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Body Weight Change During and After Hospitalization for Acute Heart Failure: Patient Characteristics, Markers of Congestion, and Outcomes – Findings from ASCEND-HF

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Abstract

Background—Body weight changes during and after hospitalization for acute heart failure (AHF) and the relationships with outcomes have not been well-characterized.

Methods—A *post-hoc* analysis was performed of the ASCEND-HF trial, which enrolled patients admitted for AHF regardless of ejection fraction. In-hospital body weight change was defined as the difference between baseline and discharge/day 10, while post-discharge body weight change was defined as the difference between discharge/day 10 and day 30. Spearman rank correlations of weight change, urine output (UOP), and dyspnea relief as assessed by a 7-point Likert scale are described. Logistic and Cox proportional hazards regression was used to evaluate the relationship between weight change and outcomes.

Results—Study participants with complete body weight data (n = 4,172) had a mean age of 65±14 years and 66% were male. Ischemic heart disease was reported in 60% of patients and the average ejection fraction was 30±13%. The median change in body weight was −1.0 kg (interquartile range [IQR]: −2.1, 0.0) at 24 hr and −2.3 kg (IQR: −5.0, −0.7) by discharge/day 10. At hour 24, there was a weak correlation between change in body weight and UOP (r = −0.381) and minimal correlation between body weight change and dyspnea relief (r = −0.096). After risk

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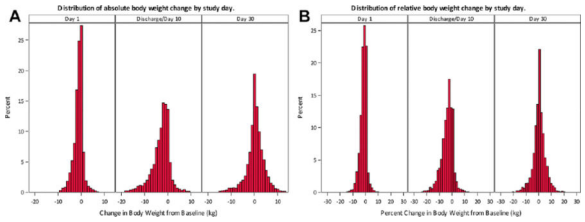
adjustment, increasing body weight during hospitalization was associated with a 16% increase per kg in the likelihood of 30-day mortality or HF readmission for patients showing weight loss ≤1 kg or weight gain during hospitalization (Odds Ratio per kg increase 1.16, 95% Confidence Interval [CI] 1.09–1.27; p<0.001). Among the subset of patients experiencing > 1 kg increase in body weight post-discharge, increasing body weight was associated with higher risk of 180-day mortality (Hazard Ratio per kg increase 1.16, 95% CI 1.09–1.23; p<0.001).

Conclusion—A substantial number of patients experienced minimal weight loss or frank weight gain in the context of an AHF trial, and increasing body weight in this subset of patients was independently associated with a worse post-discharge prognosis.

Graphical abstract



Keywords

acute heart failure; body weight; urine output; dyspnea

Introduction

There are more than 1 million hospitalizations for acute heart failure (AHF) annually in the United States representing 1–2% of all admissions (1). Signs and symptoms of congestion due to elevated cardiac filling pressures are the most common precipitant for hospitalization and readmission (2,3). As a result, relieving congestion has traditionally been one of the primary goals of therapy during hospitalization (4). Although the outpatient management of HF has been transformed by guideline-directed medical therapies, there have been few advances in the inpatient management of AHF and the cornerstone of decongestion remains diuretics (5). Despite the fundamental role congestion plays in AHF, there is little consensus among clinicians with respect to assessing and grading congestion during hospitalization. Moreover, limited data exist regarding the association between congestion, symptoms, changes in weight, and outcomes in patients following a hospitalization for AHF.

Elements of the history and physical exam, body weight change, and net fluid balance must ultimately be integrated into a comprehensive evaluation of volume status in order to make vital treatment decisions regarding the duration and intensity of therapy and patient disposition. However, the accuracy and reproducibility of surrogate measures of congestion and their associations with post-discharge outcomes remain unclear (6–8). Thus, the objective of this secondary analysis of the global *ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide and Decompensated Heart Failure)* trial was to systematically characterize the relationship between body weight change during hospitalization and following discharge and patient characteristics, markers of congestion, and outcomes.

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Methods

Overview

The study design (9) and primary results (10) of the *ASCEND-HF* trial have been previously reported. Briefly, *ASCEND-HF* was a global, prospective, randomized, double-blind, placebo-controlled trial designed to examine the short- and long-term efficacy and safety of nesiritide, a recombinant natriuretic peptide. A total of 7141 patients hospitalized for HF as evidenced by dyspnea at rest or with minimal activity, ≥1 accompanying sign, and ≥1 objective measure were randomized to nesiritide or placebo, in addition to standard therapy, within 24 hours of the first intravenous HF-related treatment. Relevant exclusion criteria included a high likelihood to be discharged from the hospital in ≤24 hours or a comorbid condition with an associated life expectancy of <6 months. The ASCEND-HF trial was conducted in accordance with the Declaration of Helsinki, the protocol was independently approved by the institutional review board or ethics committee at each participating center, and written informed consent was obtained from all participants.

Study Definitions and Endpoints

Patient weight was routinely collected according to local practice as part of study assessments. In-hospital body weight change was defined as the absolute difference between baseline and discharge or day 10, whichever occurred first, while post-discharge body weight change was defined as the absolute difference between discharge/day 10 and day 30. Study participants with a body weight change less than the 1st percentile or greater than the 99th percentile were excluded. In-hospital body weight change was categorized as significant loss (i.e. change < −5 kg), moderate loss (i.e. −5 kg ≤ change < −1 kg), no loss (i.e. −1 kg ≤ change < 1 kg), and gain (i.e. change ≥1 kg). Dyspnea relief was measured 24 hours after enrollment using a selfreported 7-point categorical Likert scale (i.e. markedly worse = −3, moderately worse = −2, minimally worse = −1, no change = 0, minimally better = 1, moderately better = 2, and markedly better = 3). Urine output (UOP) was measured in milliliters (mL) from baseline to hour 24 (11).

The primary outcome of the ASCEND-HF trial was 30-day all-cause mortality or HF hospitalization. Additional outcomes of interest for the present analysis were 30-day HF hospitalizations, all-cause mortality, and the composite of all-cause mortality or all-cause hospitalization and 180-day all-cause mortality. An independent and blinded adjudication committee determined the cause of all hospitalizations and deaths occurring within 30 days. Hospitalization for HF was defined as admission for worsening signs or symptoms of HF resulting in the new administration of intravenous therapies, mechanical or surgical intervention, or provision of ultrafiltration, hemofiltration, or dialysis specifically for the management of persistent or worsening HF.

Statistical Analysis

All continuous data were reported as median (25th, 75th) percentiles and as frequencies and percentages for categorical data. Baseline patient characteristics including demographics, medical history, laboratory values, and medication use were compared by in-hospital body weight change. Categorical variables were assessed using Chi-square test or Fisher’s exact

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test, while continuous variables were evaluated using analysis of variance or Kruskal-Wallis testing, as appropriate. The relationship between in-hospital body weight change, dyspnea relief and UOP was evaluated using Spearman's rank correlation. The association between in-hospital body weight change and 30-day outcomes was assessed using logistic regression. Cox proportional hazards regression was utilized to assess the association between in-hospital body weight change and 180-day mortality, similarly for post-discharge body weight change. To investigate the relationship between post-discharge body weight change and 180-day mortality, the reference time for 180-day mortality was reset to the date of discharge/day 10. Piecewise linear splines were used to model the nonlinear relationship between body weight change and both 30-day and 180-day clinical outcomes. Models were adjusted for potential confounders including age, gender, body mass index (BMI), ejection fraction (EF), New York Heart Association (NYHA) functional class, heart rate (HR), systolic blood pressure (SBP), Na, serum creatinine (sCr), blood urea nitrogen (BUN), b-type natriuretic peptide (BNP)/amio terminal-proBNP (NT-proBNP), comorbidities (coronary artery disease [CAD], atrial fibrillation [afib], diabetes mellitus type II [DMII], chronic kidney disease [CKD], chronic obstructive pulmonary disease [COPD]), baseline medications (i.e. beta-blocker, angiotensin-converting enzyme inhibitor [ACEI]/angiotensin receptor blocker [ARB], mineralocorticoid receptor antagonist [MRA], digoxin, and inotropes), loop diuretics (i.e. total loop diuretics in oral furosemide equivalents from randomization to 24 hours post-randomization), and treatment assignment (i.e. nesiritide vs. placebo). The method of multiple imputations was utilized for missing data for prespecified covariates under the assumption that data were missing at random. Each adjustment variable had some degree of missingness. The majority of the pre-specified variables had less than 1% missing data. Three variables had more than 1% but less than 10% missing data (Na; sCr; BUN). In addition, three variables had > 10% missing data (EF: 13.4%; NYHA functional class: 17.3%; NT-proBNP: 47.9%). Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

Funding and Manuscript Preparation

Scios Inc. (Mountain View, CA) provided financial and material support for the ASCEND-HF trial. Database management and statistical analysis was performed by the Duke Clinical Research Institute. The authors take responsibility for the manuscript's integrity, and had complete control and authority over its preparation and the decision to publish.

Results

Study Population

A total of 4172 patients had body weight measured at baseline and discharge/day 10. Study participants had a mean age of 65±14 years, 65% were male, and 47% self-identified as non-white (Table 1). Ischemic heart disease was reported in 60% of patients and the average ejection fraction was 30±13%. The prevalence of cardiac and non-cardiac comorbidities was high and patients were well-treated with guideline-directed medical therapies.

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Clinical Course of Body Weight Change

The median change in body weight was −1.0 kg (-2.1, 0.0) at hour 24 and −2.3 kg (−5.0, −0.7) at discharge/day 10 (Figure 1). Overall, 67% of patients (n = 2776) showed significant (i.e. change < −5 kg) or moderate weight loss (i.e. −5 kg ≤ change < −1 kg) during hospitalization, while 26% (n = 1068) showed no loss (i.e. −1 kg ≤ change < 1 kg) and 8% (n = 328) experienced weight gain (i.e. change ≥1 kg). Between discharge/day 10 and day 30, study participants reported a change of +0.2 kg (−1.3, 2.0). At 30 days, 26% of patients (n = 945) showed significant or moderate weight loss, while 34% (n = 1211) showed no loss and 40% (n = 1438) experienced weight gain.

In-Hospital Body Weight Change and Patient Characteristics

Patients experiencing no weight loss or weight gain during hospitalization tended to self-identify as non-white and were more likely to be female. This subgroup of patients also had a higher prevalence of cardiac and non-cardiac medical comorbidities. Although patients experiencing no weight loss or weight gain had less severe signs and symptoms of volume overload and lower natriuretic peptide levels at baseline, there were no clinically significant between-group differences in the rate of prescription or dose of loop diuretics. With the exception of β-blocker usage, there was no significant difference between groups in utilization of guideline-directed medical therapies.

Correlation Between Surrogate Markers of Congestion

At hour 24, there was a weak correlation between change in body weight and UOP (r = −0.381) and minimal correlation between body weight change and dyspnea relief (r = −0.096) (Table 2, Figure 2–4). In addition, there was minimal correlation between dyspnea relief and UOP (r = 0.111). The overlapping 95% CIs for the mean trajectory of sCr and BUN during hospitalization and post-discharge suggest that these markers did not differ over time by in-hospital body weight change (Figure 5–6).

Association Between Body Weight Change and Outcomes

The relationship between body weight change and 30-day and 180-day events was non-linear—demonstrating a general decrease in risk for patients who lost weight and an increase in risk for patients who gained weight. Among patients with weight loss ≤1 kg or weight gain during hospitalization, increasing body weight during hospitalization was associated with a 16% increase (per kg) in the likelihood of 30-day mortality or HF readmission after risk adjustment (Odds Ratio [OR] per kg increase 1.16, 95% Confidence Interval [CI] 1.09–1.27; p<0.001) (Table 3). The association between in-hospital body weight change and 180-day mortality did not reach the threshold for statistical significance (p = 0.086) in this subset of patients after risk adjustment (Table 4). In contrast, there was no statistically significant association between inhospital body weight change and 30-day and 180-day outcomes among patients reporting weight loss > 1 kg.

Among the subset of patients experiencing > 1 kg increase in body weight post-discharge, increasing body weight was associated with a 16% increase (per kg) in the risk of 180-day mortality after risk adjustment (HR per kg increase 1.16, 95% CI 1.09–1.23, p<0.001) (Table 5). In contrast, for patients reporting <1 kg weight gain or weight loss, decreasing body

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weight was associated with greater risk of death at day 180 (HR per kg increase 0.93, 95% CI 0.89–0.97).

Discussion

This study found that more than 30% of patients admitted for a primary diagnosis of AHF experience minimal weight loss or even frank weight gain during hospitalization. Despite reporting fewer signs and symptoms of congestion and lower natriuretic peptide levels at baseline, the prescription and dosing of loop diuretics was comparable to patients experiencing more marked in-hospital weight loss. Although there was a weak correlation between in-hospital body weight change and UOP, there was minimal correlation between dyspnea relief and either in-hospital body weight change or UOP. Finally, for the subset of patients experiencing weight gain during hospitalization or following discharge, body weight increases were associated with higher readmission rates and reduced survival.

The observation that 30% of patients experience minimal weight loss or gain weight during hospitalization for AHF is consistent with previously published estimates (6,12). When first considered, this observation could be surprising and even counterintuitive, however there are several contributing factors that help explain this finding. First, there are inherent practical barriers to weighing patients in a standardized fashion (i.e. timing, scale calibration, amount of clothing, patient positioning, etc.) that limit the precision and accuracy of body weight measurements. Second, at least a fraction of patients may be discharged with minimal weight loss and incomplete clinical decongestion. Third, it is possible that some patients may exhibit diuretic resistance or refractoriness to medical therapy (13). Finally, this finding may also be explained by the complex pathophysiology of congestion, which likely is a result of both an absolute increase in intravascular volume as well as a relative redistribution of fluid from capacitance vessels to the effective circulation (14,15). Thus, it is possible that patients reporting minimal weight loss or weight gain may in part represent a distinct HF phenotype characterized by a relative redistribution of fluid as opposed to a more gradual absolute increase in intravascular volume. This hypothesis is supported by the fact that these patients had substantially lower levels of natriuretic peptides and less peripheral edema at baseline, findings more suggestive of an acute decompensation, but were otherwise quite similar to patients experiencing more substantial weight loss during hospitalization.

It is also noteworthy that there was minimal correlation between dyspnea relief and either in-hospital body weight change or UOP (8,16). Worsening dyspnea is the most common presenting symptom in AHF (2,6,17) and dyspnea relief has traditionally been an important endpoint for clinical trials and regulatory approval (18). However, there are several shortcomings to exclusively relying on dyspnea for assessing volume status and treatment response. First, there is no universally agreed upon method for measuring dyspnea in the context of routine practice or in the setting of a clinical trial (19). Second, dyspnea is subjective and non-specific, which is particularly problematic in HF where the prevalence of cardiac (i.e. ischemic heart disease, atrial fibrillation, etc.) and non-cardiac comorbidities (i.e. chronic obstructive pulmonary disease, sleep disordered breathing, etc.) is high and may confound interpretation (20–22). Third, dyspnea may be elicited in patients who are asymptomatic at rest by performing provocative maneuvers (e.g. lying them supine,

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ambulation, etc.) (23,24). In addition, measuring body weight and UOP in the context of a pragmatic clinical trial likely represents a 'best-case scenario' and the reproducibility and accuracy of these recordings are likely superior to 'real-world' measurements. Thus, this study clearly highlights the challenges faced by providers who must integrate potentially discrepant data points as part of a global assessment of congestion in order to make management decisions.

Finally, in both the in-hospital and post-discharge phase there was a clear association between increasing body weight and adverse events among the subset of patients experiencing weight gain. Over the last couple of decades there has been a trend towards shorter length of stay (LOS) for hospitalization in general and HF-related admissions in particular. The pressure placed on providers by hospital administrators, healthcare payers, and policy makers alike to decrease LOS has likely had the unintended consequence of a subset of patients being discharged prematurely. These patients likely experience minimal weight loss and/or incomplete clinical decongestion and are subsequently at higher risk for short-term readmissions. In examining the patients in this analysis, the LOS of patients with minimal weight loss or frank weight gain was on average one day shorter than patients experiencing > 1 kg weight loss. This supposition is strongly supported by the existing literature, which has shown a robust association between LOS and post-discharge outcomes (25,26). Of note, prior research has shown a relationship between post-discharge body weight increases and HF readmissions, but this is the first study to demonstrate an association with mortality (27). However, it does not necessarily follow that further reductions in body weight during hospitalization or soon after discharge would translate into improved outcomes. Additional research is required to evaluate body weight targets as a potential endpoint for therapy. Finally, the association between increasing post-discharge body weight and improved survival, among patients experiencing <1 kg weight gain or weight loss, may be explained by nutritional status as severe malnutrition (28,29) and cardiac cachexia (30,31) as well as subtle decreases in serum albumin within the normal range (32,33) have been associated with increased morbidity and mortality.

There are several limitations of the data that should be addressed. First, this study was conceived *post-hoc* and is therefore subject to the potential biases intrinsic to exploratory analyses of observational data including unmeasured or residual confounding. Second, per study protocol patients were enrolled within 24 hours of the first intravenous HF-related treatment and likely experienced some degree of weight loss during the timeframe between initial presentation and enrollment. Third, the *ASCEND-HF* study protocol did not require a systematic process for weighing patients, which may have impacted the reliability and reproducibility of changes over time. Fourth, the case report form did not include estimates of intake and thus UOP is used as a best approximate of net fluid balance. Fifth, dyspnea relief was assessed in the ASCEND-HF trial using a categorical Likert scale and using a continuous instrument such as a visual analogue scale to assess dyspnea may have modified the correlation between dyspnea relief and other surrogate markers of congestion. Finally, these data were collected in the context of a clinical trial with specific inclusion and exclusion criteria potentially restricting the generalizability of the results.

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In conclusion, more than 30% of patients admitted for a primary diagnosis of AHF reported minimal weight loss or gained weight during hospitalization. These patients tended to exhibit fewer signs and symptoms of volume overload and had lower natriuretic peptide levels, suggesting a rapid redistribution of fluid as the pathophysiologic basis of congestion. There was also a dissociation between early dyspnea relief and both body weight change and UOP, underscoring the challenges of evaluating congestion and determining the appropriate intensity and duration of therapy. Finally, among patients experiencing weight gain during hospitalization or soon after discharge, increasing body weight portended a poor prognosis and additional research is necessary to prospectively validate goal-oriented decongestion strategies.

Clinical Perspectives

More than 30% of patients admitted for a primary diagnosis of AHF reported minimal weight loss or frank weight gain during hospitalization. These patients tended to exhibit fewer signs and symptoms of volume overload and had lower natriuretic peptide levels, suggesting a unique clinical phenotype characterized by a rapid redistribution of fluid as the pathophysiologic basis of congestion. There was also a dissociation between early dyspnea relief and both body weight change and UOP, underscoring the challenges of evaluating congestion and determining the appropriate intensity and duration of therapy. Among patients experiencing minimal weight loss or frank weight gain during hospitalization or following discharge, increasing body weight was associated with increased risk of adverse outcomes.

Translational Outlook

Additional research is required to prospectively validate the role of body weight targets as part of a comprehensive goal-oriented decongestion strategy.

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Abbreviations

HF	heart failure
AHF	acute heart failure

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ASCEND-HF	Acute Study of Clinical Effectiveness of Nesiritide and Decompensated Heart Failure
UOP	urine output
BMI	body mass index
EF	ejection fraction
NYHA	New York Heart Association
HR	heart rate
SBP	systolic blood pressure
sCr	serum creatinine
BUN	blood urea nitrogen
BNP	b-type natriuretic peptide
NT-proBNP	amino terminal-proBNP
CAD	coronary artery disease
Afib	atrial fibrillation
DMII	diabetes mellitus type II
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
ACEI	angiotensin-converting enzyme inhibitor
ARB	angiotensin receptor blocker
MRA	mineralocorticoid receptor antagonist
HR	hazard ratio
CI	confidence interval

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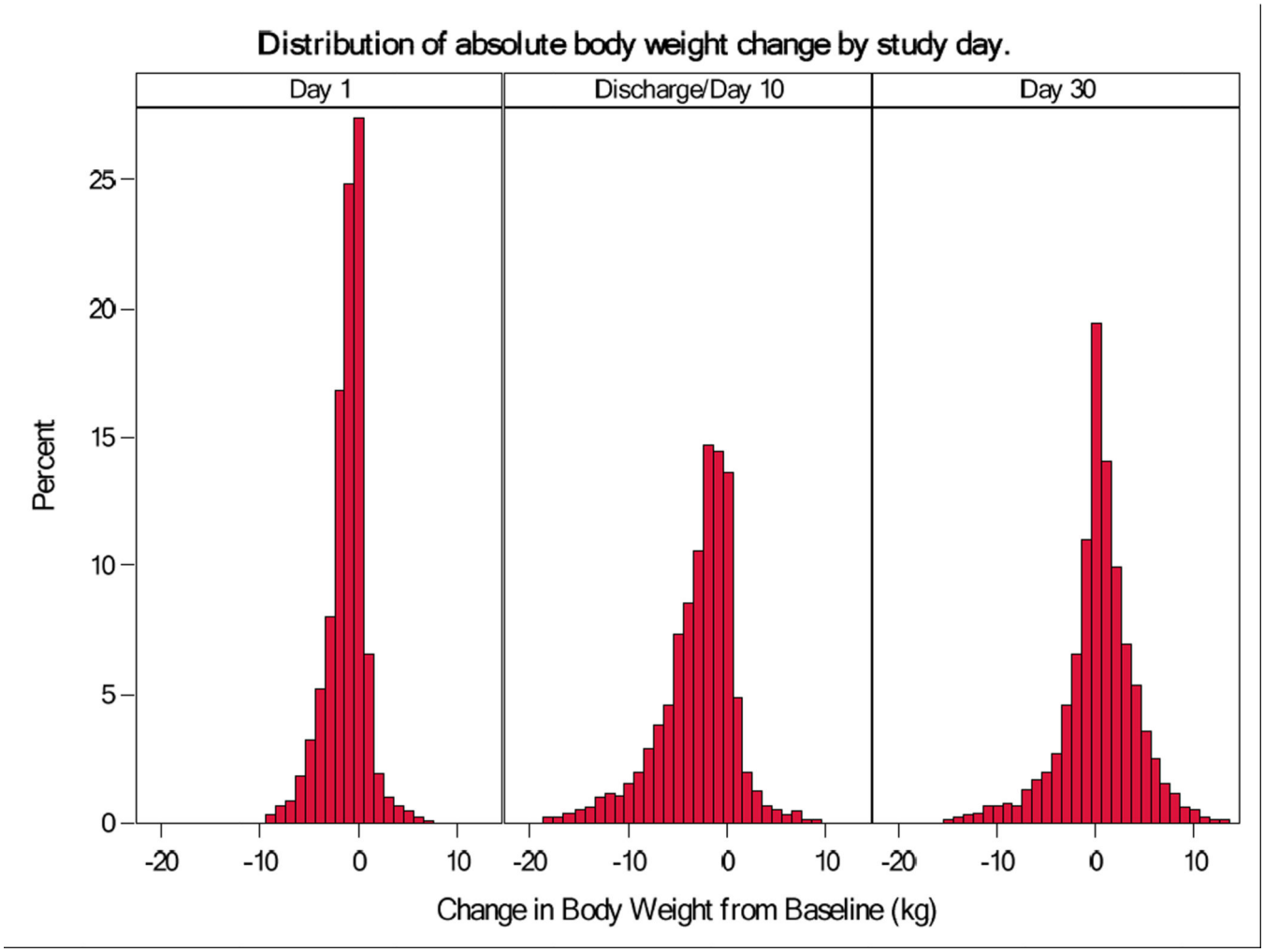
A.



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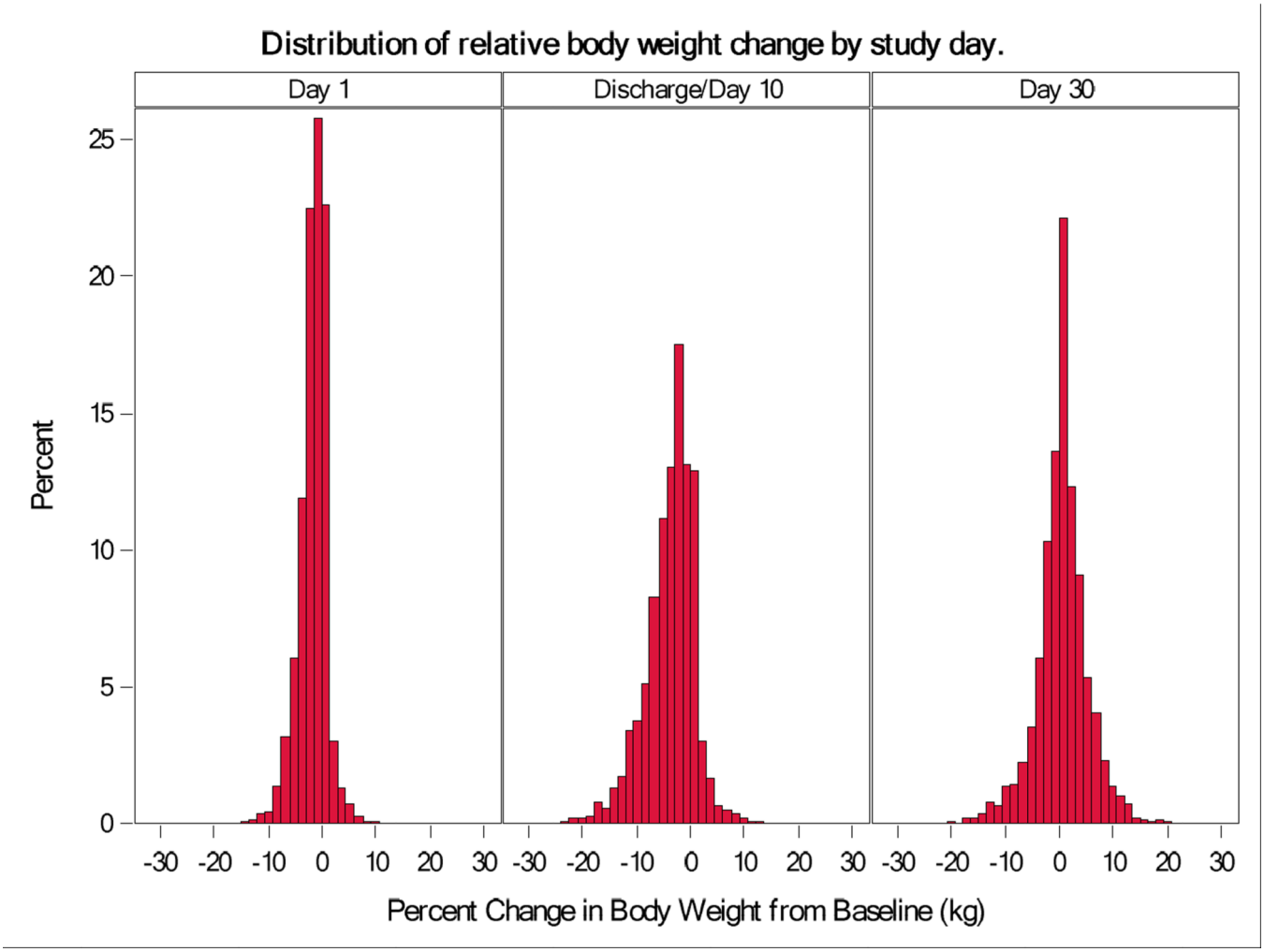

Figure 1. In-Hospital Body Weight Change

The distribution of (A) absolute and (B) relative in-hospital body weight change at hour 24, discharge/day 10, and day 30.

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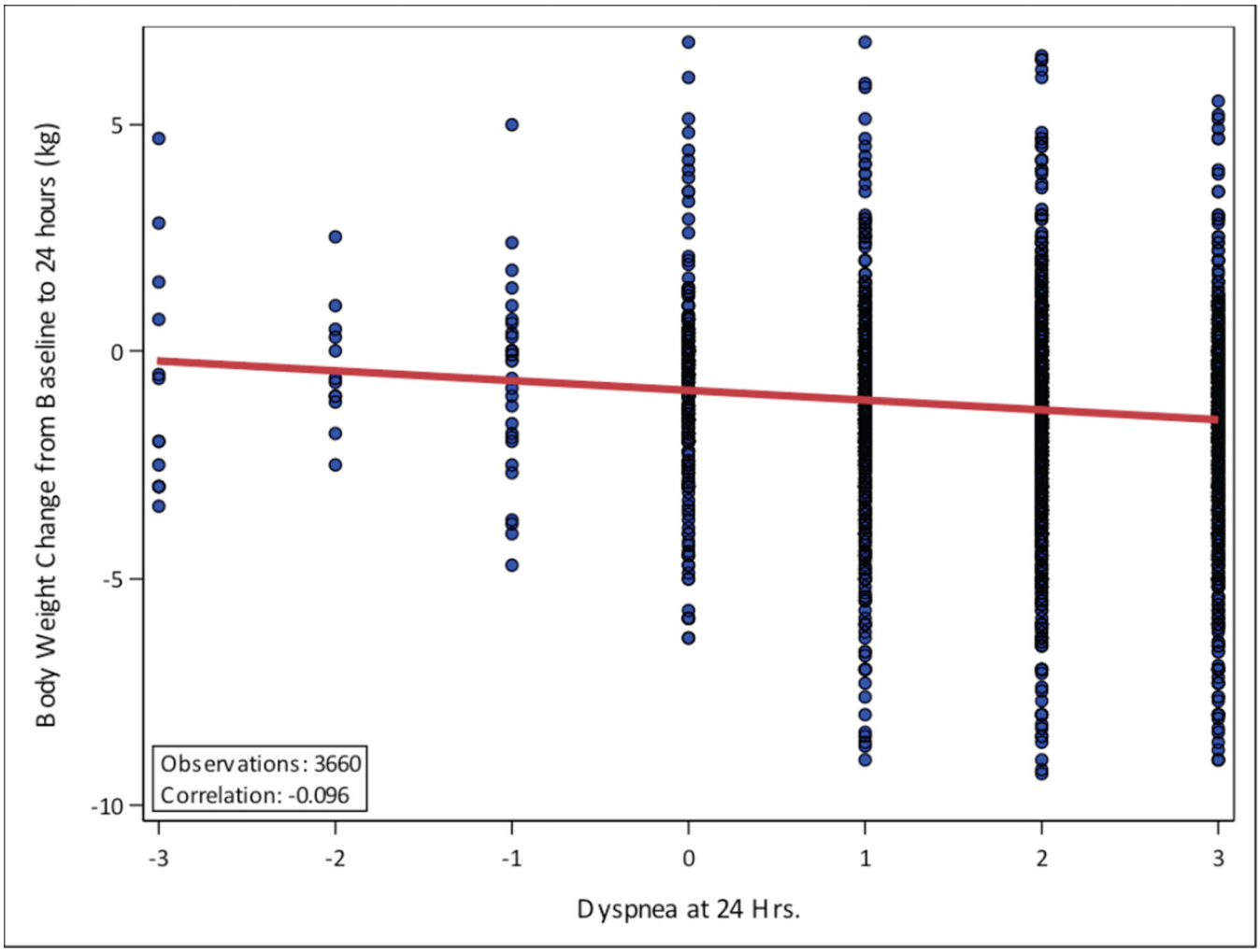

Figure 2. Body Weight Change and Dyspnea

The correlation between in-hospital body weight change and dyspnea relief at 24 hours.

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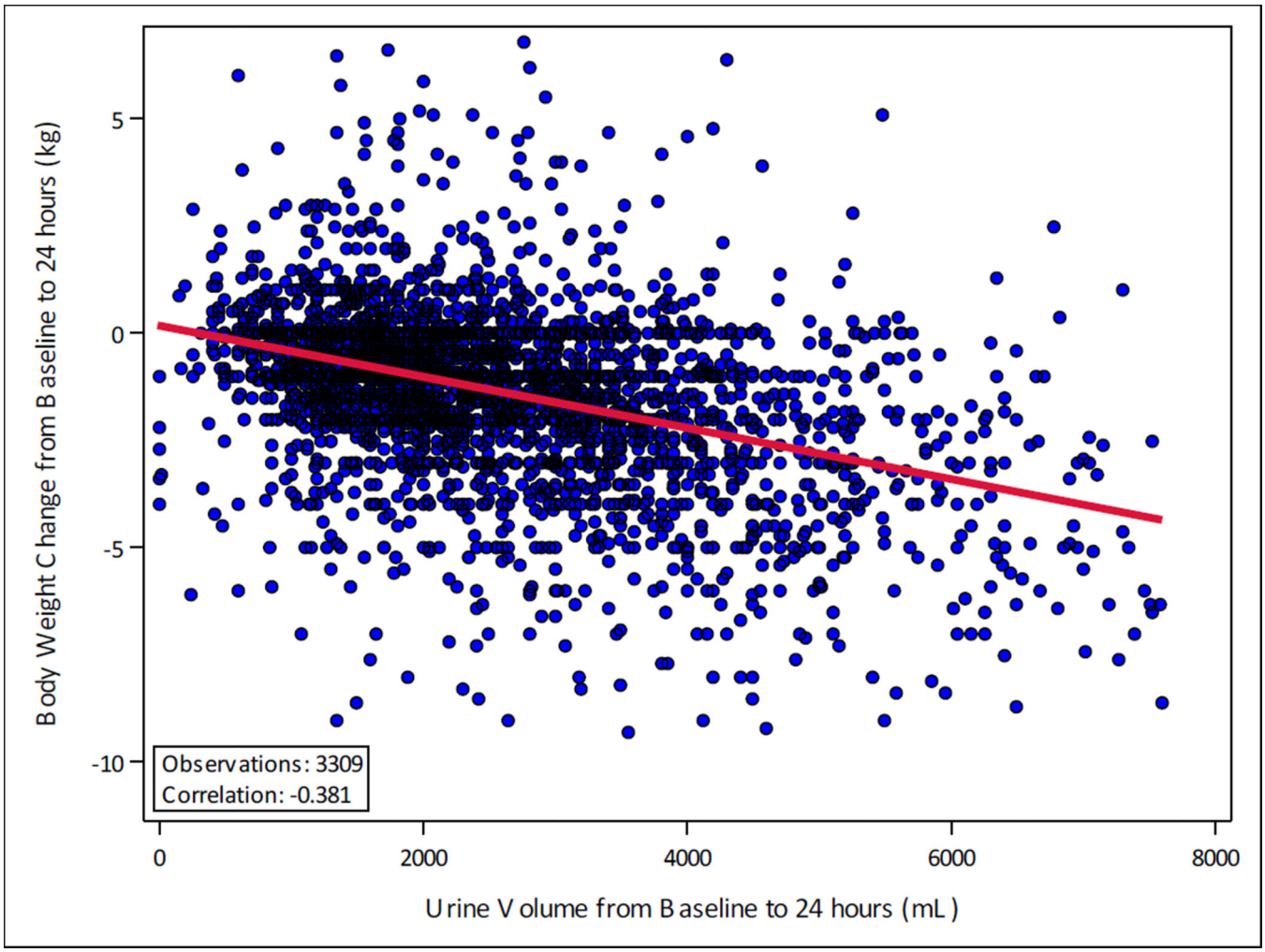

Figure 3. Body Weight Change and Urine Output

The correlation between in-hospital body weight change and urine output at 24 hours.

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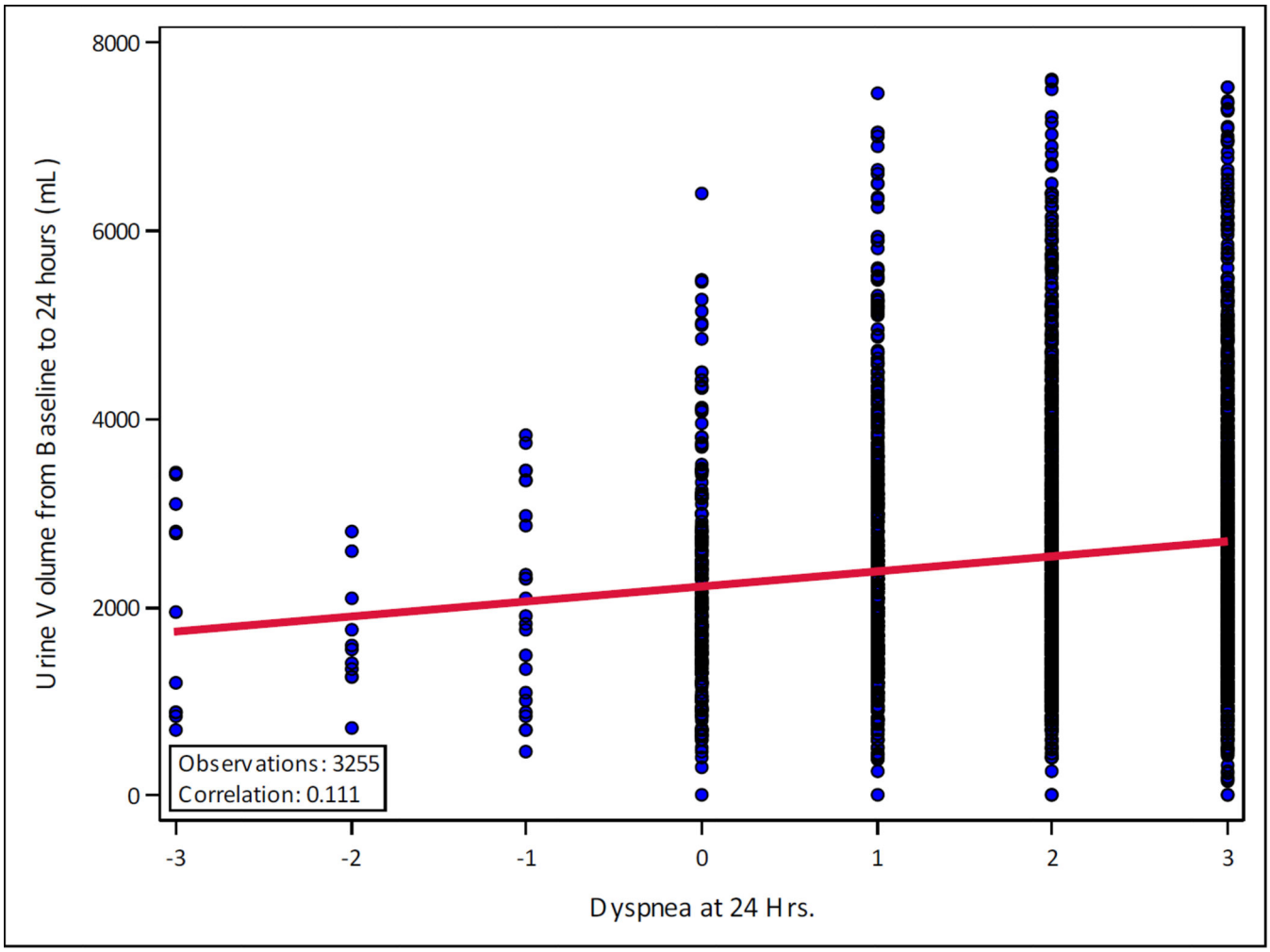

Figure 4. Urine Output and Dyspnea

The correlation between urine output and dyspnea relief at 24 hours.

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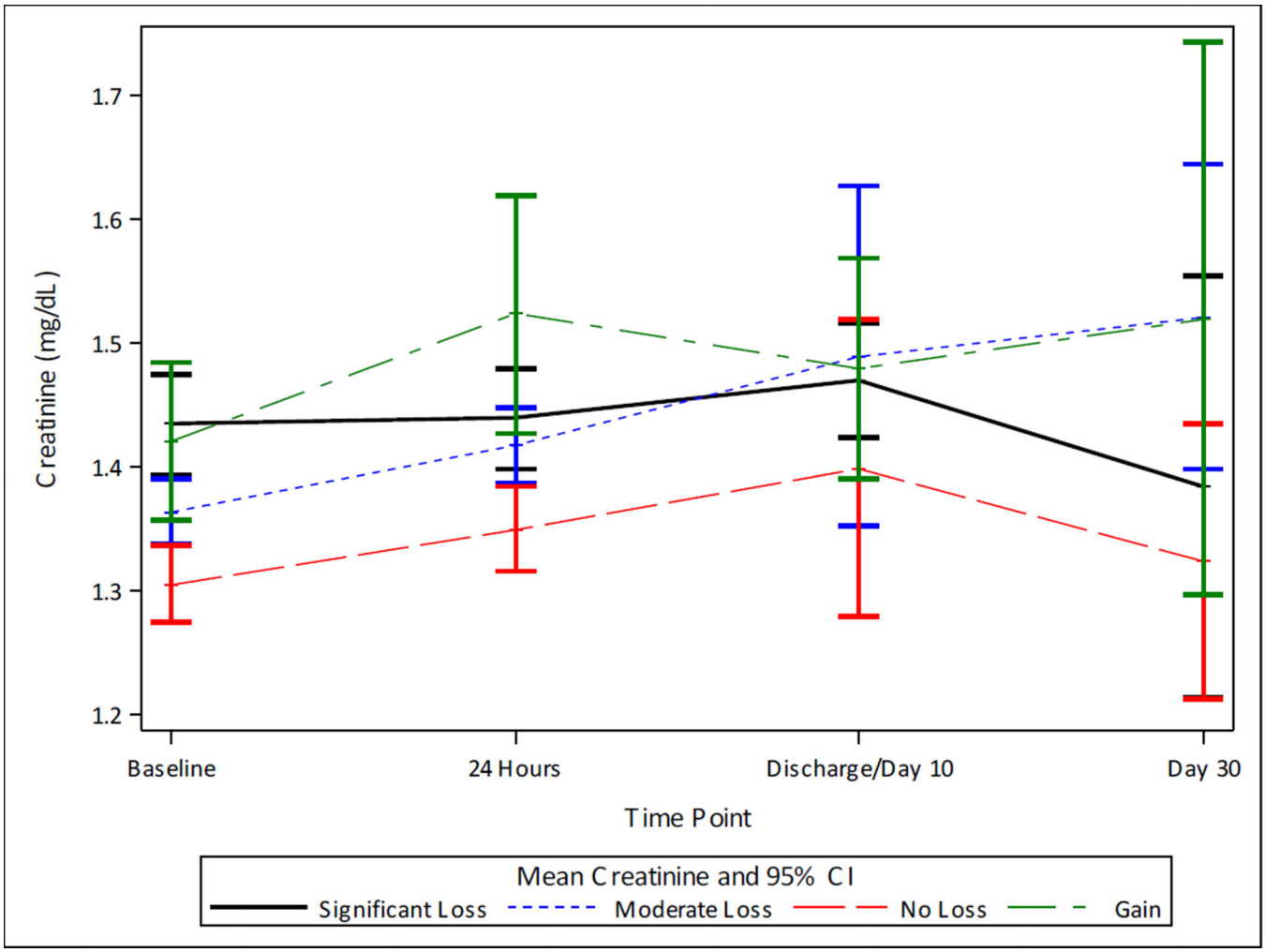

Figure 5. Serum Creatinine and Change in Body Weight

Serum creatinine over time by in-hospital body weight change.

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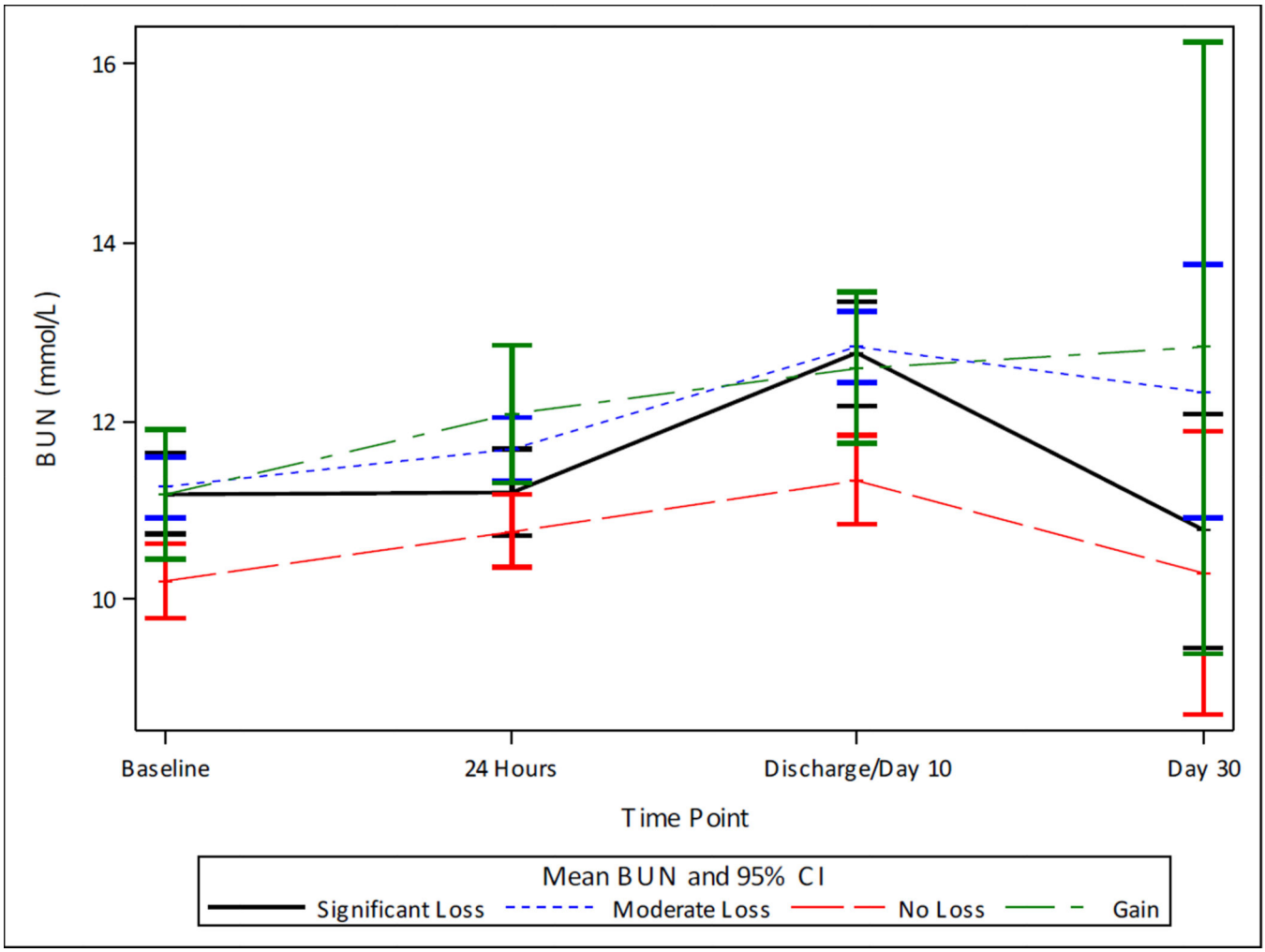

Figure 6. Blood Urea Nitrogen and Change in Body Weight

Blood urea nitrogen over time by in-hospital body weight change

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Table 1

Patient Characteristics by Body Weight Change from Baseline to Discharge/Day 10

		Weight Change Classification*				
Characteristic	**All Patients (N=4172)**	**Significant Loss (N=957)**	**Moderate Loss (N=1819)**	**No Loss (N=1068)**	**Gain (N=328)**	**P-Value**
Demographics						
Age, yrs (median, 25th–75th)	67 (56– 76)	65 (54– 75)	68 (57– 77)	66 (56– 75)	67 (57– 76)	<.001
Female	1436 (34.4%)	266 (27.8%)	615 (33.8%)	421 (39.4%)	134 (40.9%)	<.001
Race Groups						<.001
White	2214 (53.1%)	576 (60.3%)	996 (54.8%)	459 (43.0%)	183 (55.8%)	
Black or African American	686 (16.4%)	184 (19.2%)	258 (14.2%)	162 (15.2%)	82 (25.0%)	
Asian	1027 (24.6%)	118 (12.3%)	451 (24.8%)	403 (37.7%)	55 (16.8%)	
Other	244 (5.8%)	78 (8.2%)	114 (6.3%)	44 (4.1%)	8 (2.4%)	
Baseline BMI (median, 25th–75th)	27 (24– 32)	30 (26– 35)	27 (24– 32)	26 (22– 30)	28 (24– 32)	<.001
Left Ventricular Ejection Fraction, previous 12 months (median, 25th–75th)	28 (20– 35)	25 (20– 37)	29 (20– 35)	27 (20– 35)	27(20– 40)	0.132
Baseline SBP (median, 25th–75th)	122 (110– 139)	124 (112– 140)	123 (110– 138)	120 (110– 138)	120 (110– 138)	0.017
Baseline DBP (median, 25th–75th)	74 (67– 83)	76 (67– 87)	74 (67– 82)	74 (69– 82)	72 (63– 81)	<.001
Baseline Heart Rate, bpm (median, 25th–75th)	82 (72– 95)	82 (71– 96)	82 (72– 95)	82 (72– 95)	80 (70– 92)	0.112
Baseline Weight, kg (median, 25th–75th)	78 (64– 95)	87 (74– 106)	76 (63– 92)	70 (58– 86)	79 (64– 97)	<.001
Clinical Profile						
Orthopnea	3215 (77.1%)	785 (82.1%)	1433 (78.8%)	744 (69.7%)	253 (77.1%)	<.001
Rales >1/3 lung fields						0.384
No Pulmonary Congestion	516 (12.4%)	129 (13.5%)	217 (11.9%)	128 (12.0%)	42 (12.8%)	
Less than 1/3 up lung fields	1361 (32.6%)	333 (34.8%)	592 (32.5%)	332 (31.1%)	104 (31.7%)	
Greater than or eq to 1/3 up lung fields	2295 (55.0%)	495 (51.7%)	1010 (55.5%)	608 (56.9%)	182 (55.5%)	

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		Weight Change Classification*			
Characteristic	**All Patients (N=4172)**	**Significant Loss (N=957)**	**Moderate Loss (N=1819)**	**No Loss (N=1068)**	**Gain (N=328)**	**P-Value**
JVD	2440 (58.5%)	609 (63.7%)	1128 (62.0%)	521 (48.8%)	182 (55.5%)	<.001
Peripheral Edema	3122 (74.8%)	870 (90.9%)	1381 (75.9%)	644 (60.3%)	227 (69.2%)	<.001
NYHA Classification						0.001
NYHA Class not assessed	722 (17.3%)	199 (20.8%)	309 (17.0%)	158 (14.8%)	56 (17.1%)	
I	175 (4.2%)	39 (4.1%)	81 (4.5%)	41 (3.8%)	14 (4.3%)	
II	669 (16.0%)	153 (16.0%)	275 (15.1%)	185 (17.3%)	56 (17.1%)	
III	1772 (42.5%)	389 (40.6%)	823 (45.2%)	428 (40.1%)	132 (40.2%)	
IV	834 (20.0%)	177 (18.5%)	331 (18.2%)	256 (24.0%)	70 (21.3%)	
Medical History						
History of Myocardial Infarction	1478 (35.4%)	307 (32.1%)	674 (37.1%)	378 (35.4%)	119 (36.3%)	0.075
History of Atrial Fibrillation/Flutter	1490 (35.7%)	380 (39.7%)	666 (36.6%)	331 (31.0%)	113 (34.5%)	<.001
History of Hypertension	3005 (72.0%)	715 (74.7%)	1311 (72.1%)	728 (68.2%)	251 (76.5%)	0.002
History of Diabetes Mellitus	1758 (42.1%)	430 (44.9%)	765 (42.1%)	407 (38.1%)	156 (47.6%)	0.003
History of Hyperlipidemia	1751 (42.0%)	406 (42.5%)	795 (43.7%)	378 (35.4%)	172 (52.4%)	<.001
Smoking History						<.001
Current Smoking	551 (13.2%)	132 (13.8%)	220 (12.1%)	146 (13.7%)	53 (16.2%)	
Prior History of Smoking	1507 (36.1%)	368 (38.5%)	704 (38.7%)	306 (28.7%)	129 (39.3%)	
No History of Smoking	2112 (50.6%)	455 (47.6%)	895 (49.2%)	616 (57.7%)	146 (44.5%)	
History of ICD/CRT	399 (9.6%)	104 (10.9%)	170 (9.3%)	90 (8.4%)	35 (10.7%)	0.257
History of Cerebrovascular Disease	509 (12.2%)	129 (13.5%)	219 (12.0%)	97 (9.1%)	64 (19.5%)	<.001
History of Peripheral Arterial Vascular Disease	452 (10.8%)	105 (11.0%)	198 (10.9%)	89 (8.3%)	60 (18.3%)	<.001
Medication at Baseline						
ACEI/ARB	2557 (61.3%)	597 (62.4%)	1122 (61.7%)	633 (59.3%)	205 (62.5%)	0.441
β-Blockers	2448 (58.7%)	558 (58.4%)	1115 (61.3%)	566 (53.0%)	209 (63.7%)	<.001
MRAs [Aldosterone Antagonists]	1109 (26.6%)	270 (28.2%)	498 (27.4%)	270 (25.3%)	71 (21.6%)	0.075

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		Weight Change Classification*				
Characteristic	All Patients (N=4172)	Significant Loss (N=957)	Moderate Loss (N=1819)	No Loss (N=1068)	Gain (N=328)	P-Value
Calcium Channel Blockers	527 (12.6%)	119 (12.4%)	248 (13.6%)	107 (10.0%)	53 (16.2%)	0.007
Nitrates	976 (23.4%)	225 (23.5%)	451 (24.8%)	223 (20.9%)	77 (23.5%)	0.124
Digoxin	1085 (26.0%)	232 (24.3%)	475 (26.1%)	298 (27.9%)	80 (24.4%)	0.267
Loop Diuretic Use (Doses in Furosemide Equivalents)						
Loop Diuretics [Chronically Before QE]	2643 (63.4%)	646 (67.6%)	1139 (62.6%)	622 (58.3%)	236 (72.0%)	<.001
Total Loop Diuretic Dose, chronically pre-qualifying episode (mg) (median, 25th–75th)	40 (40– 80)	60 (40– 80)	40 (40– 80)	40 (40– 80)	40 (40– 100)	<.001
Loop Diuretics [QE to Randomization]	3736 (89.6%)	853 (89.1%)	1627 (89.4%)	961 (90.1%)	295 (89.9%)	0.907
Loop Diuretic Dose, QE to Randomization (median, 25th–75th)	80 (40–120)	80 (40–120)	80 (40–120)	60 (40–80)	80 (40–120)	<.001
Loop Diuretics [QE to 24Hrs Post Randomization]	3868 (92.7%)	905 (94.6%)	1691 (93.0%)	971 (90.9%)	301 (91.8%)	0.014
Loop Diuretic Dose, QE to 24Hrs Post Randomization (median, 25th–75th)	140 (80–215)	160 (102–269)	140 (80–200)	120 (80–180)	140 (100–220)	<.001
Laboratory Values						
Baseline Creatinine, mg/dL (median, 25th–75th)	1.2 (1.0– 1.6)	1.3 (1.0– 1.7)	1.2 (1.0– 1.6)	1.2 (1.0– 1.5)	1.3 (1.0– 1.6)	<.001
Baseline GFR, ml/min (median, 25th–75th)	58 (44–75)	59 (43–74)	58 (44–75)	60 (46– 76)	57 (41– 73)	0.023
Baseline BUN, mg/dL (median, 25th–75th)	25 (18– 38)	26 (18– 39)	26 (18– 40)	23 (16–35)	27 (19–41)	<.001
Baseline sodium, mmol/L (median, 25th–75th)	139 (136–141)	139 (136–141)	139 (136–141)	139 (136–141)	139 (136–141)	0.294
Baseline Hemoglobin, g/dL (median, 25th–75th)	13 (11– 14)	13 (11– 14)	13 (11– 14)	13 (11– 14)	13 (11– 14)	0.736
Baseline NT-proBNP, pg/mL (median, 25th–75th)	4596 (2148–9403)	5211 (2744–10581)	4694 (2259–9579)	3797 (1772–7902)	3452 (1606–10379)	<.001
Baseline BNP, pg/mL (median, 25th–75th)	976 (524–1850)	1244 (721–2180)	988 (523–1775)	764 (415–1546)	914 (527–1891)	<.001

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		Weight Change Classification*				
Characteristic	**All Patients (N=4172)**	**Significant Loss (N=957)**	**Moderate Loss (N=1819)**	**No Loss (N=1068)**	**Gain (N=328)**	**P-Value**
Clinical Course						
Change in SBP (Baseline to 24Hrs), mmHg (median, 25th–75th)	−10 (−20– 0)	−10 (−20– 0)	−9 (−20– 0)	−10 (−20– 0)	−9 (−23– 0)	0.470
Change in DBP (Baseline to 24Hrs), mmHg (median, 25th–75th)	−6 (−14– 1)	−5 (−14– 2)	−6 (−14– 1)	−5 (−13– 0)	−6 (−16– 2)	0.820
Change in Creatinine (Baseline to 24Hrs), mg/dL (median, 25th–75th)	0.0 (−0.1– 0.2)	0.0 (−0.1– 0.1)	0.0 (−0.1– 0.2)	0.0 (−0.1– 0.2)	0.0 (−0.1– 0.2)	<.001
Urine Volume (Baseline to 24Hrs), mL (median, 25th–75th)	2300 (1600–3350)	3150 (2100–4500)	2300 (1625–3280)	1950 (1400–2638)	2000 (1350–2810)	<.001
LOS (median, 25th–75th)	5 (3–8)	7 (4–10)	5 (3–7)	4 (3–6)	4 (3–7)	<0.001

*Significant Loss: <−5kg; Moderate Loss: [−5kg, −1kg); No Loss: [−1kg, 1kg); Gain: ≥ 1kg.

Abbreviations: yrs = years; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; bpm = beats per minute; JVD = jugular venous distension; NYHA = New York Heart Association; ICD/CRT = implantable cardioverter defibrillator/cardiac resynchronization therapy; ACEI/ARB = angiotensin converting-enzyme inhibitor/angiotensin receptor blocker; MRA = mineralocorticoid receptor antagonist; QE = qualifying episode; GFR = glomerular filtration rate; BUN = blood urea nitrogen; NT-proBNP = amino terminal-b-type natriuretic peptide; BNP = b-type natriuretic peptide; LOS = length of stay.

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Table 2

Correlation Between Body Weight Change and Surrogates of Congestion at 24 Hours

Variable 1	Variable 2	$r^{\dagger}$	P-value
Change in Body Weight (kg)	Dyspnea Relief	−0.09600	<.0001
Change in Body Weight (kg)	Urine Output	−0.38100	<.0001
Dyspnea Relief	Urine Output	0.11100	<.0001

†Spearman's rank correlation coefficient.

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Table 3

Association between in-hospital weight change and 30-day outcomes

		> 1kg Weight Loss[1]		≤ 1kg Weight Loss or Weight Gain[1]	
Outcome	**Analysis**	**Odds Ratio (95% CI)**	**P-value**	**Odds Ratio (95% CI)**	**P-value**
30-Day Death / All Cause Rehosp	Unadjusted	0.99 (0.96–1.02)	0.642	1.18 (1.11–1.27)	<.001
	Adjusted	1.00 (0.97–1.04)	0.788	1.15 (1.08–1.22)	<.001
30-Day Death / HF Rehosp	Unadjusted	0.99 (0.95–1.03)	0.715	1.20 (1.12–1.30)	<.001
	Adjusted	1.01 (0.97–1.05)	0.483	1.16 (1.09–1.27)	<.001
30-Day Death	Unadjusted	0.97 (0.90–1.04)	0.391	1.27 (1.12–1.41)	<.001
	Adjusted	0.98 (0.91–1.05)	0.662	1.28 (1.14–1.43)	<.001
30-Day HF Rehosp	Unadjusted	1.00 (0.96–1.05)	0.857	1.16 (1.08–1.27)	<.001
	Adjusted	1.03 (0.98–1.08)	0.258	1.11 (1.02–1.22)	0.020

[1]Odds ratios reported with respect to a 1kg increase in in-hospital body weight

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Table 4

Association between in-hospital weight change and 180-day mortality

		> 1kg Weight Loss[1]		≤ 1kg Weight Loss or Weight Gain[1]	
Outcome	**Analysis**	**Hazard Ratio (95% CI)**	**P-value**	**Hazard Ratio (95% CI)**	**P-value**
180-Day Mortality	Unadjusted	0.99 (0.95–1.02)	0.383	1.08 (1.00–1.15)	0.053
	Adjusted	1.00 (0.97–1.03)	0.961	1.06 0.99–1.15)	0.086

[1]Hazard ratios reported with respect to a 1kg increase in in-hospital body weight.

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Table 5

Association between post-discharge weight change and 180-day mortality

		> 1kg Weight Gain[1]		≤ 1kg Weight Gain or Weight Loss[1]	
Outcome	**Analysis**	**Hazard Ratio (95% CI)**	**P-value**	**Hazard Ratio (95% CI)**	**P-value**
180-Day Mortality	Unadjusted	1.17 (1.11–1.23)	<.001	0.91 (0.88–0.95)	<.001
	Adjusted	1.16 (1.09–1.23)	<.001	0.93 (0.89–0.97)	<.001

[1]Hazard ratios reported with respect to a 1kg increase in post-discharge body weight.