Clinical Investigation

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

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ABSTRACT

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

Methods and Results: We used ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) 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/m^2) 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 (hazard ratio [HR]1.03, 95% confidence interval 0.96–1.11 per 0.2 L/min/m^2 decrease, *P* = .39), but final PCWP ≥ 20 mmHg was associated with increased risk of these events (HR 2.03, 95% confidence interval 1.31–3.15, *P* < .01), as was higher final right atrial pressure (HR 1.09, 95% confidence interval 1.06–1.12 per mmHg increase, *P* < .01).

Conclusion: Final PCWP and final right atrial pressure were stronger predictors of postdischarge 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 (*J Cardiac Fail 2016;22:182–189*)

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In the United States, heart failure affects more than 5 million people and results in more than 1 million hospitalizations per year.[1] In patients age 65 years and older, there are more hos-

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pitalizations for a primary diagnosis of heart failure than any other condition.[2] Although 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 inpatient 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. 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 1 sign and 1 symptom of congestion, and collected information from invasive hemodynamic assessments. The

ESCAPE data provide 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 3 months of symptoms despite treatment with an angiotensin-converting enzyme inhibitor and diuretics and had at least 1 sign and 1 symptom of congestion. Patients were required to have a left ventricular ejection fraction ≤30% and systolic blood pressure ≤125 mmHg. Exclusion criteria included creatinine level ≥3.5 mg/dL, prior use of dobutamine or dopamine ≥3 µg/kg/min, or prior use of milrinone during hospitalization. A total of 433 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) ≤15 mmHg, and right atrial pressure ≤8 mmHg. 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/m^2) 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 4 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 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 < .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 < 20 mmHg 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 (Fig. 1, Table 2). Patients with an elevated final PCWP had higher baseline right atrial pressure, pulmonary artery pressure, and PCWP compared with 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 S1 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

Table 1. Baseline Characteristics of the Study Population*

	Preserved Cardiac Index (≥2 L/min/m²)		Reduced Cardiac Index (<2 L/min/m²)		
Variable	PCWP < 20 (n = 74)	PCWP ≥ 20 (n = 37)	PCWP < 20 (n = 23)	PCWP ≥20 (n = 17)	P
Age, y	56 (47–66)	54 (49–66)	67 (49–71)	60 (49–64)	.45
Gender, female	23 (31.1)	5 (13.5)	12 (52.2)	5 (29.4)	.02
Race, non-white	34 (45.9)	10 (27.0)	13 (56.5)	5 (29.4)	.07
Ischemic etiology	35 (47.3)	20 (54.1)	12 (52.2)	13 (76.5)	.19
Medical history					
Angina pectoris	28 (37.8)	10 (27.0)	3 (13.0)	8 (47.1)	.07
Myocardial infarction	32 (43.2)	22 (59.5)	8 (34.8)	12 (70.6)	.05
PCI	16 (21.6)	11 (29.7)	5 (21.7)	8 (47.1)	.17
CABG	19 (25.7)	14 (37.8)	5 (21.7)	5 (29.4)	.49
Peripheral vascular disease	7 (9.5)	5 (13.5)	2 (8.7)	6 (35.3)	.06
COPD	11 (14.9)	5 (13.5)	5 (21.7)	4 (23.5)	.67
Diabetes	21 (29.2)	12 (33.3)	7 (30.4)	7 (41.2)	.81
Hypertension	37 (50.0)	18 (48.6)	11 (47.8)	7 (41.2)	.93
ICD	21 (28.4)	11 (29.7)	4 (17.4)	4 (23.5)	.71
Atrial fibrillation	17 (23.0)	17 (45.9)	8 (34.8)	5 (29.4)	.10
Ventricular tachycardia/fibrillation	11 (14.9)	8 (21.6)	3 (13.0)	3 (17.6)	.79
Cerebrovascular disease	8 (10.8)	7 (18.9)	5 (21.7)	4 (23.5)	.31
Renal insufficiency†	5 (6.8)	3 (8.1)	0 (0)	1 (6.7)	.68
Physical examination					
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)	.12
Baseline heart rate, bpm	81 (70–93.5)	79 (72–88)	84 (76–93)	74.5 (64.5–93)	.37
Baseline SBP, mmHg	109 (95–120)	98 (94–108)	110 (99–125)	98 (90–116)	.05
Baseline DBP, mmHg	68 (60–76)	64 (57–70)	70 (61–84)	64 (58–70)	.17
Baseline testing					
Baseline EF, %	20 (15–25)	20 (15–22)	15 (15–20)	19 (15–20)	.07
6-min walk distance, feet	249 (0–650)	390 (0–650)	360 (0–650)	50 (0–725)	.80
Sodium, mEq/L	137 (136–140)	136 (134–139)	138 (136–141)	136 (131–138)	.05
Creatinine, mg/dL	1.4 (1–1.8)	1.6 (1.3–2)	1.3 (1–1.5)	1.5 (1.2–2)	.12
BUN, mg/dL	27 (17–41)	33 (24–51)	25 (20–31)	31 (28–43)	.12
ALT, units/L	25.5 (18–37.5)	24 (18–34)	34 (22–59)	24 (22–38)	.43
AST, units/L	29 (21–41)	27 (22–34)	30 (24–49)	29 (25–31)	.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)	.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)	.02

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

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

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 intervention; PVD, peripheral vascular disease; SBP, systolic blood pressure.
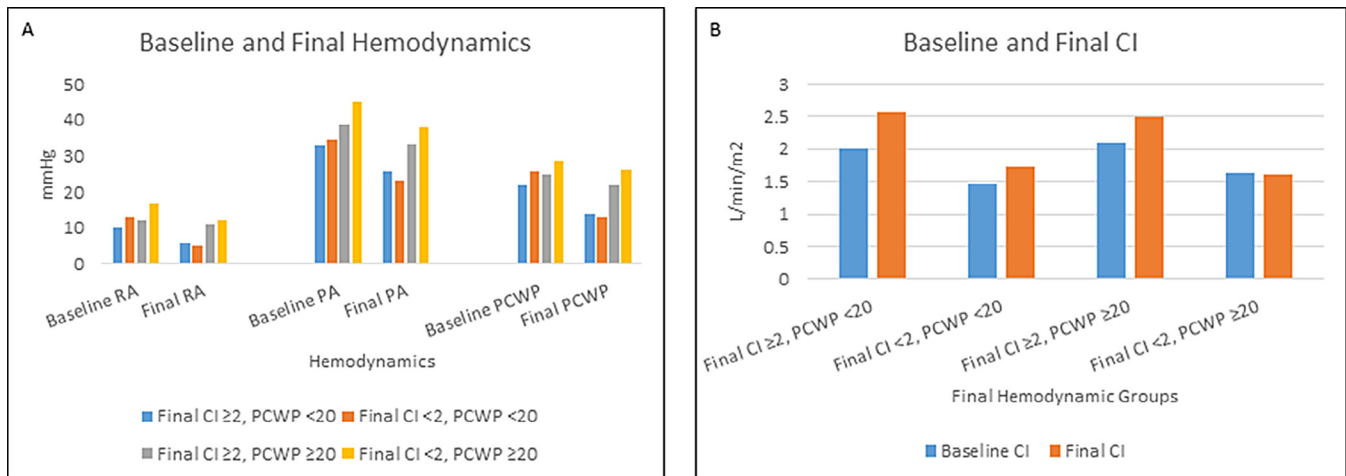

Fig. 1. Bar graph of baseline and final median hemodynamic pressure and cardiac index (CI) measurements by group. (A) The median baseline and final hemodynamic pressure measurements for patients stratified by final hemodynamic measurements. (B) The median baseline and final CI measurements for patients stratified by final hemodynamic measurements. PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure; RA, right artery.

Table 2. Baseline and Final Hemodynamics of the Study Population*

Variable	Preserved CI (≥2 L/min/m²)		Reduced CI (<2 L/min/m²)		P
	PCWP < 20 (n = 74)	PCWP ≥ 20 (n = 37)	PCWP < 20 (n = 23)	PCWP ≥ 20 (n = 17)	
Baseline hemodynamics					
RAP, mmHg	10 (6–15)	12 (8–20)	13 (8–18)	17 (12.5–20)	.01
PA mean, mmHg	33 (26–41)	39 (33–46)	34.5 (32–44)	45 (31.5–49)	.04
CI, L/min/m²	2.0 (1.8–2.4)	2.1 (1.7–2.4)	1.5 (1.2–1.8)	1.6 (1.4–1.9)	<.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)	<.001
SVR, dynes × sec/cm²	1322 (1116–1631)	1162 (921–1440)	1923 (1350–2088)	1546 (1464–2003)	<.001
PCWP, mmHg	22 (16–27)	25 (21–36)	25.5 (20–30)	28.5 (24–33.5)	<.001
Final hemodynamics					
RAP, mmHg	6 (4–10)	11 (9–15)	5 (4–8)	12 (9–20)	<.001
PA mean, mmHg	25.5 (22–30)	33.5 (30–39)	23 (20–32)	38 (33–40)	<.001
CI, L/min/m²	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)	<.001
SVR, dynes × sec/cm²	1083 (813–1207)	867 (568–1022)	1735 (1490–1903)	1446 (1213–1748)	<.001
PCWP, mmHg	14 (10–17)	22 (21–24)	13 (11–15)	26 (23–30)	By definition

*Presented as median (25th, 75th percentile).
CI: cardiac index, CO: cardiac output, PA: pulmonary artery, PCWP: pulmonary capillary wedge pressure, RAP: right atrial pressure, SVR: systemic venous resistance.

hemodynamic measurements, and medication use, respectively. Supplemental Table S3 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 S4 presents in-hospital complications and procedures. Few patients experienced in-hospital complications or underwent cardiac procedures. Although 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 (MCS) with intraaortic 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 chronic obstructive pulmonary disease, whereas variables associated with decreased risk of adverse events included higher baseline sodium, higher baseline blood pressure, and angiotensin-converting enzyme inhibitor

use (Fig. 2). Final CI was not associated with the combined risk of death, cardiovascular hospitalization, or cardiac transplantation (HR 1.03, 95% confidence interval 0.96–1.11 per 0.2 L/min/m² decrease, $P = .39$). Conversely, final PCWP ≥ 20 mmHg was univariably associated with increased morbidity and mortality (HR 2.03, 95% confidence interval 1.31–3.15, $P < .01$), as was final right atrial pressure (HR 1.09, 95% confidence interval 1.06–1.12 per mmHg increase, $P < .01$). 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

Table 3. Follow-up Outcomes of Study Population

Final Hemodynamics	Death	Cardiovascular Hospitalization	Heart Transplant
CI ≥ 2 L/min/m², PCWP < 20 mmHg (n = 74)	10 (13.5%)	23 (31.1%)	3 (4.1%)
CI ≥ 2 L/min/m², PCWP ≥ 20 mmHg (n = 37)	12 (32.4%)	20 (54.1%)	4 (1.1%)
CI < 2 L/min/m², PCWP < 20 mmHg (n = 23)	5 (21.7%)	11 (47.8%)	1 (4.3%)
CI < 2 L/min/m², PCWP ≥ 20 mmHg (n = 17)	7 (41.2%)	6 (35.3%)	1 (5.9%)
All PCWP < 20 mmHg (N = 97)	15 (15.5%)	34 (35.1%)	4 (4.1%)
All PCWP ≥ 20 mmHg (N = 54)	19 (35.2%)	26 (48.1%)	5 (9.3%)
All CI ≥ 2 L/min/m² (N = 111)	22 (19.8%)	43 (38.7%)	7 (6.3%)
All CI < 2 L/min/m² (N = 40)	12 (30.0%)	17 (42.5%)	2 (5.0%)

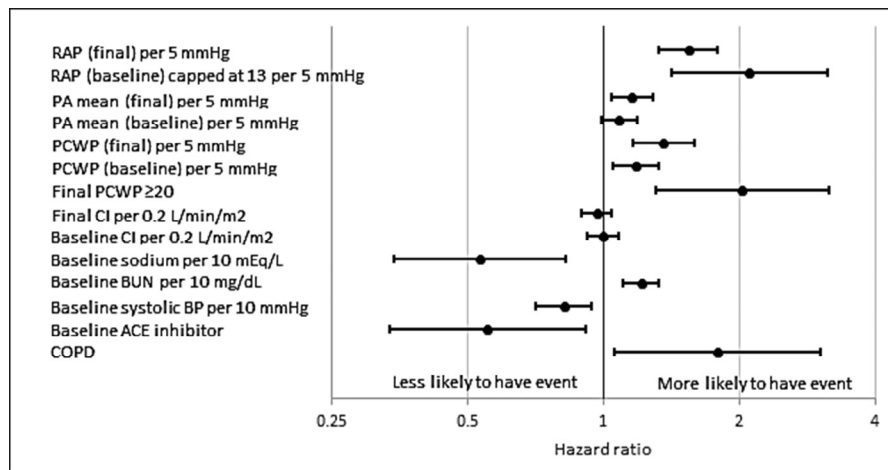CI: cardiac index, PCWP: pulmonary capillary wedge pressure.

Fig. 2. Univariate associations with death or cardiac hospitalization or cardiac transplant. ACE, angiotensin-converting enzyme; BP, blood pressure; BUN, blood urea nitrogen; CI, cardiac index; COPD, chronic obstructive pulmonary disease; PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure.

decreased cardiac output. These hemodynamic alterations indirectly form the basis of targeted pharmacotherapy. Although 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 CI 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.

Although 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]
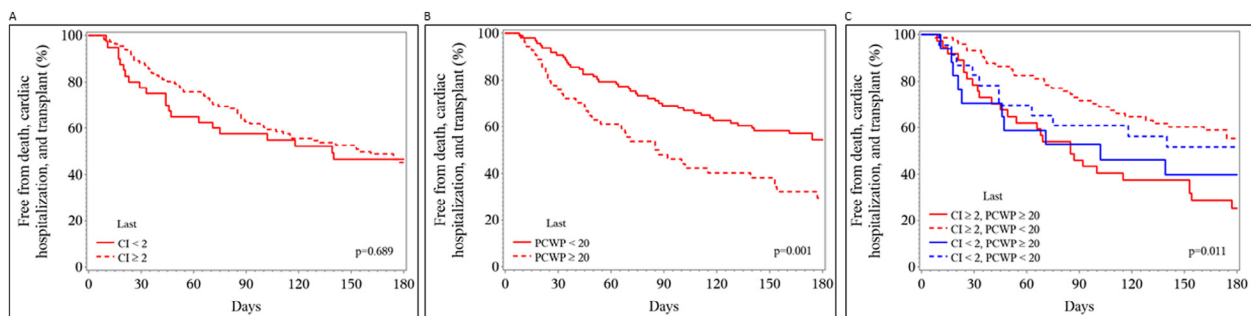

Fig. 3. Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation. (A) The Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation for patients with final cardiac index (CI) < 2 L/min/m² and final CI ≥ 2 L/min/m². (B) The Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation for patients with final pulmonary capillary wedge pressure (PCWP) < 20 mmHg and final PCWP ≤ 20 mmHg. (C) The Kaplan-Meier estimates of freedom from death, cardiac hospitalization, and cardiac transplantation for patients with final CI ≥ 2 L/min/m² and PCWP ≥ 20 mmHg, CI ≥ 2 L/min/m² and PCWP < 20 mmHg, CI < 2 L/min/m² and PCWP ≥ 20 mmHg, and CI < 2 L/min/m² and PCWP < 20 mmHg.

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 with 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 in-hospital 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 period the ESCAPE study was conducted. Although 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 although temporary 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] Although 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. Although 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 examination 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, such as 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, because of the small sample size and few number of events, a multivariable analysis could not be done. Third, although 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 1 sign and 1 symptom of congestion, potentially influencing the importance of congestion for prognosis in this cohort. Furthermore, patients with worse final hemodynamics may have been more likely to be referred to transplant or had a lower threshold 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. Although 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 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 6 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.

Disclosure

None.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Supplementary Data

Supplementary data to this article can be found online at doi:10.1016/j.cardfail.2015.11.012.

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