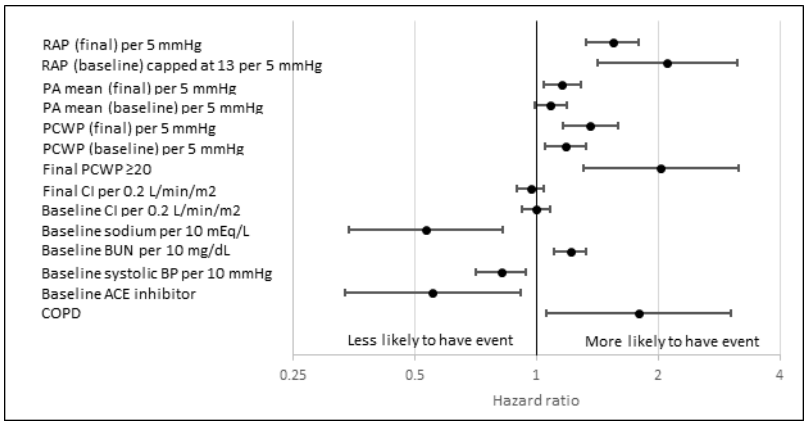

Figure 2.
Univariate Associations with Death or Cardiac Hospitalization or Cardiac Transplant

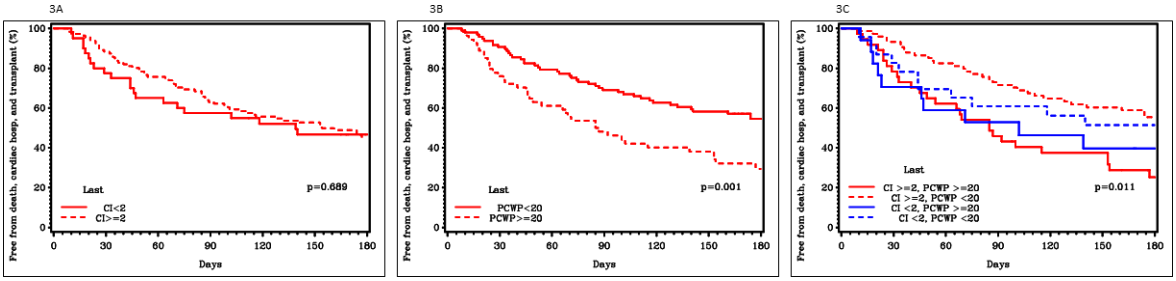

Figure 3.

Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation.

Panel A shows the Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation for patients with final CI < 2 L/min/m^2 and final CI ≥ 2 L/min/m^2.

Panel B shows the Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation for patients with final PCWP < 20 mmHg and final PCWP ≤ 20 mmHg.

Panel C shows the Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation for patients with final CI ≥ 2 L/min/m^2 and PCWP ≥ 20 mmHg, CI ≥ 2 L/min/m^2 and PCWP < 20 mmHg, CI < 2 L/min/m^2 and PCWP ≥ 20 mmHg, and CI < 2 L/min/m^2 and PCWP < 20 mmHg.

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Table 1

Baseline Characteristics of the Study Population*

	Preserved Cardiac Index (≥2 L/min/m^2)		Reduced Cardiac Index (<2 L/min/m^2)		
Variable	**PCWP < 20 (N=74)**	**PCWP ≥ 20 (N=37)**	**PCWP < 20 (N=23)**	**PCWP ≥ 20 (N=17)**	**p**
Age, years	56 (47 – 66)	54 (49 – 66)	67 (49 – 71)	60 (49 – 64)	0.45
Gender, female	23 (31.1)	5 (13.5)	12 (52.2)	5 (29.4)	0.02
Race, non white	34 (45.9)	10 (27.0)	13 (56.5)	5 (29.4)	0.07
Ischemic Etiology	35 (47.3)	20 (54.1)	12 (52.2)	13 (76.5)	0.19
Past Medical History					
Angina pectoris	28 (37.8)	10 (27.0)	3 (13.0)	8 (47.1)	0.07
Myocardial infarction	32 (43.2)	22 (59.5)	8 (34.8)	12 (70.6)	0.05
PTCI‡	16 (21.6)	11 (29.7)	5 (21.7)	8 (47.1)	0.17
CABG	19 (25.7)	14 (37.8)	5 (21.7)	5 (29.4)	0.49
Peripheral vascular disease	7 (9.5)	5 (13.5)	2 (8.7)	6 (35.3)	0.06
COPD	11 (14.9)	5 (13.5)	5 (21.7)	4 (23.5)	0.67
Diabetes	21 (29.2)	12 (33.3)	7 (30.4)	7 (41.2)	0.81
Hypertension	37 (50.0)	18 (48.6)	11 (47.8)	7 (41.2)	0.93
ICD	21 (28.4)	11 (29.7)	4 (17.4)	4 (23.5)	0.71
Atrial fibrillation	17 (23.0)	17 (45.9)	8 (34.8)	5 (29.4)	0.10
Ventricular tachycardia/fibrillation	11 (14.9)	8 (21.6)	3 (13.0)	3 (17.6)	0.79
Cerebrovascular disease	8 (10.8)	7 (18.9)	5 (21.7)	4 (23.5)	0.31
Renal insufficiency†	5 (6.8)	3 (8.1)	0 (0)	1 (6.7)	0.68
Physical Exam					
BMI, kg/m2	27.9 (23.9 – 33.5)	27.7 (24.1 – 33.4)	24.4 (21.3 – 28.4)	28.4 (24.2 – 32.1)	0.12
Baseline heart rate, bpm	81 (70 – 93.5)	79 (72 – 88)	84 (76 – 93)	74.5 (64.5 – 93)	0.37
Baseline SBP, mmHg	109 (95 – 120)	98 (94 – 108)	110 (99 – 125)	98 (90 –116)	0.05
Baseline DBP, mmHg	68 (60 – 76)	64 (57 – 70)	70 (61 – 84)	64 (58 – 70)	0.17
Baseline Testing					
Baseline EF, %	20 (15 – 25)	20 (15 – 22)	15 (15 – 20)	19 (15 – 20)	0.07
6 min walk distance, feet	249 (0 – 650)	390 (0 – 650)	360 (0 – 650)	50 (0 – 725)	0.80
Sodium, mEq/L	137 (136 – 140)	136 (134 – 139)	138 (136 – 141)	136 (131 – 138)	0.05

Variable	Preserved Cardiac Index (≥2 L/min/m^2)		Reduced Cardiac Index (<2 L/min/m^2)		p
	PCWP < 20 (N=74)	PCWP ≥ 20 (N=37)	PCWP < 20 (N=23)	PCWP ≥ 20 (N=17)	
Creatinine, mg/dL	1.4 (1 – 1.8)	1.6 (1.3 – 2)	1.3 (1 – 1.5)	1.5 (1.2 – 2)	0.12
BUN, mg/dL	27 (17 – 41)	33 (24 – 51)	25 (20 – 31)	31 (28 – 43)	0.12
ALT, units/L	25.5 (18 – 37.5)	24 (18 – 34)	34 (22 – 59)	24 (22 – 38)	0.43
AST, units/L	29 (21 – 41)	27 (22 – 34)	30 (24 – 49)	29 (25 – 31)	0.61
Albumin, g/dL	3.5 (3.3 – 3.8)	3.8 (3.30 – 4.10)	3.4 (3.1 – 3.7)	3.7 (3.5 – 3.9)	0.18
Total bilirubin, mg/dL	0.7 (0.40 – 1.10)	1.1 (0.6 – 1.4)	1.1 (0.70 – 1.40)	0.4 (0.3 – 1.1)	0.02

*Presented as N (%) or median (25th, 75th percentile).

†Past medical history of renal insufficiency defined as history of creatinine >3.5mg/dL or history of chronic dialysis. Current creatinine >3.5mg/dL was an exclusion criterion for the study.

Abbreviations: ALT: alanine aminotransferase, AST: aspartate aminotransferase, BMI: body mass index, CABG: coronary artery bypass graft, COPD: chronic obstructive pulmonary disease, DBP: diastolic blood pressure, EF: ejection fraction, ICD: implantable cardioverter defibrillator, PCI: percutaneous coronary intervention, PVD: peripheral vascular disease, SBP: systolic blood pressure

Table 2

Baseline and Final Hemodynamics of the Study Population*

	Preserved Cardiac Index (≥2 L/min/m^2)		Reduced Cardiac Index (<2 L/min/m^2)		
Variable	**PCWP < 20 (N=74)**	**PCWP ≥ 20 (N=37)**	**PCWP < 20 (N=23)**	**PCWP ≥ 20 (N=17)**	**p**
Baseline Hemodynamics					
RAP, mmHg	10 (6 – 15)	12 (8 – 20)	13 (8 – 18)	17 (12.5 – 20)	0.01
PA mean, mmHg	33 (26 – 41)	39 (33 – 46)	34.5 (32 – 44)	45 (31.5 – 49)	0.04
CI, L/min/m^2	2.0 (1.8 – 2.4)	2.1 (1.7 – 2.4)	1.5 (1.2 – 1.8)	1.6 (1.4 – 1.9)	<0.001
CO, L/min	3.9 (3.1 – 4.7)	4 (3.6 – 5.1)	2.9 (2.4 – 3.2)	3.23 (2.7 – 4.0)	<0.001
SVR, dynes x sec/cm^2	1322 (1116–1631)	1162 (921–1440)	1923 (1350–2088)	1546 (1464–2003)	<0.001
PCWP, mmHg	22 (16 – 27)	25 (21 – 36)	25.5 (20 – 30)	28.5 (24 – 33.5)	<0.001
Final Hemodynamics					
RAP, mmHg	6 (4 – 10)	11 (9 – 15)	5 (4 – 8)	12 (9 – 20)	<0.001
PA mean, mmHg	25.5 (22 – 30)	33.5 (30 – 39)	23 (20 – 32)	38 (33 – 40)	<0.001
CI, L/min/m^2	2.6 (2.2 – 2.8)	2.5 (2.3 – 2.9)	1.73 (1.5 – 1.9)	1.60 (1.5 – 1.9)	by definition
CO, L/min	4.81 (4.3 – 5.6)	5.10 (4.58 – 5.9)	3.18 (2.61 – 3.6)	3.3 (2.8 – 3.9)	<0.001
SVR, dynes x sec/cm^2	1083 (813 – 1207)	867 (568 – 1022)	1735 (1490–1903)	1446 (1213–1748)	<0.001
PCWP, mmHg	14 (10 – 17)	22 (21 – 24)	13 (11 – 15)	26 (23 – 30)	by definition

*Presented as median (25th, 75th percentile).

Abbreviations: CI: cardiac index, CO: cardiac output, PA: pulmonary artery, PCWP: pulmonary capillary wedge pressure, RAP: right atrial pressure, SVR: systemic venous resistance

Table 3

Follow-up Outcomes of Study Population

Final Hemodynamics	Death	Cardiovascular hospitalization	Heart transplant
CI ≥ 2 L/min/m^2, PCWP <20 mmHg (N=74)	10 (13.5%)	23 (31.1%)	3 (4.1%)
CI ≥ 2 L/min/m^2, PCWP ≥ 20 mmHg (N=37)	12 (32.4%)	20 (54.1%)	4 (1.1%)
CI <2 L/min/m^2, PCWP <20 mmHg (N=23)	5 (21.7%)	11 (47.8%)	1 (4.3%)
CI <2 L/min/m^2, PCWP ≥ 20 mmHg (N=17)	7 (41.2%)	6 (35.3%)	1 (5.9%)
ALL PCWP <20mmHg (N=97)	15 (15.5%)	34 (35.1%)	4 (4.1%)
ALL PCWP ≥ 20mmHg (N=54)	19 (35.2%)	26 (48.1%)	5 (9.3%)
ALL CI ≥ 2 L/min/m^2 (N=111)	22 (19.8%)	43 (38.7%)	7 (6.3%)
ALL CI <2 L/min/m^2 (N=40)	12 (30.0%)	17 (42.5%)	2 (5.0%)

Abbreviations: CI: cardiac index, PCWP: pulmonary capillary wedge pressure