Characteristics of Patients with Improvement or Worsening in Renal Function during the Treatment of Acute Decompensated Heart Failure

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Abstract

Worsening renal function (RF) and improved RF during the treatment of decompensated heart failure have traditionally been thought of as hemodynamically distinct events. We hypothesized that if pulmonary artery catheter derived measures are relevant in the evaluation of cardiorenal interactions comparison of patients with improved vs. worsening RF should highlight any important hemodynamic differences. All subjects in the ESCAPE trial limited data set with admission and discharge creatinine values available were included (401 patients). There were no differences in baseline, final, or change in pulmonary artery catheter derived hemodynamic variables, inotrope and intravenous vasodilator use, or survival between patients with improved and worsening RF (p=NS for all). Both groups were equally likely to be in the bottom quartile of cardiac index (CI) (p=0.32), have a 25% improvement in CI (p=0.97), or have any worsening in CI (p=0.90). When patients with any significant change in renal function (positive or negative) were compared to patients with stable renal function, strong associations between variables such as reduced CI (OR=2.2, p=0.02), increased intravenous inotrope and vasodilator use (OR=2.9, p<0.001), and worsened all cause mortality (HR=1.8, p=0.01) became apparent. Contrary to traditionally held views, patients with improved RF and worsening RF have similar hemodynamic parameters and outcomes. Combining these groups identifies a hemodynamically compromised population with significantly worse survival than patients with stable renal function. In Conclusion, changes in renal function, regardless of direction, likely identify a population with an advanced disease state and poor prognosis.

Keywords

Cardio-renal syndrome; worsening renal function; improved renal function; acute heart failure; kidney

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Worsening renal function (RF) complicates approximately one third of acute decompensated heart failure admissions and has been associated with increased length of stay, readmission rate, and decreased short and long term survival (1-4). Traditional teaching has held that the hemodynamic profile associated with worsening RF is that of decreased cardiac output and intravascular volume depletion, concepts which have not born out in recent publications (5-7). Likely arising from similar logic, improved renal function RF has been suggested to result from a treatment induced increase in "forward flow" to the kidney. Since the current literature regarding the profile of patients developing worsening RF has been largely inconsistent with previously proposed mechanisms, we hypothesized that this may also be true of improved RF. Our first aim was to directly compare patients with improved RF to those with worsening RF. Since the hemodynamic changes offered to explain worsening RF and improved RF are largely discordant we felt this would optimize the probability of documenting any important hemodynamic differences. Additionally, a requisite for improvement in renal function during the treatment of decompensated heart failure is reversible renal dysfunction at baseline. Unless this renal dysfunction was present at birth, by definition this indicates that worsening RF had occurred prior to admission. Resultantly, we hypothesized that the outcomes of patients with improved RF and worsening RF may be similar and our second aim was to investigate if any change in renal function, either improved or worsened, may be the prognostically more relevant variable to investigate.

Methods

The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) Trial was a National Heart, Lung and Blood Institute (NHLBI) sponsored, randomized, multicenter trial of therapy guided by pulmonary artery catheter (PAC) vs. clinical assessment in hospitalized patients with acute decompensated heart failure. Methods and results have been previously published (8,9). Briefly, 433 patients were enrolled at 26 sites from January 2000 to November 2003. Inclusion criteria included an ejection fraction of 30% or less, systolic blood pressure of 125 mmHg or less, treatment in the preceding month with >160 mg of furosemide (or equivalent), and at least 1 sign and 1 symptom of congestion(6). Exclusion criteria included an admission creatinine level ≥ 3.5 mg/dL, use of dopamine or dobutamine ≥3 ug/kg/min, or any use of milrinone before randomization. Patients were randomized to therapy guided by clinical assessment alone vs. PAC and clinical assessment. Treatment goals were resolution of the signs and symptoms of congestion. In patients randomized to the PAC arm, additional goals of treatment were a pulmonary capillary wedge pressure ≤15 mmHg and a right atrial pressure ≤8 mmHg. Routine use of inotropes was "explicitly" discouraged but diuretics and vasodilating agents were recommended. The ESCAPE trial was conducted and supported by the NHLBI in collaboration with the ESCAPE study investigators. This manuscript was prepared using a limited access dataset obtained from the NHLBI and does not necessarily reflect the opinions or views of the ESCAPE investigators or the NHLBI.

A relative change in GFR was used rather than an absolute change in serum creatinine to account for the non-linear relationship between creatinine and renal function (10). A significant change in renal function, regardless of direction, was defined as a ≥20% change in GFR and patients meeting this criteria were categorized as having Dynamic RF. Patients not meeting this criteria were classified as Stable RF. GFR was estimated using the four variable Modification of Diet in Renal Disease study equation (11). The in-hospital loop diuretic dose represents the maximum total IV loop diuretic dose received in any one day of the study period.

Values reported are mean ± standard deviation for continuous variables and percentile for categorical variables, unless otherwise noted. Independent Student's t-test or the Mann-

Whitney U test was used to compare means of independent continuous variables. Pearson's Chi Square was used to evaluate categorical variables. Trend analysis of ordinal variables was done using linear-by-linear association. Wilcoxon Signed Rank tests were used for comparison of GFR over time within worsening RF or improved RF groups. In order to highlight the similarity or dissimilarity between patients with improved RF and worsening RF, these groups were compared directly for the primary analysis. Contingent upon satisfying our hypothesis that the groups would be similar hemodynamically, the improved RF and worsening RF groups were combined and compared to patients with no change in renal function. Cox proportional hazard modeling was used to evaluate the univariate hazard ratio of predictors of mortality and rehospitalization. Patients alive or not rehospitalized at 180 days, respectively, were censored. Cox proportional modeling was used to test the independence of renal variables in their association with mortality. Candidate variables for multivariate Cox proportional modeling were obtained via entry of all univariate baseline predictors of mortality with a p<0.2 and ≤5% missing values. Using backwards elimination, starting with the variable with the largest p-value, variables altering the hazard ratio (HR) by more than 10% were retained in the final model. Statistical analysis was performed with SPSS version 17.0 (SPSS Inc, Chicago, Illinois) and significance defined as 2-tailed p<0.05.

Results

Of the 433 patients enrolled in the ESCAPE trial, 401 had admission and discharge serum creatinine values available and these subjects were included in subsequent analysis. Baseline characteristics of the trial population have been previously reported (9). Additionally, Nohria et al. have described the lack of association between PAC derived hemodynamic variables and the development of worsening RF in this population (6). Overall, worsening RF occurred in 21.2% (n=85) and improved RF occurred in 16.2% (n=65) of the population.

Overall, baseline demographics, comorbidities, symptom severity, physical exam, and medication use were similar between patients with improved RF and worsening RF. Notable exceptions were a greater admission systolic blood pressure, an increased prevalence of hypertension, and a higher incidence of suspected ascites in patients with worsening RF (Table 1).

There were no PAC derived variables that demonstrated any significant discriminative ability between improved RF and worsening RF (Table 2). Contrary to the postulated association between cardiac index and changes in renal function; baseline, final, and admission to final change in cardiac index was no different in patients with improved RF or worsening RF (Table 2). Both groups were equally likely to be in the bottom quartile of cardiac index (p=0.32), have a 25% improvement in cardiac index (p=0.97), or have any worsening in cardiac index during hospitalization (p=0.90). Similarly, baseline, final, and change in right atrial pressure and pulmonary capillary wedge pressure did not differentiate patients with improved RF or worsening RF (Table 2).

Overall, treatment characteristics of patients with improved RF and worsening RF were similar. There were no differences in baseline or in hospital medications with the exception of a higher utilization of thiazide diuretics in the group with worsening RF (Table 1). Notably, loop diuretic dosage, intravenous vasodilator use, and inotrope use were similar between both groups (Table 1).

As might be expected by the nature of the dichotomy, renal variables differed substantially between groups. Mean admission glomerular filtration rate (GFR) was significantly lower in the group developing improved RF (39.9 ± 17.2 mL/min vs. 69.5 ± 29.5 mL/min, p<0.001). However, by the time of discharge, GFR was higher in the improved RF group compared to

the worsening RF group (57.1 ± 22.2 mL/min vs. 45.7 ± 22.4 mL/min, p=0.002). In patients with 6 month creatinine values available, the group with improved RF had a significant decrease in GFR from discharge to 6 months (59.2 ± 24.6 mL/min vs. 47.5 ± 20.9 mL/min, p<0.001), but GFR remained significantly higher than the admission value (40.8 ± 18.8 mL/min vs. 47.5 ± 20.9 mL/min, p<0.001). From discharge to 6 months, GFR in the worsening RF group improved somewhat (47.7 ± 22.7 mL/min vs. 60.2 ± 29.6 mL/min, p<0.001), but did not recover fully to baseline levels (73.0 ± 29.6 mL/min vs. 60.2 ± 29.6 mL/min, p<0.001).

Patients with improved RF had significantly higher admission norepinephrine levels (Table 1) and were much more likely to have values in the highest quartile at admission compared to patients with worsening RF (OR=6.3, p<0.001). Serum sodium was also lower in the group with improved RF (Table 1). The differences in sodium (p=0.99) and norepinephrine (p=0.38) were no longer significantly different at discharge.

Overall, short and long term outcomes of these groups were also similar with no differences in length of stay (p=0.87) or rehospitalization (p=0.47) between patients with improved RF and worsening RF. Additionally, mortality was similar in the group developing improved RF compared to those with worsening RF (HR=1.1, p=0.85). One notable difference was a significantly greater weight loss (5.4 ± 5.2 kg vs. 2.7 ± 5.0 kg, p=0.002) and higher rate of weight loss (0.75 ± 0.78 kg/day vs. 0.34 ± 0.68 kg/day, p=0.002) in the worsening RF compared to the improved RF group.

Patients with worsening RF had no significant differences in baseline, final, or change in hemodynamic parameters when compared to patients without worsening RF (p=NS for all, data not shown). The group with improved RF shared the same lack of associations when compared to patients without improved RF (p=NS for all, data not shown). As such, analysis of patients with a 20% change in GFR (Dynamic RF), regardless of improvement or deterioration, was undertaken to explore the hypothesis that susceptibility to changes in renal function rather than the actual direction of change may be a more relevant clinical variable.

Compared to patients with stable renal function (Stable RF), patients with Dynamic RF had a significantly lower baseline ejection fraction and cardiac index (Tables 1,2). Additionally, they were more likely to be in the bottom quartile of cardiac index (OR=2.2, p=0.021) or have a 25% improvement in cardiac index from admission to PAC removal (OR=3.3, p=0.001). Other hemodynamic variables were similar (Table 2). Notable differences in treatment characteristics were a significantly greater use of intravenous vasodilators and inotropes in patients with Dynamic RF (Table 1). Moreover, the dose of loop diuretics was greater and adjunctive thiazide diuretics were more commonly used (Table 1). Length of stay was significantly longer in the group with Dynamic RF (9.8 vs. 8.0 days, p<0.001).

The univariate associations between improved RF and mortality (HR=0.16, p=0.11) and between worsening RF and mortality (HR=1.5, p=0.14) were not statistically significant. However, comparison of patients with improved RF or worsening RF to the group with Stable RF demonstrated significant associations with mortality (improved RF HR=1.9, p=0.032; worsening RF HR=1.7, p=0.043). Similarly, the group with Dynamic RF had a substantially increased mortality rate compared to patients with Stable RF (HR=1.8, p=0.01) (Figure 1).

As previously reported by Nohria et al, both admission and discharge GFR were strong univariate predictors of mortality (6). Despite the relatively strong correlation between admission and discharge GFR (r=0.80, p<0.001), they had discordant effects on the prognostic ability of worsening RF and improved RF. Using Stable RF as the comparison

group, controlling for admission GFR caused improved RF to lose its significant association with mortality (HR=1.3, p=0.37) but the relationship between worsening RF and mortality was strengthened (HR=2.2, p=0.004). Similarly, after adjusting for discharge GFR, worsening RF was no longer significantly associated with mortality (HR=1.4, p=0.26), whereas the relationship between improved RF and mortality was unaffected (HR=1.9, p=0.033). Much of this effect is likely explained by the highly significant, but discordant, relationships between improved RF/worsening RF and GFR at admission versus discharge (Table 3). Addition of admission and/or discharge GFR to a model containing Dynamic RF did not eliminate the association between Dynamic RF and mortality (Table 4). After multivariate Cox regression using backwards elimination adjusting for baseline variables (ischemic etiology, history of coronary artery bypass grafting or myocardial infarction, jugular venous distention, ascites, edema, angiotensin converting enzyme inhibitor or receptor blocker use, beta blocker use, loop diuretic dose, thiazide diuretic use, systolic blood pressure, serum sodium, and admission GFR), Dynamic RF remained a significant predictor of mortality (p=0.01).

There appeared to be a dose response effect with regards to the association with mortality since escalating thresholds used to define Dynamic RF (p=0.013 for trend) or define improved RF (p=0.028 for trend) were associated with progressively greater odds for death at 180 days (Figure 2). This association did not meet statistical significance for worsening RF (p= 0.071).

Discussion

The primary finding of this study is the absence of substantial differences in standard PAC derived hemodynamic parameters between patients developing improved RF versus worsening RF. Despite the traditional assumptions that cardiac output driven increases or decreases in renal perfusion explain differing changes in renal function, PAC derived hemodynamic parameters, traditional baseline characteristics, treatment with inotropes or vasodilators, and outcomes were largely similar between these groups. In fact, patients with improved RF and worsening RF were hemodynamically more closely related to each other than to patients with Stable RF. After combining patients with worsening RF and improved RF into a single "cardio-renal" group, significant associations with variables such as reduced cardiac index, utilization of inotropes, and decreased survival became apparent.

The overall lack of substantial hemodynamic differences between the worsening RF and improved RF groups is not surprising given that recent publications have failed to validate the predicted relationship between PAC derived variables and worsening RF (5-7). It is however somewhat surprising that a poor prognostic indicator such as worsening RF has not co-segregated with hemodynamic markers of disease severity, such as a low cardiac index, even if the hemodynamic perturbations had no causal relationship. These observations can be interpreted to indicate the presence of a truly minimal, or paradoxical, association between worsening RF and parameters such as cardiac index. Alternatively, worsening RF may only be capturing a portion of the "cardio-renal" population and those patients left in the comparison group are obscuring any differences due to shared hemodynamic derangements with worsening RF patients. We believe the later hypothesis is supported by the above data.

It is however of interest that the worsening RF group had a significantly greater rate and quantity of weight loss compared to the improved RF group despite no difference in baseline, PAC removal, or baseline to PAC removal change in cardiac filling pressures. Given the well described disconnect between filling pressures and volume status, it is possible that relative intravascular volume depletion secondary to aggressive diuresis

contributed to the deterioration in renal function in the worsening RF group (12-18). Additional non-PAC derived measures of intravascular volume merit further study for potential guidance of diuresis in these patients.

In this cohort, patients with any significant change in renal function (Dynamic RF) had a lower cardiac index, lower ejection fraction, were more apt to be treated with inotropes and intravenous vasodilators, received higher loop diuretic doses and more frequent adjunctive thiazide diuretics than patients with Stable RF. Any of the above cited associations could be employed in speculation on mechanisms related to improved RF or worsening RF and their associated mortality. It is equally likely, however, that the majority of the above factors are all simply describing a "sicker" patient population. Despite the mechanistic uncertainty underlying these changes in renal function, it seems clear that there is prognostic relevance in the changes. In this series, prognostic information was best captured by focusing on the dynamic, as opposed to the directional aspect, of changes in renal function. This was highlighted by the fact that both improved RF and worsening RF were not significantly associated with mortality when patients with changes in renal function of the opposite direction were left in the comparator group. However, comparison of patients with improved RF or worsening RF to patients with Stable RF revealed strong associations with mortality. From a prognostic standpoint, separation of patients into worsening versus improving renal function may be an artificial delineation.

Many published reports support the prognostic importance of chronic renal insufficiency; however, this analysis raises some question as to what actually constitutes chronic renal insufficiency in a heart failure population (19-25). Central to the theme of chronic kidney disease is the concept of loss of nephron mass since the majority of diseases associated with chronic kidney disease cause irreversible loss of functional nephrons (26). In this study, patients with improved RF had on average a 48% improvement in GFR from admission to discharge, but at 6 months GFR had once again decreased and was not significantly different from admission levels. Since a transient regeneration of nephrons is unlikely, a significant percentage of the renal impairment at admission, and quite possibly at 6 months, may be secondary to reversible decreases in renal function rather than irreversible parenchymal disease. Assuming the association between Dynamic RF and mortality stems from the advanced heart failure disease state severe enough to facilitate worsening in renal function at some time, these observations raise the question if a significant portion of the predictive ability of chronic renal insufficiency stems from its relationship to outpatient worsening RF, rather than intrinsic parenchymal disease. Given the interdependence between changes in renal function, admission, and discharge GFR, determination of the relative importance of parenchymal disease verses functional renal impairment is impossible from this data.

The most direct clinical implication of this study is the incremental prognostic information that Dynamic RF adds to established risk stratification tools. Additionally, this study further supports the concept that pulmonary artery catheters provide limited information related to renal function given that patients with improved RF and worsening RF serially had similar PAC derived variables. Reversible renal dysfunction appears to be common and further research is necessary to develop methods to prospectively identify it. If such tools become available they could help inform practical decisions such as cardiac transplantation listing status, cardiac versus combined cardiac renal transplantation, left ventricular assist device implantation, and hemodialysis initiation. Additionally, identification of outpatients with renal insufficiency that has the potential for improvement may represent a tremendous therapeutic target.

The ESCAPE trial was not designed to evaluate improved RF or worsening RF and given that the treating physicians were not blinded to either renal or PAC data, it is likely that

treatment strategies were significantly modified in response to those variables. Patients with advanced renal insufficiency were excluded limiting generalization to this group of patients. The presence of multicollinearity between improved RF, worsening RF, and admission and discharge GFR limits the ability to determine the relative contribution of each covariate. Consequently, these analyses should be interpreted as hypothesis generating and further research is required to determine the true importance of various causes of reduced renal function in heart failure populations. By nature of the trial design, PAC data is only available on slightly more than half the patients, limiting power. Additionally, given the small number of patients with improved RF and worsening RF, comparison of these groups may have missed smaller hemodynamic differences. While many of the associations in this study had very highly significant p-values and are unlikely to have arisen by chance, some of the more modestly significant associations may have arisen as a result of multiple comparisons and should be interpreted with caution.

Acknowledgments

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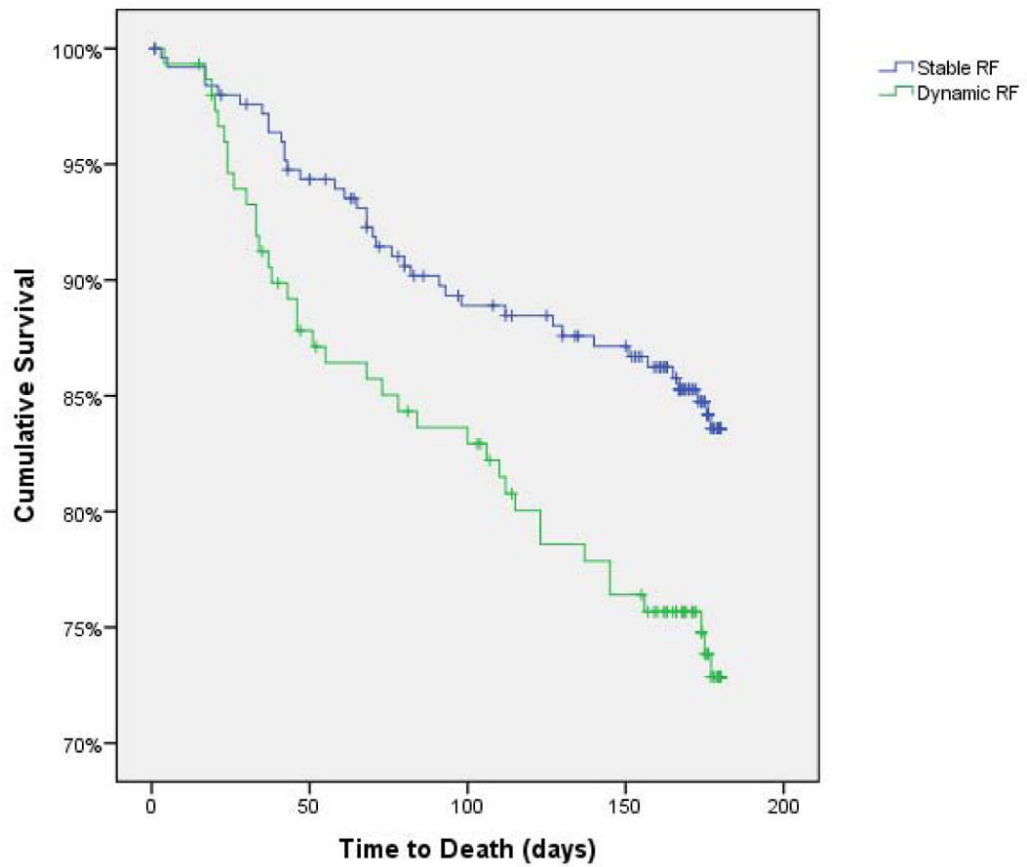
Figure 1.
Kaplan-Meier survival curves grouped by Stable RF versus Dynamic RF. Dynamic RF: ≥20% increase or decrease in glomerular filtration rate from admission to discharge, Stable RF: ≤20% change in renal function from admission to discharge.

Figure 2.
Odds ratio for 6 month mortality at increasing percentage change in GFR cut points.
Dynamic RF: Increase or decrease in glomerular filtration rate from admission to discharge,
GFR: Glomerular filtration rate, RF: Renal function. Dynamic RF p=0.013 for trend,
improved RF p=0.028 for trend.

Table1

Baseline characteristics

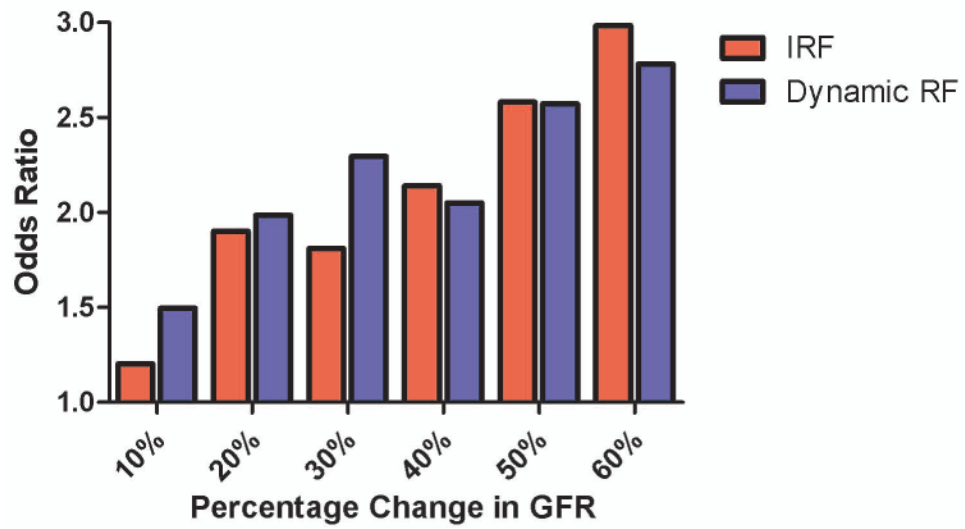| Characteristics	Worsening RF (n=85)	Improved RF (n=65)	p	Stable RF (n=251)	Dynamic RF (n=150)	p
Age (years)	55 ± 13	58 ± 15	0.109	56 ± 14	56 ± 14	0.946
Males	73%	85%	0.087	72%	78%	0.192
White race	51%	60%	0.251	63%	55%	0.12
Ischemic etiology of heart failure	55%	47%	0.342	47%	51%	0.447
Hypertension	50%	31%	0.022[*]	50%	42%	0.108
Diabetes mellitus	39%	25%	0.067	32%	33%	0.799
Myocardial infarction	48%	42%	0.511	43%	45%	0.663
Coronary bypass grafting	33%	25%	0.272	30%	30%	0.908
Gout	17%	22%	0.423	18%	19%	0.883
Dyspnea at rest	53%	59%	0.5	60%	55%	0.36
Fatigue at rest	67%	72%	0.49	64%	69%	0.254
Orthopnea	87%	82%	0.352	86%	85%	0.714
NYHA class (mean)	3.9 ± 0.3	3.9 ± 0.3	0.855	3.8 ± 0.4	3.9 ± 0.3	0.18
Six minute walk (feet)	417 ± 418	428 ± 381	0.569	416 ± 429	422 ± 401	0.572
Maximal oxygen consumption (mL/kg/min)	9.7 ± 1.9	10.9 ± 5.0	0.831	9.9 ± 3.2	10.3 ± 3.7	0.655
Ejection fraction (%)	18.3 ± 6.0	18.2 ± 6.3	0.94	20.1 ± 6.6	18.3 ± 6.1	0.008[*]
Systolic blood pressure (mm Hg)	110 ± 18	101 ± 16	0.001[*]	106 ± 15	106 ± 18	0.775
Heart rate (bpm)	84 ± 16	80 ± 16	0.111	81 ± 14	82 ± 16	0.569
Respiration rate (breaths/min)	21 ± 4	20 ± 4	0.862	21 ± 4	20 ± 4	0.722
Jugular venous pressure > 12 cm	25%	21%	0.509	19%	23%	0.294
Rales > 1/3 lung fields	18%	11%	0.241	14%	15%	0.726
Ascites ≥ moderate	29%	14%	0.036[*]	18%	22%	0.241
Severe edema	17%	11%	0.322	10%	14%	0.258
Cool extremities	14%	22%	0.229	16%	18%	0.684
Medications (baseline)						
ACE inhibitor / ARB	89%	89%	0.972	90%	89%	0.721
β-Blocker	54%	67%	0.107	64%	60%	0.423

Characteristics	Worsening RF (n=85)	Improved RF (n=65)	p	Stable RF (n=251)	Dynamic RF (n=150)	p
Loop diuretic (mg)†	200 (120, 400)	160 (120, 320)	0.16	200 (100, 320)	190 (120, 320)	0.334
Spironolactone	38%	32%	0.664	33%	34%	0.726
Thiazide diuretic	16%	12%	0.438	11%	14%	0.33
Medications (in-hospital)						
ACE inhibitor / ARB	93%	88%	0.27	93%	91%	0.345
Loop diuretic (mg) †	280 (160, 450)	190 (120, 400)	0.056	200 (100, 340)	240 (140, 425)	0.039*
Thiazide diuretic	46%	27%	0.017*	24%	38%	0.003*
Inotropes	45%	55%	0.221	38%	49%	0.028*
Vasodilators	37%	43%	0.486	22%	39%	>0.001*
Inotropes or vasodilators	71%	78%	0.3	50%	74%	>0.001*
Laboratory Findings						
Hemoglobin (g/dL)	12.5 ± 1.8	12.6 ± 1.9	0.565	12.6 ± 1.8	12.5 ± 1.8	0.748
Serum sodium (mEq/L)	137 ± 5	135 ± 6	0.002*	137 ± 4	136 ± 5	0.189
Serum creatinine (mg/dL)	1.27 ± 0.51	2.08 ± 0.83	>0.001*	1.44 ± 0.49	1.62 ± 0.78	0.126
Glomerular filtration rate (mL/min)	69.5 ± 29.5	39.9 ± 17.2	>0.001*	57.2 ± 23.0	56.7 ± 28.9	0.837
B-Type Natriuretic peptide (pg/mL)	1076 ± 1301	1309 ± 1953	0.48	906 ± 1144	1174 ± 1605	0.209
Norepinephrine (pg/mL)	547 ± 366	977 ± 579	>0.001*	660 ± 535	721 ± 508	0.175

ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker, Dynamic RF: ≥ 20% increase or decrease in glomerular filtration rate from admission to discharge, RF: Renal function, NYHA: New York Heart Association, Stable RF: ≤ 20% change in renal function from admission to discharge.

*
Represents a significant p-value.

†
Loop diuretic dose reported as median with interquartile range. Baseline loop dose represents daily oral dose prior to hospitalization. In-hospital loop dose represents the maximum IV loop diuretic dose received on any one day of the study. All other values represent mean +/- standard deviation or %.

Table 2

Pulmonary artery catheter derived parameters at admission, catheter removal, and the associated change

Characteristics	Worsening RF	Improved RF	p	Stable RF	Dynamic RF	p
Hemodynamics (baseline)	(n=41)	(n=42)		(n=99)	(n=83)	
Right atrial pressure (mm Hg)	13.2 ± 6.3	12.7 ± 7.4	0.612	13.4 ± 10.4	12.9 ± 6.8	0.664
Pulmonary artery systolic pressure (mm Hg)	57.4 ± 13.8	55.1 ± 12.7	0.447	54.4 ± 15.7	56.2 ± 13.2	0.407
Pulmonary capillary wedge pressure (mm Hg)	26.3 ± 7.1	25.4 ± 10.2	0.717	23.7 ± 9.8	25.9 ± 8.8	0.219
Cardiac index (L/min/m²)	1.82 ± 0.63	1.91 ± 0.55	0.249	2.08 ± 0.60	1.86 ± 0.59	0.019*
Systemic vascular resistance (dyn-s/cm5)	1554 ± 1064	1490 ± 679	0.97	1464 ± 802	1522 ± 885	0.974
Hemodynamics (PAC removal)	(n=37)	(n=37)		(n=89)	(n=72)	
Right atrial pressure (mm Hg)	10.5 ± 5.4	9.0 ± 5.3	0.216	8.6 ± 5.5	9.7 ± 5.4	0.137
Pulmonary artery systolic pressure (mm Hg)	49.0 ± 12.3	46.4 ± 11.8	0.381	44.6 ± 13.0	47.8 ± 12.1	0.113
Pulmonary capillary wedge pressure (mm Hg)	18.5 ± 6.5	16.4 ± 7.5	0.323	17.0 ± 8.2	17.4 ± 7.0	0.844
Cardiac index (L/min/m²)	2.26 ± 0.71	2.27 ± 0.53	0.915	2.41 ± 0.65	2.26 ± 0.62	0.07
Systemic vascular resistance (dyn-s/cm5)	1091 ± 466	1156 ± 488	0.746	1119 ± 491	1126 ± 475	0.82
Hemodynamics (change)	(n=36)	(n=35)		(n=85)	(n=68)	
Right atrial pressure (mm Hg)	-2.8 ± 7.4	-3.9 ± 7.5	0.712	-4.8 ± 10.5	-3.4 ± 7.4	0.547
Pulmonary artery systolic pressure (mm Hg)	-9.6 ± 13.5	-9.0 ± 11.9	0.851	-9.7 ± 12.4	-9.3 ± 12.7	0.338
Pulmonary capillary wedge pressure (mm Hg)	-8.3 ± 7.1	-7.5 ± 10.0	0.729	-6.9 ± 9.3	-7.9 ± 8.6	0.526
Cardiac index (L/min/m²)	0.46 ± 0.69	0.47 ± 0.59	0.909	0.36 ± 0.70	0.46 ± 0.63	0.092
Systemic vascular resistance (dyn-s/cm5)	-484 ± 1121	-384 ± 549	0.641	-336 ± 757	-431 ± 858	0.372

Dynamic RF: ≥ 20% increase or decrease in glomerular filtration rate from admission to discharge, RF:Renal function, Stable RF: ≤ 20% change in renal function from admission to discharge. Values represent mean +/-standard deviation or %.

*
Represents a significant p-value.

Table 3

Relationship between changes in renal function and renal function at baseline and discharge

Variable	Improved RF	p	Worsening RF	p
Admission glomerular filtration rate	r = -0.30	<0.001[*]	r = 0.26	<0.001[*]
Discharge glomerular filtration rate	r = 0.05	0.302	r = -0.20	<0.001[*]
Admission glomerular filtration rate <60 mL/min	OR = 4.4	<0.001[*]	OR = 0.33	<0.001[*]
Discharge glomerular filtration rate <60 mL/min	OR = 0.99	0. 961	OR = 2.0	0.010[*]

RF: Renal function

[*] Represents a significant p-value.

Table 4

Cox regression results for dynamic renal function and mortality controlling for glomerular filtration rate at admission and discharge

Variable	Covariates	SE	HR	p	95% CI
Dynamic RF		0.229	1.79	0.011[*]	1.14-2.81
Dynamic RF		0.231	1.71	0.020[*]	1.09-2.69
	Admission GFR[†]	0.054	0.83	<0.001[*]	0.75-0.92
Dynamic RF		0.232	1.59	0.047[*]	1.006-2.499
	Discharge GFR[†]	0.059	0.81	<0.001[*]	0.73-0.91
Dynamic RF		0.232	1.67	0.027[*]	1.06-2.63
	Discharge GFR[†]	0.086	0.9	0.207	0.76-1.06
	Admission GFR[†]	0.077	0.89	0.136	0.77-1.04

CI: Confidence interval, Dynamic RF: ≥ 20% increase or decrease in estimated glomerular filtration rate, RF: Renal function, SE: Standard error.

[*] Represents a significant p-value.

[†] Hazard ratio (HR) calculated per 10 mL/min increase in glomerular filtration rate.