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Comparison of Clinical Features and Outcomes of Patients Hospitalized with Heart Failure and Normal Ejection Fraction ($\geq 55\%$) –vs- Those with Mildly Reduced (40–55%) and Moderately to Severely Reduced ($< 40\%$) Fractions

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Abstract

Heart failure (HF) with normal ejection fraction (EF) is an increasingly common presentation of acute decompensated heart failure (ADHF). Differences between patients with HF and truly normal EF and those with mildly impaired EF have not been described. The Acute Decompensated Heart Failure Registry (ADHERE) contains information on over 100,000 heart failure hospitalizations and may provide insight into this distinction. The ADHERE database was used to investigate differences between patients hospitalized with heart failure and severely (EF $< 25\%$), moderately (EF 25–40%) and mildly reduced ejection fraction (EF 40–55%) vs. those with normal ejection fraction (EF $\geq 55\%$). The group with normal EF was 69% female with a mean age of 74 ($p < 0.017$ vs. all other groups). Coronary artery disease was less frequent in the normal EF group, and hypertension played a larger role. Patients with EF $\geq 55\%$ had elevated pulse pressure, suggesting a role for arterial stiffening. Treatment differed by ejection fraction. Creatinine increased ≥ 0.5 mg/dl more often in the group with HF and normal EF than the group with HF and severely reduced EF. In-hospital mortality and intensive care unit length of stay varied inversely with ejection fraction; overall length of stay was similar. In conclusion, patients with HF and normal EF are more likely to be female, have a history of high pulse pressure hypertension, less coronary artery disease and a lower risk of inpatient death but a higher likelihood of deterioration in renal function during hospitalization. These observations may be important considerations in the design of future clinical trials.

Studies of heart failure with normal ejection fraction (EF) utilize widely varying EF definitions from $\geq 40\%$ to $> 55\%$.^{1–3} This broad range may obscure important results by mixing different patient populations, particularly because patients with an EF in the 40–55% range may have both left ventricular (LV) systolic and diastolic abnormalities. Even patients with heart failure (HF) and normal EF, long thought to have normal LV systolic function with a primary

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abnormality of LV diastolic function, may have disturbed contractility.^{4–7} Patients with HF and truly normal EF ($\geq 55\%$) may differ importantly from patients with mildly reduced EF (40–55%). To test the hypothesis that these populations differ and to determine differences between patients with HF and normal EF, mildly depressed systolic function and significantly reduced ventricular function, we used the Acute Decompensated Heart Failure Registry (ADHERE) database to explore differences between hospitalized patients with HF and severely (EF $< 25\%$), moderately (EF 25–40%) and mildly reduced EF (40–55%), vs. those with truly normal ejection fraction (EF $\geq 55\%$).

Methods

The ADHERE protocol and data included in the registry have been previously described.¹² The ADHERE database is a multicenter registry providing observational data regarding patients hospitalized with acute decompensated heart failure (ADHF). Data for this analysis were derived from 274 sites. ADHF was defined as hospitalization for either new-onset HF or decompensation of chronic established HF. Data were collected on consecutive eligible adult patients by retrospective chart review, and included information on demographics, medical history, clinical presentation, medical therapy both prior to and in the hospital, and hospital course including procedures, in-hospital outcomes, and disposition. Medical history was recorded as noted in the chart. For example if it was noted in the chart that a patient had a history of hyperlipidemia, dyslipidemia, or abnormal cholesterol, this was coded as hyperlipidemia. Specific levels of cholesterol were not required. Likewise, a patient who was noted to have a history of coronary artery disease, either clinically or angiographically, was coded as “CAD”. No documentation of these diagnoses was required of the abstractor. Ejection fraction could be determined by echocardiography, nuclear ventriculography or ventricular angiography. Institutional review board approval was required from each site for participation with de-identified data collection so that individual patient consent was not necessary. Identifiers were assigned by hospitalization, so that a single patient with multiple hospitalizations is coded as separate events. No information was collected beyond the point of hospital discharge; data on readmission and out of hospital clinical events are unknown.

The study population included all patients enrolled in the Acute Decompensated Heart Failure Registry (ADHERE) as of January 1, 2004. Patients were excluded if there was no documentation of quantitative EF assessment, either during or prior to index hospitalization. The remaining patients were divided by ejection fraction into a group with normal EF ($\geq 55\%$), a group with mildly reduced EF (≥ 40 and $<55\%$), a group with moderately reduced EF (≥ 25 and $<40\%$) and a group with severe LV systolic dysfunction (EF $< 25\%$). Patients in the 4 groups were compared with respect to demographics, medical history, clinical characteristics at presentation, oral medication use prior to hospitalization and inpatient medication use, both intravenous and oral. In addition, important events during the hospital course, such as ICU stay, weight change, hospital length of stay and in-hospital mortality were examined.

Characteristics of the group with HF and normal EF were compared to those of the groups with decreased EF using one-way ANOVA and Wilcoxon tests for continuous variables and chi-square tests for categorical variables. Two-sided p values are reported. To adjust for multiple comparisons, only p-values < 0.017 are considered statistically significant. Records with missing data were excluded from relevant analyses. Most variables had $< 0.01\%$ of data missing, but exceptions included insurance and blood pressures ($< 1\%$ missing), creatinine (2% missing), race (3% missing), thyroid disease (10% missing), weight and QRS duration (12% missing) and body mass index (32% missing). Heart failure etiology was not recorded for 46% of hospitalizations with history of HF. Use of centrally acting antihypertensives during hospitalizations was not recorded in 51% of the cases. At discharge, blood pressure data were

missing in 15% of records, change in weight in 38% of records and change in creatinine in 54% of records.

Results

105,388 admissions were reviewed. Quantitative EF assessment during or prior to index hospitalization was available in 74,863 (71.0%) of these admissions: 17,022 with EF $\geq 55\%$, 17,045 with EF 40–55%, 21,195 with EF 25–40%, and 19,601 with EF $< 25\%$. In the remaining patient hospitalizations, 10,407 (9.9%) had only qualitative assessment and 20,118 (19.1%) had no documented EF assessments. Data from these patients were not used in this analysis.

Differences in demographics and medical history are described in Table 1. The percentage of women increased more than two-fold as ejection fraction increased. While the majority of patients in both higher EF groups were female, the female preponderance was significantly greater in the group with EF $\geq 55\%$. All groups were elderly and age also increased significantly as EF rose. Approximately 70% of patient episodes occurred in Caucasians. African Americans were more likely to have lower EF. Weight and body mass index rose steadily with EF. The groups with the highest and lowest ejection fractions were less likely to have hyperlipidemia, or peripheral vascular disease as compared to the middle EF groups.

Most patients in all groups had a history of hypertension, but the proportion with hypertension was greatest in the HF and normal EF group. Patients with normal EF were less likely to have a history of HF or coronary artery disease compared to the other groups (Figure 1A). Of the 56,977 hospitalizations with a history of HF included in this analysis, an underlying HF etiology was identified by treating clinicians in only 30,557 (53.6%) cases. Etiology was identified less often in the higher EF groups. The normal EF group was less likely to have an ischemic etiology and more likely to have hypertensive etiology than other groups (Figure 1B). Among patients with EF 40–55% or EF $\geq 55\%$, the largest contrast in etiology of HF was between men with mildly reduced EF (18% with hypertensive and 54% with ischemic etiology) and women with HF and normal EF (30% with hypertensive, 26% with ischemic etiology).

Patients in all but the lowest EF group tended to be hypertensive on presentation (Table 2). Patients with HF and normal EF had the highest systolic blood pressure and low diastolic blood pressure on admission, on average, giving them a higher mean pulse pressure than all other groups (Table 2). Blood pressure and pulse pressure were lower at discharge than admission in all groups, but the trend observed at admission remained: mean pulse pressure at discharge increased with EF and was highest in the HF and normal EF patients (all $p < 0.0001$, Table 4).

Intravenous medication use during HF hospitalizations is shown in Figure 2. Parenteral diuretic therapy was used equally in the two highest EF groups, and slightly less in the patients with lower EF. Intravenous vasoactive medications (both vasodilatory and inotropic) were used less often in the HF and normal EF group than in other groups. Although the percentage was low (6.3%), over 1000 patients with HF and normal EF received inotropic therapy while in the hospital. Oral medications prescribed during hospitalization are shown in Table 3. Compared to HF and normal EF patients, those in all other groups, including those with EF 40–55%, were more likely to be prescribed medications known to reduce cardiovascular mortality in ischemic heart disease and in HF with reduced EF, such as ACE inhibitors, aspirin, beta blockers, and lipid lowering drugs. Patients with EF $\geq 55\%$ were more likely to receive angiotensin receptor blockers, calcium channel blockers, and centrally acting antihypertensives. Chronic outpatient therapy patterns were qualitatively similar to those shown for oral medications in the hospital.

Baseline creatinine was lowest in the HF and normal EF group; these patients were less likely to have a history of renal insufficiency than other groups. However, increased creatinine by 0.5 mg/dl or more occurred as frequently in the HF and normal EF group as in the two middle

EF groups, and more often than in the group with the lowest EF (Table 4). The HF and normal EF group lost less weight than the other EF groups. In-hospital mortality steadily increased as EF fell with statistically significant differences observed between HF and normal EF and both groups with EF < 40%, as reported previously.¹³ Only minor differences were observed in median hospital length of stay among the four groups.

Discussion

These data, from >74,000 episodes of hospitalization for ADHF, demonstrate that patients with truly normal EF hospitalized with ADHF differ from patients with mildly reduced ventricular function and those with lower EF. Studies of HF and normal EF often include patients with EF as low as 40%.^{3,13} Our study was focused on HF patients with higher EF, in an attempt to determine whether the group of patients with truly normal EF is similar enough to those with mildly reduced EF to justify grouping them together in clinical trials of HF and normal EF. Epidemiologic studies of HF and normal EF have focused on patients with EF >50%. The impact of including patients with EFs lower than 50% in clinical trials of HF is difficult to assess based on available epidemiologic studies and our data help clarify some of the differences between the population with normal EF and those with mildly reduced EF.

A prior analysis from ADHERE¹³ demonstrated increased mortality and length of stay in hospital admissions for ADHF when EF was $\leq 40\%$ vs. EF >40%. This analysis included only hospitalizations during which the EF was assessed, and made no comparisons between patients with EF <55% and those with EF $\geq 55\%$. In that analysis, systolic hypertension was noted in patients with preserved systolic function, but pulse pressure was not examined.

In our analysis, as in many prior analyses, patients with normal EF were more often female, were definitely older and had a lower incidence of coronary disease than those with HF and lower EFs.^{14–18} While studies demonstrate an increasing prevalence of African Americans in hypertensive HF and normal EF populations relative to controls, our study shows that nationally African Americans with HF are more likely to have lower EF. Significant differences were found in many parameters between the patients with the highest EFs and those with lower EFs. No conclusions can be drawn from these data, but they suggest potentially important areas to explore in future studies, such as the impact of lung disease, stroke index and right ventricular dysfunction on symptoms. Importantly, patients with EF $\geq 55\%$ also have elevated pulse pressure; this observation suggests that decreased vascular compliance may play an important pathophysiologic role in the genesis of HF in the highest EF group.

Our data also confirm that patients with normal EF are treated differently, both in the hospital and as outpatients, when compared with patients with mildly, moderately and severely reduced EF, which may be appropriate given the absence of data in this population. When hospitalized with HF, they are less likely to be treated with vasoactive medications, including vasodilators, despite the fact that they have higher systolic blood pressure on presentation. A surprising number are treated with inotropic agents. This suggests a quality of care issue that merits further study. The observed pattern of medication use reflects the absence of data in HF and normal EF and the differing opinions about the optimal therapy for this condition. Inclusion of patients with EF 40–55% with those with normal EF in clinical trials of HF and normal EF may introduce treatment biases related to background therapy.

More patients with HF and normal EF experienced an increase in creatinine during the hospitalization than in the severely depressed EF group, despite a lower rate of pre-existing recognition of renal insufficiency. However, the rate of increased creatinine in the group with HF and normal EF was not different from those with HF and mildly or moderately reduced EF. It is interesting to speculate on possible reasons for this. There may be under-recognition

of renal impairment in the elderly group with normal EF, many of whom may have lower muscle mass. Alternatively, inaccurate assessment of the extent of volume overload and failure to appreciate critical pressure-volume relationships in smaller non-compliant ventricles may play a role. The potential for increased pulse pressure to contribute to worsening renal function is supported by recent studies.^{19,20} Finally, worsening creatinine may lead to early stopping of diuretics contributing to less fluid removal in the HF with normal EF, however this was not seen in the groups with EF 25–40% and 40–55%, who had similar rates of increased creatinine to the normal EF group. Those with HF and normal EF lost the least weight in the hospital, suggesting that these patients were less volume expanded than HF patients with severely reduced EF. Mechanistic conclusions from these data remain speculative. Inpatient mortality risk increases steadily as EF falls, which is consistent with a prior report from the ADHERE database.¹³

While demographics and echocardiographic features have previously been described in smaller groups of patients with HF and normal EF, typically geographically localized groups^{13,14,18} or trial populations,²¹ this is the first national snapshot of this important group of patients to distinguish between those with truly normal and those with mildly impaired EF. It provides information on the group of patients with EF of 40–55%, often included in clinical trials, but in large part excluded from epidemiologic descriptions of patients with HF and normal EF.

There are limited clinical trial data regarding HF and normal EF. In the Candesartan in Heart failure Assessment of Reduction in Mortality and morbidity (CHARM) programme, the CHARM-Preserved study³ demonstrated a non-significant benefit of angiotensin receptor blockade with candesartan on mortality and heart failure hospitalizations in patients with heart failure and an ejection fraction >40%. The CHARM study population was 60% male with an average age of 67 and an average ejection fraction of 54%. Over 50% of enrolled patients had an ischemic etiology of heart failure, with 22% having a hypertensive etiology. Inclusion of subjects with ejection fractions as low as 40% may have reduced the number of women included, lowered the average subject age and increased the patient heterogeneity. Recent data from the CHARM study also demonstrate a very heterogeneous group as determined by echocardiography. Despite having a diagnosis of HF and normal EF, 33% had normal diastolic function by echo.²¹ Our study would suggest that inclusion of patients with mild LV dysfunction would also change the baseline pharmacologic treatment profile. Clearly a more effective strategy for identification of appropriate HF and normal EF patients for study is necessary.

The ADHERE data are taken from an observational registry of patients hospitalized for heart failure; the data are collected by retrospective abstraction of medical charts. These data must be interpreted as provocative and hypothesis generating, but not definitive. Entry into the registry is based on diagnostic coding in participating hospitals, which may be incomplete or inaccurate. No tests or treatments are prescribed. Even small, clinically insignificant differences can be statistically significant due to the large number of records in the database. We are limited in our analysis to information prospectively identified for collection into the database. Some information important in the group of patients with normal systolic function was not prospectively identified for inclusion, including use of non-loop oral diuretic therapy, method and timing of ejection fraction assessment, and information regarding echocardiographic features of interest in this population, such as left ventricular hypertrophy and measures of diastolic function. Data regarding ventricular function are recorded by the site coordinator from the clinical record. Measurement of ejection fraction was performed if deemed clinically indicated by the treating physicians. Although most assessments were echocardiographic, data from nuclear ventriculography and angiographic ventriculograms are also included. In addition, a minority of the assessments of ejection fraction included in this study (30%) were performed prior to the index hospitalization. Because study entry is based

on hospitalization rather than individual patients, patients being rehospitalized are included in the dataset. In many of these patients with recent assessment of ejection fraction, a repeat assessment may not be clinically indicated. Thus, the recorded ejection fraction, particularly when performed prior to the current hospitalization, may not be truly representative of ventricular function during the hospitalization. Although this may introduce imprecision into the dataset, it does provide a realistic snapshot of actual clinical practice.

As the ADHERE registry contains no longitudinal outcomes data, no conclusions regarding the long-term natural history of HF and normal EF can be drawn from these findings. Nevertheless, these data do segregate the different populations of heart failure patients with various iterations of reduced vs. normal systolic function.

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Figure 1.

A. Prevalence of a history of hypertension and history of coronary artery disease stratified by ejection fraction (EF) in the ADHERE population. B. Heart failure etiology was identified in the minority of cases in the ADHERE registry. Shown is attribution of heart failure etiology to hypertension or ischemic heart disease in patients in whom an etiology was identified. * = $p < .017$ compared to EF $\geq 55\%$ group.

Figure 2.

Use of intravenous medications to treat heart failure in the ADHERE populations stratified by ejection fraction. Diuretic use was high in all groups, but slightly greater in the two higher EF groups than in the two lower EF groups. Both inotropic and IV vasodilator medications were used significantly less often in the group with EF ≥ 55% than in all other groups. * = $p < .017$ compared to EF ≥ 55% group.

TABLE 1

PATIENT CHARACTERISTICS

Variable	< 25% (n = 19,601)	Ejection Fraction		
		25–40% (n = 21,195)	40–55% (n = 17,045)	≥ 55% (n = 17,022)
Mean Age, years	67.8 ± 14.7 ^{*†‡}	71.8 ± 13.5 ^{*†}	73.8 ± 12.9 [*]	74.3 ± 13.3
Female	6592 (33.6%) ^{*†‡}	9247 (43.6%) ^{*†}	9249 (54.3%) [*]	11821 (69.4%)
Caucasian	13059 (68.6%) ^{*†‡}	15376 (75.0%) ^{*†}	12882 (78.1%) [*]	12697 (77.2%)
Black	5026 (26.4%) ^{*†‡}	4165 (20.3%) ^{*†}	2907 (17.6%) [*]	3088 (18.8%)
Weight, (pounds)	179.2 ± 49.6 ^{*†‡}	180.8 ± 51.1 ^{*†}	185.6 ± 54.5 [*]	186.8 ± 58.0
Body Mass Index, (kg/m ²)	27.7 ± 6.8 ^{*†‡}	28.6 ± 7.2 ^{*†}	29.9 ± 7.9 [*]	31.0 ± 8.7
Medicare Insurance	12442 (63.9%) ^{*†‡}	15033 (71.4%) ^{*†}	12675 (74.8%) [*]	12911 (76.3%)
Coronary Artery Disease	11980 (61.1%) ^{*†‡}	13808 (65.1%) ^{*†}	10177 (59.7%) [*]	7990 (46.9%)
Valvular Disease	4825 (24.6%) [*]	5206 (24.6%) [*]	4232 (24.8%) [*]	3942 (23.2%)
Hyperlipidemia	6965 (35.5%) ^{*†‡}	8494 (40.1%) ^{*†}	6485 (38.0%) [*]	5720 (33.6%)
Diabetes Mellitus	7605 (38.8%) ^{*†‡}	9513 (44.9%) ^{*†}	8137 (47.7%) [*]	7566 (44.4%)
Peripheral Vascular Disease	3250 (16.6%) ^{*†‡}	4172 (19.7%) [*]	3391 (19.9%) [*]	2913 (17.1%)
Stroke/Transient Ischemic Attack	2992 (15.3%) ^{*†‡}	3554 (16.8%) ^{*†}	3075 (18.0%) [*]	2897 (17.0%)
Chronic Obstructive Pulmonary Disease/Asthma	5613 (28.6%) ^{*†}	6234 (29.4%) ^{*†}	5377 (31.5%) [*]	5828 (34.2%)
Atrial Fibrillation	5559 (28.4%) ^{*†‡}	6292 (29.7%) ^{*†}	5608 (32.9%) [*]	5402 (31.7%)
Renal Insufficiency	5986 (30.5%) [*]	6621 (31.2%) [*]	5269 (30.9%) [*]	4610 (27.1%)
Chronic Dialysis	572 (2.9%) ^{*†‡}	859 (4.1%) [*]	713 (4.2%) [*]	675 (4.0%)
Creatinine, [†] (mg/dL)	1.4 (1.1, 1.9) ^{*†‡}	1.4 (1.0, 1.9) [*]	1.3 (1.0, 1.9) [*]	1.2 (0.9, 1.7)
Creatinine > 2.0 (mg/dL)	3812 (19.9%) [*]	4312 (20.7%) [*]	3386 (20.2%) [*]	2923 (17.4%)
Current Smoker	3511 (17.9%) ^{*†‡}	3076 (14.5%) ^{*†}	2062 (12.1%) [*]	1810 (10.6%)
Thyroid Disease	2617 (14.9%) ^{*†}	2960 (15.5%) ^{*†}	2817 (18.2%) [*]	3150 (20.1%)
QRS Duration, [†] (msec)	122 (98, 160) ^{*†‡}	110 (92, 146) ^{*†}	100 (86, 130) [*]	90 (80, 110)

Values are expressed as either mean ± SD or as n (percent). Abbreviations: CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease, TIA: transient ischemic attack.

* Significantly different from normal EF group at p<0.017 level.

[†] Significantly different from EF 40–55% group at p<0.017 level.

[‡] Significantly different from EF 25–40% group at p<0.017 level.

[†] Creatinine and QRS duration are expressed as median (Q1, Q3 (interquartile range))

TABLE 2
BLOOD PRESSURE (mmHg) AT PRESENTATION

Variable	Ejection Fraction			
	< 25% (n = 19,601)	25–40% (n = 21,195)	40–55% (n = 17,045)	≥ 55% (n = 17,022)
Systolic blood pressure, (mmHg)	129 ± 29 ^{*†‡}	143 ± 31 ^{*†}	150 ± 33 [*]	152 ± 33
Diastolic blood pressure, (mmHg)	77 ± 19 ^{†‡}	79 ± 21 [*]	79 ± 21 [*]	77 ± 20
Pulse pressure, (mmHg)	53 ± 20 ^{*†‡}	63 ± 22 ^{*†}	71 ± 25 [*]	75 ± 26

Values are expressed as mean ± SD.

* Significantly different from normal EF group at p<0.017 level.

[†] Significantly different from EF 40–55% group at p<0.017 level.

[‡] Significantly different from EF 25–40% group at p<0.017 level.

TABLE 3

ORAL MEDICATIONS PRESCRIBED

Medication	< 25% (n = 19,601)	Ejection Fraction		≥ 55% (n = 17,022)
		25–40% (n = 21,195)	40–55% (n = 17,045)	
ACE Inhibitors	13095 (66.8) [*] ^{†‡}	13652 (64.4) [*] [†]	9724 (57.1) [*]	8628 (50.7)
Angiotensin Receptor Blocker	2570 (13.1) [*] [†]	2930 (13.8) [*]	2502 (14.7) [*]	2687 (15.8)
Aspirin	11500 (58.7) [*] ^{†‡}	12972 (61.2) [*] [†]	9898 (58.1) [*]	9076 (53.3)
Beta Blocker	13274 (67.7) [*] [†]	14235 (67.2) [*] [†]	10597 (62.2) [*]	9363 (55.0)
Calcium Channel Blocker	2064 (10.5) [*] ^{†‡}	4173 (19.7) [*] [†]	5198 (30.5) [*]	6603 (38.8)
Centrally Acting Antihypertensives	324 (3.5) [*] ^{†‡}	586 (5.7) [*] [†]	768 (9.1)	874 (10.2)
Lipid Lowering	6421 (32.8) [*] ^{†‡}	8079 (38.1) [*] [†]	6151 (36.1) [*]	5323 (31.3)
Nitrate	8850 (45.2) [*] ^{†‡}	10975 (51.8) [*]	8856 (52.0) [*]	8163 (48.0)

Values are expressed as n(%). Abbreviations: ACE: angiotensin converting enzyme.

* Significantly different from normal EF group at p<0.017 level.

[†] Significantly different from EF 40–55% group at p<0.017 level.

[‡] Significantly different from EF 25–40% group at p<0.017 level.

TABLE 4

PATIENT OUTCOMES

Outcome	Ejection Fraction			
	< 25% (n = 19,601)	25–40% (n = 21,195)	40–55% (n = 17,045)	≥ 55% (n = 17,022)
Systolic BP at discharge, (mmHg)	114 ± 20 ^{*†‡}	123 ± 21 ^{*†}	129 ± 22 [*]	131 ± 23
Diastolic BP at discharge, (mmHg)	66 ± 13 ^{*†‡}	67 ± 13	67 ± 13 [*]	66 ± 13
Pulse pressure at discharge, (mmHg)	49 ± 16 ^{*†‡}	56 ± 18 ^{*†}	62 ± 19 [*]	65 ± 19
Increase in Creatinine of >0.5 mg/dl during hospitalization	1046/8657 (12.1) ^{*†‡}	1408/9585 (14.7)	1185/7946 (14.9)	1232/8111 (15.2)
Weight change assessed	12,264 (62.6) [*]	13,114 (61.9) [*]	10,555 (61.9) [*]	10,267 (60.3)
Weight Change, lbs	−7.0 ± 10.2 ^{*†‡}	−6.6 ± 9.6 [*]	−6.4 ± 9.8 [*]	−6.1 ± 9.4
Mortality	929 (4.7) ^{*†‡}	744 (3.5) [*]	537 (3.2)	509 (3.0)
ICU/CCU Admissions	4730 (24.1) ^{*†‡}	4430 (20.9) ^{*†}	3233 (19.0) [*]	2820 (16.6)
ICU/CCU LOS, days	3.0 (1.6, 5.0) ^{*†‡}	2.5 (1.4, 4.5)	2.6 (1.4, 4.6)	2.5 (1.3, 4.8)
Total Hospital LOS, days [†]	4.8 (3.0, 7.7) ^{*†‡}	4.5 (2.9, 7.2) [†]	4.7 (3.0, 7.3)	4.6 (3.0, 7.2)

Values are expressed as either mean ± SD or as n (percent). Abbreviations: BP: blood pressure, CCU: coronary care unit, ICU: intensive care unit, LOS: length of stay.

* Significantly different from normal EF group at p<0.017 level.

[†] Significantly different from EF 40–55% group at p<0.017 level.

[‡] Significantly different from EF 25–40% group at p<0.017 level.

[†] Hospital LOS and ICU/CCU LOS are expressed as median (Q1, Q3 (interquartile range))