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Patient Journey after admission for acute heart failure: length of stay, 30-day readmission and 90-day mortality

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Abstract

The course of patients after and admission for acute heart failure (AHF), especially length of initial hospital stay (LOS), rate of early readmission and death are of major importance to patients and health providers. We explored these outcomes in 1,990 patients enrolled in the PROTECT study.

Methods: The PROTECT study examined the effect of the adenosine blocker rolofylline in patients within 24 hours of admission for AHF with mild to moderate renal impairment. We examined predictors and associations of LOS, 30-day readmission and 90-day mortality in the study.

Results: LOS was only partially predicted by severity of HF and other background morbidities at baseline (diabetes mellitus, renal impairment, ischemic heart disease) as well as severity of metabolic dysfunction (cholesterol and albumin) at baseline and their changes during the first days of admission. Occurrence of in-hospital worsening heart failure (WHF) was associated with significant increase in LOS. Thirty-day readmissions and especially HF readmissions were associated with more severe HF and previous HF admission but not with LOS. Death within 90 days after discharge was associated with older age, more severe HF, worse renal function and lower sodium and bicarbonate at admission. LOS was a strong predictor of 90-day post-discharge mortality.

Conclusions: In patients admitted for AHF, LOS is not well-predicted by traditional markers of disease severity, but strongly associated with the occurrence of in-hospital WHF. After discharge, early readmissions are mostly predicted by previous HF admissions and severity of HF, while 90-day mortality is more strongly associated with HF severity, renal impairment and advanced age. Longer LOS is a strong predictor of early mortality even after discharge but not of readmissions. These findings may help focus efforts to reduce LOS and post-discharge outcomes on patients' subgroups at increased risk. Hospitalization for acute heart failure (AHF) is a major cause of morbidity and mortality and a significant burden on healthcare systems worldwide [1] [2]. The patients' journey after being admitted encompasses several important possible outcomes including a long length of stay (LOS) during the initial hospitalization, followed by a high risk for repeat readmissions (most of which are for heart failure) and an increased risk of death [2]. Although all of these outcomes have been examined as measures of treatment success and, in some jurisdictions suggested as surrogate measures of hospital performance, they tend to vary substantially, especially among countries and geographic regions [3-6], and, given a lack of understanding of their predictors, tools to influence these outcomes globally are missing. This is especially true for LOS, where uncertainty surrounds what constitutes the optimal length of stay, given that some studies suggest that short LOS may be associated with a higher rate of readmission or even death [7, 8]. To better understand the implications of predictors of these outcome measures and differences in LOS across different countries, we studied patient outcomes in hospital and up to 90 days after admission, adjusted for regional LOS disparities, among the 1,990 patients with AHF enrolled within 24h of admission into the Placebo-controlled Randomized study of the selective A1 adenosine receptor antagonist KW-3902 for patients hospitalized with acute HF and volume Overload to assess Treatment Effect on Congestion and renal function (PROTECT)[9].

Methods:

Inclusion Criteria and Study Design: PROTECT was initially designed as two identical, concurrent randomized, placebo-controlled trials (PROTECT-1 and PROTECT-2; ClinicalTrials.gov numbers, NCT00328692 and NCT00354458, respectively), which were then combined for analysis. The design and main results of PROTECT have been published [9], [10]. Patients with pre-existing heart failure, mild or moderate renal impairment (estimated creatinine clearance, 20–80 mL/min), increased plasma concentrations of brain natriuretic peptides, and dyspnea at rest or minimal exertion associated with

symptoms and signs of volume overload requiring intravenous diuretic therapy, were enrolled within 24 hours of admission. The protocol was approved by the ethics committee at each participating center, and patients provided written informed consent.

During the initial hospitalization, patients were assessed daily through the earlier of day 7 or discharge, followed up on day 14, and then contacted by telephone to identify death and readmission up to day 60 and to assess vital status alone at day 180. Investigators reported the occurrence of worsening heart failure (WHF) during the initial hospitalization based on worsening signs or symptoms of heart failure leading to intensification of HF-directed therapy. Samples for central laboratory assessment of chemistry and hematology were drawn daily through day 4 and then at day 7. Results of primary and secondary end points of PROTECT have been reported in detail. [9] For the purposes of this analysis, the following outcomes were considered: length of initial hospital stay, 30-day post-discharge all-cause readmission, 30-day post-discharge heart failure readmission, and 90-day post-discharge all-cause mortality.

Statistical Methods: Patients in the intention-to-treat analysis set were excluded who were missing information about whether or not the patient had died during the initial hospital stay and therefore were missing a record for LOS. Length of stay is presented by patient status (survived or died during initial hospital stay) and by geographical region, showing means, standard deviations, medians, and first and third quartiles. For all subsequent analyses, patients who died during the initial hospital stay have been excluded. Because readmissions were assessed only through 60 days after baseline, patients with a LOS longer than 30 days were further excluded from analyses of 30-day post-discharge readmissions.

The following endpoints were considered for analysis: (i) LOS, (ii) 30-day post-discharge all-cause readmission, (iii) 30-day post-discharge HF readmission, and (iv) 90-day post-discharge all-cause mortality. Baseline characteristics are presented for patients who survived to discharge and further

categorized as having a short, medium, or long LOS (supplementary tables). This categorization was determined based on the first and third tertiles within geographic region, which were 4 and 7 days in North America, 4 and 6 days in Israel, 8 and 13 days in Western Europe, 7 and 10 days in Eastern Europe, 4 and 6 days in Argentina, and 15 and 18 days in Russia. Baseline characteristics are further presented by all-cause readmission up to 30 days after discharge, by HF readmission up to 30 days after discharge, and by all-cause mortality up to 90 days after discharge (supplementary tables). For continuous baseline variables means, standard deviations, medians, and first and third quartiles are presented and differences between groups are compared using ANOVA F-tests. For discrete baseline variables absolute and relative frequencies are presented and proportions are compared between groups using chi-square tests.

Univariable and multivariable associations between baseline characteristics and each endpoint were assessed using linear regression (for LOS), logistic regression (for 30-day post-discharge readmission endpoints), and Cox proportional hazards models (for 90-day post-discharge mortality). Multivariable models were developed using a common approach. Non-linearity of the association between each continuous predictor and the outcome was assessed through testing the significance of non-linear components of a restricted cubic spline transformation. Plots of the predicted outcome against the value of the predictor and values of Akaike's Information Criterion (AIC) were used to select non-linear transformations where needed. From the 44 baseline variables considered (presented in the supplementary tables), four parameters (pulse pressure, mean arterial pressure, eGFR, and BUN/creatinine ratio) were excluded from further consideration due to correlation and/or collinearity issues. Multiple imputation assuming multivariate normality was used for missing predictors; the proportion missing each covariate is given in the supplementary tables. In each of the 10 imputed data sets, backwards selection was performed at a 0.05 significance level for linear regression and a 0.10 significance level for Cox and logistic regression models. Predictors selected in at least six of the ten

imputed data sets were included in the final overall multivariable model. Estimated effect sizes, confidence intervals and p-values were obtained by averaging across the imputation datasets using Rubin's algorithm.[11] Model performance was assessed through adjusted R-squared for linear regression models and through C-statistics for logistic regression and Cox proportional hazards models. C-statistics for Cox regression were computed using Harrell's method. [12, 13] Observed adjusted Rsquared and C-statistics were averaged across the 10 imputed data sets and further examined by obtaining bias-corrected estimates and corresponding confidence intervals using bootstrapping.

A multivariable-adjusted estimate of the association between LOS and the outcome of interest was obtained by adding the LOS as a predictor in the multivariable model. The occurrence of WHF up to day 7 after baseline was then added to evaluate whether any association between LOS and the outcome might be explained by WHF. In addition, changes from baseline to day 2 for certain laboratory parameters (albumin, AST, cholesterol, and creatinine) as well as for weight were added both individually and all at once into the model to determine how these parameters affect the association between LOS and the outcome of interest. Differences between models with added parameters were examined by obtaining bootstrap estimates and confidence intervals for the differences in adjusted Rsquared or C-statistics. All models were either adjusted or stratified by geographic region.

The rate of HF readmission as a function of days after discharge was evaluated using Poisson regression. Patients were considered at risk until the first readmission for HF, last follow-up, or death. Due to the low number of events per day post-discharge, the model was not adjusted by geographic region.

SAS® version 9.3 (SAS Institute, Cary, NC, USA) software was used for all analyses.

Results:

Between May 2007 and January 2009, 2033 patients were enrolled in PROTECT. . Of the 2021 patients in the intention-to-treat analysis set, 31 were excluded from analysis for whom deaths could not be classified as having occurred or not during the initial hospitalization. Therefore, no LOS value was available for these patients. For further analysis of LOS and all post-discharge endpoints, 88 patients who did not survive to discharge were excluded from the set of 1990 patients, leaving 1902 patients for analysis. For analysis of 30-day post-discharge readmissions, additional 53 patients whose LOS was > 30 days were excluded, leaving 1849 patients for analysis.

LOS: Length of stay (LOS) for patients who did and did not survive the initial hospitalization is presented by geographic region in table 1. Baseline characteristics of patients discharged alive by LOS categories (short, intermediate and long) are presented in Supplementary table 1. Univariable and multi variable associations of baseline characteristics with LOS are presented in table 2a. Variables associated with shorter length of stay included male sex, history of HF, and higher systolic blood pressure, WBC, albumin and cholesterol (up to 4.5 mg/dl). Variables associated with longer LOS included history of angina pectoris, history of diabetes mellitus, higher BMI, higher heart rate (above 90 beats per minute at admission), more orthopnea and higher JVP, and higher BUN and Uric acid. In general the model had poor to modest ability to predict LOS in patients with AHF, with a bias-corrected adjusted R-square of 0.27. Adding to the model changes occurring during the first days of admission that representing congestion and end organ damage – such as AST, weight and creatinine changes, previously shown to be associated with post-discharge outcomes in protect [14] did not significantly improve the model. However, changes in markers of metabolic abnormalities such as Cholesterol and albumin and especially the occurrence of in-hospital WHF through day 7 increased the bias-corrected adjusted R-squared to 0.32 (95% CI 0.27, 0.35) which constitutes a significant increase of 0.050 (95% CI 0.028, 0.072), (table 2b). Mean LOS was 15.2 days in patients with in-hospital WHF versus 9.8 days in patients without inhospital WHF.

Readmission within 30 days after discharge: Baseline characteristics for patients who were or were not readmitted in the first 30 days post discharge are presented in supplemental table 2a, and baseline characteristics for patients readmitted for HF during the first 30 days after discharge are presented in supplemental table 2b. The HF readmission rate tended to follow a quadratic pattern of early increase during the first few days after discharge followed by a decrease (p=0.0458, figure 1). Multivariate predictors of all cause readmission 30 days after discharge were diabetes mellitus, presence of orthopnea but lack of edema and increased BUN (Table 3a). The bias-corrected C-index for the model was 0.68 suggesting that the model had low predictive value. Longer LOS was borderline significant predictor for increased rate of all cause readmissions after discharge (p=0.0525) without improving the c-index of the model.

Previous HF admission, orthopnea at admission, lower sodium, higher BUN and higher albumin were associated with an increased risk for HF readmission within 30 days after discharge (table 3b). The biascorrected C-index for this model was higher (0.74) than for all-cause readmission. Neither LOS nor occurrence of WHF were significantly associated with higher rates of 30-day post-discharge readmission and did not add predictive value to the model. Cumulative risks of post-discharge HF readmission by history of HF admission prior to the initial admission are presented in figure 2.

90-day post-discharge mortality: Baseline characteristics of patients who died within 90 days of discharge are presented in supplemental table 3. Older age, history of lung disease, lower systolic blood pressure at admission, higher WBC count, lower sodium and bicarbonate and higher BUN and uric acid were associated with increased risk of mortality 90 days post discharge. Longer LOS, up to 14 days was associated with higher 90-day post-discharge mortality and this association persisted even after adjustment for WHF (table 4) as well as changes in albumin, AST, cholesterol, creatinine, and weight to day 2 (table 5). The model has modest discrimination for the outcome (bias-corrected c-index = 0.73).

Discussion

The journey of patients admitted for acute heart failure (AHF) through the hospitalization and early post-discharge period has been of significant interest in recent years as AHF has become an increasingly common cause for hospital admission [1] and admission for AHF is a large driver of the health cost associated with HF. Therefore, determining the drivers of longer LOS and, for patients being discharged alive, the drivers for early readmission and death has gained substantial importance.

Length of the initial hospital stay has been difficult to analyze because of its extreme variation among geographic regions [3-6]. Indeed, in the present analysis LOS varied between 5-6 days in Argentina, Israel and the US to 17 days in Russia. After accounting for geographic region, the multivariable model to predict longer LOS had low to modest discrimination, meaning that for the most part variables such as baseline severity of HF, concomitant disease and lab abnormalities at admission did not predict well the LOS. Addition of in-hospital measures of changes in disease severity such as worsening of end organ (kidney, liver) function as well as change in weight, which in AHF patients mostly represents decongestion did not significantly improve the model, suggesting that these changes, did not add beyond HF and renal impairment severity at baseline to the patients length of stay. On the other hand, metabolic changes (change in cholesterol and albumin) and most significantly the occurrence of inhospital WHF increased the ability to predict length of stay (table 2b). WHF was shown previously to be a strong predictor of LOS and short term outcomes in AHF [15-18] and the current analysis adds substantially to this body of knowledge, reinforcing the strong interaction between occurrence of WHF in hospital in patients with AHF and prolonged LOS. These findings are of interest as they do not support our tendency in clinical practice to look at decongestion and weigh as well as changes in organ function most importantly kidney function as important determinants of patient "dischargability". In reality, patients LOS is probably determined by severity of their disease and co-morbidities at baseline,

however, during the hospital admission improvement in metabolic measures such as albumin and cholesterol and most importantly lack of occurrence of WHF are strong determinants of LOS, and hence it is possible that efforts to improve those measures and especially prevention of WHF should take precedence in our effort to shorten LOS.

Early post-discharge admissions (for all causes and HF) during the first 30 days after discharge were less common in the first days after discharge increasing after approximately a week and then decreasing slowly over time (figure 1). HF readmissions were largely predicted by whether patients were previously admitted for HF, disease severity (congestion, low sodium) and renal dysfunction. Previous HF readmission (figure 2) was an especially strong predictor of additional HF readmissions within 30 days post-discharge. Regretfully in the PROTECT study we did not collect any socioeconomic data to assess whether these factors contribute substantially to the rate of early HF readmission. However, by the fact that readmissions were common mostly very close to discharge and mostly predicted by previous HF admission, it would be reasonable to assume that early HF readmissions may occur preferentially in a subgroup of patients who tend to be hospitalized more – some because their HF and renal impairment are more severe, but as suggested previously [14] some because of socioeconomic parameters and some because of area of living [6, 17]. Interestingly, when examining the predictors of 90-day postdischarge mortality, although some predictors for HF readmission and death are similar (such as congestion at admission and kidney function), others are not (such as age, blood pressure, WBC count). Most importantly increased length of stay remains a very significant predictor of 90-day post-discharge mortality, even after multiple adjustments for in-hospital deterioration of kidney or liver function or worsening of heart failure, but LOS is not a predictor of short term readmission, and especially HF readmission. Again, these associations suggest that to a certain degree a dichotomy exists in AHF between early readmission, and especially those for HF, and death. The current data as well as similar analysis of VERITAS [19] suggest that HF severity and more complicated hospital course are major

drivers of post-discharge early mortality while early HF readmissions are driven by disease severity but possibly more so by a tendency of the patients to be repeatedly readmitted. If confirmed, this finding may have significant implications for targeting therapy. i.e., mortality should be targeted with the same tools aimed at improving heart failure and renal impairment, while readmission may need to be addressed by other interventions, aimed at patients who tend to be repeatedly admitted to hospitals.

Limitations

The current analysis is a retrospective analysis of the PROTECT study and hence limited to the patients who met the inclusion and exclusion criteria for the study and the variables collected in that study including only readmissions up to 60 days post discharge and no socioeconomic measures. The study was of relatively modest size and these results should be examined in larger prospective and possibly less selective patient populations.

Conclusions

For patients discharged alive from an admission for AHF, the main factors that are of importance to the patient and the health system as a whole are the length of initial hospital stay, and early readmission and death after discharge. The current analysis suggests that although heart failure and renal impairment contribute to prolonged LOS as well as increased rate of early readmission and death, other factors may contribute to the length of stay and tendency for early re-admission while early mortality is mostly driven by disease severity and comorbidities. These factors — in-hospital WHF for LOS and history of HF admissions for early post-discharge HF readmissions may prove important in targeting specific patients' subgroups for interventions aimed at reducing LOS and post-discharge readmissions.

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	Subjects	who survived to discharge (N = 1902)	Subjects who	o died during initial hospital stay (N = 88)		Total (N = 1990)
Region	Number of subjects	Length of stay, days [1]	Number of subjects	Length of stay, days [1]	Number of subjects	Length of stay, days [1]
North America	296 (15.6%)	6.9 (5.60), 5.0 (4.0 - 8.0)	7 (8.0%)	21.0 (11.08), 18.0 (12.0 - 31.0)	303 (15.2%)	7.3 (6.13), 5.0 (4.0 - 8.0)
Israel	306 (16.1%)	6.0 (4.11), 5.0 (4.0 - 7.0)	6 (6.8%)	10.7 (3.61), 11.0 (9.0 - 14.0)	312 (15.7%)	6.1 (4.15), 5.0 (4.0 - 7.0)
Western Europe	349 (18.3%)	12.9 (9.94), 10.0 (7.0 - 15.0)	21 (23.9%)	12.1 (9.96), 11.0 (5.0 - 15.0)	370 (18.6%)	12.9 (9.93), 10.0 (7.0 - 15.0)
Eastern Europe	631 (33.2%)	10.3 (5.94), 8.0 (7.0 - 12.0)	38 (43.2%)	11.7 (8.77), 10.5 (5.0 - 16.0)	669 (33.6%)	10.4 (6.13), 8.0 (7.0 - 13.0)
Argentina	52 (2.7%)	5.2 (3.12), 4.5 (4.0 - 6.0)	1 (1.1%)	2.0 (n.d.), 2.0 (2.0 - 2.0)	53 (2.7%)	5.2 (3.13), 4.0 (4.0 - 6.0)
Russia	268 (14.1%)	17.4 (6.82), 16.0 (14.0 - 20.0)	15 (17.0%)	11.5 (14.17), 5.0 (4.0 - 14.0)	283 (14.2%)	17.0 (7.46), 15.0 (14.0 - 20.0)
Overall	1902 (100%)	10.4 (7.60), 8.0 (6.0 - 14.0)	88 (100%)	12.3 (10.24), 10.5 (5.0 - 15.5)	1990 (100%)	10.5 (7.74), 8.0 (6.0 - 14.0)

Table 1: Length of stay by patient status and region.

Notes:

[1] Results shown are mean (standard deviation), median (25th - 75th percentile).

		Univariable mod	del [1]	Multivariable model [1]		
Parameter	Mean difference for a change of	Mean difference (95% Cl)	P-value	Mean difference (95% CI)	P-value	
Age, y	10	-0.03 (-0.29, 0.24)	0.8417			
Male sex	Yes vs. No	-0.62 (-1.26, 0.02)	0.0563	-0.76 (-1.40, -0.12)	0.0193	
White race	Yes vs. No	0.31 (-1.29, 1.90)	0.7056			
Time from presentation to rand., h	1	0.02 (0.00, 0.05)	0.0610			
Ischemic heart disease	Yes vs. No	0.12 (-0.54, 0.79)	0.7144			
History of angina	Yes vs. No	0.89 (0.12, 1.67)	0.0245	0.79 (0.03, 1.55)	0.0426	
Previous stroke or PVD	Yes vs. No	0.03 (-0.74, 0.81)	0.9311			
Diabetes mellitus	Yes vs. No	1.04 (0.44, 1.65)	0.0008	0.72 (0.09, 1.35)	0.0251	
Respiratory disease	Yes vs. No	0.36 (-0.40, 1.12)	0.3525			
Mitral regurgitation	Yes vs. No	0.18 (-0.46, 0.83)	0.5782			
History of atrial fibrillation/flutter	Yes vs. No	0.35 (-0.26, 0.95)	0.2603			
History of CHF	Yes vs. No	-1.42 (-2.83, 0.00)	0.0499	-1.56 (-2.95, -0.17)	0.0284	
History of hypertension	Yes vs. No	0.08 (-0.67, 0.83)	0.8337			
History of hyperlipidemia	Yes vs. No	-0.04 (-0.69, 0.61)	0.9039			
History of smoking	Yes vs. No	0.24 (-0.52, 1.01)	0.5337			
History of CABG or PCI	Yes vs. No	-0.11 (-0.77, 0.56)	0.7579			
HF hospitalization in previous year	Yes vs. No	0.61 (0.01, 1.21)	0.0473			
NYHA class in previous month	None/I/II vs. III/IV	0.24 (-0.53, 1.01)	0.5369			

Table 2a: Univariable and multivariable associations of baseline characteristics with length of stay

		Univariable model [1]		Multivariable mo	odel [1]
Parameter	Mean difference for a change of	Mean difference (95% CI)	P-value	Mean difference (95% CI)	P-value
BMI, kg/m**2	1	0.08 (0.04, 0.13)	0.0008	0.06 (0.01, 0.11)	0.0231
Heart rate <=90 bpm [4]	5	-0.12 (-0.28, 0.03)	0.0618	-0.09 (-0.25, 0.06)	0.0072
Heart rate >90 bpm [4]	5	0.43 (0.18, 0.69)		0.40 (0.15, 0.65)	
Systolic blood pressure, mmHg	10	-0.20 (-0.37, -0.02)	0.0268	-0.18 (-0.36, 0.01)	0.0578
Diastolic blood pressure, mmHg	5	-0.12 (-0.25, 0.01)	0.0731		
Respiratory rate, breaths per min [3]	24.00 vs. 18.00	-0.53 (-1.10, 0.04)	0.0034		
Edema	<=2 vs. >2	1.03 (0.39, 1.68)	0.0017		
JVP	<=10 cm vs. >10 cm	0.95 (0.30, 1.59)	0.0043	0.78 (0.13, 1.43)	0.0194
Orthopnea	<=1 vs. >1 pillow	1.03 (0.21, 1.85)	0.0139	0.96 (0.14, 1.78)	0.0214
Rales	<1/3 vs. >=1/3	-0.03 (-0.67, 0.60)	0.9164		
Hemoglobin, g/dL	1	-0.25 (-0.41, -0.09)	0.0029		
WBC count, x10**9/L [2]	9.26 vs. 6.11	-0.20 (-0.59, 0.18)	<.0001	-0.23 (-0.61, 0.15)	0.0002
Sodium, mEq/L	3	-0.23 (-0.45, 0.00)	0.0519		
Potassium, mEq/L	1	0.35 (-0.20, 0.90)	0.2082		
Bicarbonate, mEq/L	1	-0.03 (-0.11, 0.05)	0.4989		
Creatinine, mg/dL	1	0.94 (0.40, 1.48)	0.0006		
BUN, mg/dL	1	0.05 (0.04, 0.07)	<.0001	0.04 (0.02, 0.05)	0.0005
Uric acid, mg/dL	10	0.04 (0.02, 0.06)	<.0001	0.02 (0.00, 0.05)	0.0313
Albumin, g/dL	1	-1.40 (-2.11, -0.68)	0.0001	-1.07 (-1.79, -0.35)	0.0036

		Univariable mod	del [1]	Multivariable model [1]		
Parameter	Mean difference for a change of	Mean difference (95% CI)	P-value	Mean difference (95% CI)	P-value	
ALT, U/L	1	0.01 (0.00, 0.02)	0.0650			
Glucose, mg/dL	1	0.08 (-0.02, 0.17)	0.1154			
Cholesterol <=4.5 mg/dL [4]	1	-1.07 (-1.51, -0.62)	<.0001	-0.55 (-1.01, -0.10)	0.0552	
Cholesterol >4.5 mg/dL [4]	1	0.33 (-0.29, 0.94)		0.36 (-0.25, 0.97)		
Triglycerides, mg/dL	1	0.00 (-0.01, 0.00)	0.1688			
Observed adjusted R-squared				0.2805		
Bias-corrected adjusted R-squared (95% CI) [5]				0.2703 (0.2327, 0.3079)		

Notes:

ALT, alanine aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; CHF, chronic heart failure; CI, confidence interval; eGFR, estimated glomerular filtration rate; HF, heart failure; JVP, jugular venous pressure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; WBC, white blood cells.

[1] Results from linear regression model adjusted for region.

[2] Non-linear association modeled as quadratic transformation. HR for the 75th vs. the 25th percentile is presented.

[3] Non-linear association modeled as cubic transformation. HR for the 75th vs. the 25th percentile is presented.

[4] Non-linear association modeled as linear spline.

[5] Bootstrap estimate with 1000 resampling steps.

Table 2b: Change in R-squared for model adjusted length of stay

Model [1]	Observed adjusted R- squared	Bias-corrected adjusted R- squared (95% Cl) [2]	Bias-corrected difference in adjusted R-squared (95% CI), compared to model in first line [2]
Adjusted for original predictors	0.2805	0.2703 (0.2327, 0.3079)	
Albumin (day 2 changes)	0.2879	0.2775 (0.2392, 0.3158)	0.0072 (0.0004, 0.0139)
AST (day 2 changes and corresponding baseline values)	0.2850	0.2735 (0.2349, 0.3120)	0.0032 (-0.0036, 0.0100)
Cholesterol (day 2 changes)	0.2907	0.2799 (0.2423, 0.3176)	0.0096 (0.0009, 0.0184)
Creatinine (day 2 changes and corresponding baseline values)	0.2834	0.2723 (0.2341, 0.3105)	0.0020 (-0.0035, 0.0075)
Weight (day 2 changes and corresponding baseline values)	0.2856	0.2741 (0.2360, 0.3123)	0.0038 (-0.0026, 0.0103)
All day 2 changes and corresponding baseline values	0.2927	0.2782 (0.2402, 0.3161)	0.0079 (-0.0029, 0.0187)
Worsening heart failure by day 7	0.3220	0.3119 (0.2747, 0.3491)	0.0416 (0.0214, 0.0619)
All day 2 changes, corresponding baseline values, and worsening heart failure by day 7	0.3343	0.3204 (0.2840, 0.3568)	0.0501 (0.0282, 0.0719)

Notes:

AST, aspartate aminotransferase; CI, confidence interval.

[1] Results from linear regression model adjusted for region.

[2] Bootstrap estimate with 1000 resampling steps.

		Multivariable model [1]		Multivariable model including length of stay [1]		Multivariable model including length of stay and worsening heart failure [1]	
Parameter	OR for a change of	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Diabetes mellitus	Yes vs. No	1.25 (0.98, 1.59)	0.0675	1.24 (0.97, 1.58)	0.0811	1.24 (0.97, 1.57)	0.0830
Edema	<=2 vs. >2	0.80 (0.62, 1.03)	0.0788	0.78 (0.61, 1.00)	0.0545	0.78 (0.61, 1.00)	0.0545
Orthopnea	<=1 vs. >1 pillow	1.43 (1.02, 2.00)	0.0390	1.38 (0.99, 1.94)	0.0609	1.39 (0.99, 1.94)	0.0598
BUN, mg/dL	1	1.02 (1.01, 1.02)	<.0001	1.01 (1.01, 1.02)	<.0001	1.01 (1.01, 1.02)	<.0001
Length of stay, days	1			1.02 (1.00, 1.05)	0.0525	1.02 (1.00, 1.05)	0.0888
Worsening heart failure by day 7	Yes vs. No					1.10 (0.76, 1.60)	0.6215
Observed C-statistic		0.6864		0.6871		0.6871	
Bias-corrected C-statistic (95% CI) [2]		0.6823 (0.6535, 0.7110)		0.6821 (0.6531, 0.7110)		0.6814 (0.6525, 0.7103)	
Bias-corrected difference in C-statistics (95% Cl), compared to model in previous column [2]				-0.0002 (-0.0051, 0.0047)		-0.0007 (-0.0031, 0.0017)	
Interaction test of length of stay with region					0.3269		0.3100

Table 3a: Multivariable associations of baseline characteristics with rehospitalization up to 30 days after discharge

Notes:

BUN, blood urea nitrogen; CI, confidence interval; OR, odds ratio.

[1] Results from logistic regression model stratified by region. C-

statistics computed based on logistic regression model adjusted for region (instead of stratification).

[2] Bootstrap estimate with 1000 resampling steps.

Table 3b: Multivariable associations of baseline characteristics with rehospitalizations for heart failure up to 30 days after discharge

		Multivariable model [1]		Multivariable model including length of stay [1]		Multivariable model including length of stay and worsening heart failure [1]	
Parameter	OR for a change of	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
HF hospitalization in previous year	Yes vs. No	2.11 (1.50, 2.95)	<.0001	2.10 (1.50, 2.95)	<.0001	2.10 (1.50, 2.94)	<.0001
Orthopnea	<=1 vs. >1 pillow	1.73 (1.06, 2.83)	0.0300	1.72 (1.05, 2.82)	0.0329	1.72 (1.05, 2.83)	0.0325
Sodium, mEq/L	3	0.82 (0.73, 0.91)	0.0005	0.82 (0.73, 0.91)	0.0005	0.81 (0.73, 0.91)	0.0005
BUN, mg/dL	1	1.02 (1.01, 1.03)	<.0001	1.02 (1.01, 1.03)	<.0001	1.02 (1.01, 1.03)	<.0001
Albumin, g/dL	1	1.52 (1.03, 2.24)	0.0346	1.53 (1.03, 2.26)	0.0336	1.53 (1.04, 2.26)	0.0330
Length of stay, days	1			1.00 (0.97, 1.04)	0.8152	1.00 (0.97, 1.04)	0.9312
Worsening heart failure by day 7	Yes vs. No					1.11 (0.67, 1.83)	0.6845
Observed C-statistic		0.7462		0.7457		0.7462	
Bias-corrected C-statistic (95% CI) [2]		0.7397 (0.7042, 0.7752)		0.7385 (0.7029, 0.7741)		0.7385 (0.7028, 0.7743)	
Bias-corrected difference in C-statistics (95% CI), compared to model in previous column [2]				-0.0012 (-0.0037, 0.0013)		0.0000 (-0.0028, 0.0029)	

		Multivariab	le model [1]	Multivaria including leng		Multivaria including leng worsening he	th of stay and
Parameter	OR for a change of	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Interaction test of length of stay with region					0.0499		0.0460

Notes:

BUN, blood urea nitrogen; CI, confidence interval; HF, heart failure; OR, odds ratio.

[1] Results from logistic regression model stratified by region. C-

statistics computed based on logistic regression model adjusted for region (instead of stratification).

[2] Bootstrap estimate with 1000 resampling steps.

		Multivariable model [1]		Multivariable model including length of stay [1]		Multivariable model including length of stay and worsening heart failure [1]	
Parameter	HR for a change of	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age, y	10	1.28 (1.09, 1.50)	0.0022	1.29 (1.10, 1.52)	0.0016	1.30 (1.11, 1.52)	0.0014
Respiratory disease	Yes vs. No	1.57 (1.09, 2.26)	0.0144	1.63 (1.14, 2.34)	0.0082	1.61 (1.12, 2.31)	0.0097
Systolic blood pressure, mmHg	10	0.83 (0.74, 0.92)	0.0005	0.83 (0.75, 0.92)	0.0006	0.83 (0.75, 0.93)	0.0008
WBC count, x10**9/L	5	1.20 (1.00, 1.43)	0.0522	1.16 (0.97, 1.38)	0.1072	1.17 (0.98, 1.40)	0.0895
Sodium, mEq/L	3	0.82 (0.73, 0.92)	0.0008	0.83 (0.74, 0.93)	0.0015	0.83 (0.74, 0.93)	0.0012
Bicarbonate <=24 mEq/L [2]	1	0.88 (0.82, 0.95)	0.0035	0.88 (0.82, 0.96)	0.0044	0.88 (0.82, 0.95)	0.0043
Bicarbonate >24 mEq/L [2]	1	1.09 (1.01, 1.17)		1.08 (1.00, 1.16)		1.08 (1.00, 1.16)	
BUN, mg/dL (log2)	Doubling	1.63 (1.22, 2.16)	0.0008	1.54 (1.16, 2.05)	0.0033	1.52 (1.14, 2.03)	0.0044
Uric acid, mg/dL	10	1.01 (1.00, 1.02)	0.0366	1.01 (1.00, 1.02)	0.0489	1.01 (1.00, 1.02)	0.0553
Length of stay <=14 days [2]	1			1.11 (1.05, 1.17)	0.0003	1.10 (1.04, 1.16)	0.0030
Length of stay >14 days [2]	1			0.99 (0.96, 1.02)		0.99 (0.96, 1.02)	
Worsening heart failure by day 7	Yes vs. No					1.35 (0.88, 2.06)	0.1680
Observed C-statistic		0.7324		0.7411		0.7443	
Bias-corrected C-statistic (95% CI) [3]		0.7263 (0.6881, 0.7646)		0.7348 (0.6961, 0.7735)		0.7377 (0.6989 <i>,</i> 0.7764)	
Bias-corrected difference in C-statistics (95% CI), compared to model in previous column [3]				0.0085 (-0.0065, 0.0234)		0.0029 (-0.0043, 0.0100)	

Table 4: Multivariable associations of baseline characteristics with death up to 90 days after discharge

		Multivariab	le model [1]	Multivaria including leng		Multivaria including leng worsening he	th of stay and
Parameter	HR for a change of	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Interaction test of length of stay with region					0.1093		0.1169

Notes:

BUN, blood urea nitrogen; CI, confidence interval; HR, hazard ratio; NYHA, New York Heart Association; WBC, white blood cells.

[1] Results from Cox proportional hazards model stratified by region.

[2] Non-linear association modeled as linear spline.

[3] Bootstrap estimate with 1000 resampling steps.

Table 5: Model adjusted associations of length of stay with death up to 90 days after discharge

		Length of stay [2]	
Model [1]	LOS <=14 days HR (95% CI)	LOS >14 days HR (95% Cl)	P-value
Adjusted for original predictors	1.11 (1.05, 1.17)	0.99 (0.96, 1.02)	0.0003
Albumin (day 2 changes and corresponding baseline values)	1.12 (1.06, 1.18)	0.99 (0.96, 1.02)	0.0001
AST (day 2 changes and corresponding baseline values)	1.12 (1.06, 1.17)	0.99 (0.96, 1.02)	<.0001
Cholesterol (day 2 changes and corresponding baseline values)	1.11 (1.05, 1.17)	0.99 (0.96, 1.02)	0.0003
Creatinine (day 2 changes and corresponding baseline values)	1.11 (1.06, 1.17)	0.99 (0.96, 1.02)	0.0001
Weight (day 2 changes and corresponding baseline values)	1.11 (1.06, 1.17)	0.99 (0.96, 1.02)	0.0002
All day 2 changes and corresponding baseline values	1.10 (1.05, 1.16)	0.99 (0.96, 1.02)	0.0009
Worsening heart failure by day 7	1.10 (1.04, 1.16)	0.99 (0.96, 1.02)	0.0030
All day 2 changes, corresponding baseline values, and worsening heart failure by day 7	1.10 (1.04, 1.16)	0.99 (0.96, 1.02)	0.0043

Notes:

CI, confidence interval; HR, hazard ratio; LOS, length of stay.

[1] Results from Cox proportional hazards model including length of stay and stratified by region. For each lab change the corresponding baseline values have been included into the model if they were not already among the set of original predictors.

[2] Non-linear association modeled as linear spline. Hazard ratio presented for a change of one day.

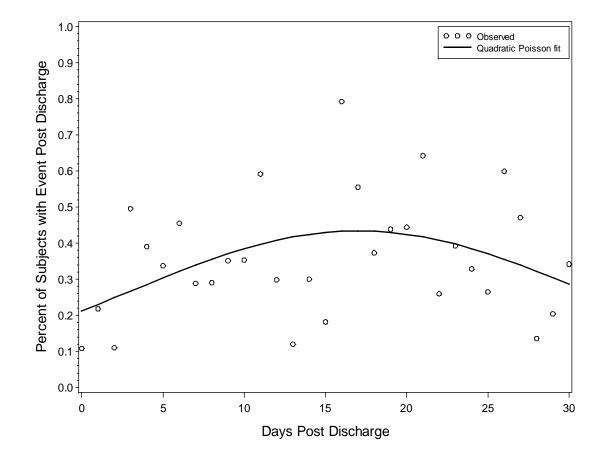
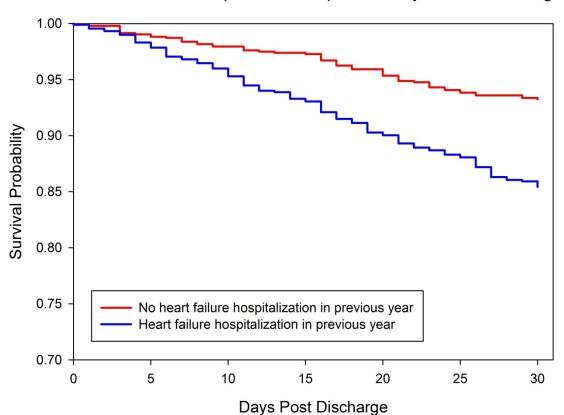


Figure 1: Rate of heart failure readmissions after discharge during the first 30 days post discharge

Figure 2: HF Readmission over 30 days in patients with and without previous HF admission prior to the study related admission



Heart Failure Rehospitalization up to 30 Days After Discharge

Supplementary table 1: Baseline characteristics by length of stay categories

			Length of stay [1] -		-
Parameter	n (% missing) Catego	y Short (N = 852)	 Medium (N = 484)	Long (N = 566)	P-value [2]
Age, y	1902 (0.0%)	69.6 (11.96), 71.0 (61.0 - 79.0)	70.8 (11.39), 73.0 (64.0 - 79.0)	69.8 (11.38), 71.0 (62.0 - 78.0)	0.1792
Male sex	1902 (0.0%)	592 (69.5%)	318 (65.7%)	365 (64.5%)	0.1129
White race	1889 (0.7%)	802 (95.0%)	450 (93.9%)	546 (96.5%)	0.1589
Time from presentation to rand., h	1885 (0.9%)	14.0 (8.17), 16.2 (5.2 - 21.4)	15.5 (18.80), 17.5 (6.0 - 21.8)	15.6 (12.57), 17.8 (6.6 - 22.2)	0.0355
Ischemic heart disease	1900 (0.1%)	581 (68.3%)	331 (68.4%)	399 (70.6%)	0.6102
History of angina	1898 (0.2%)	164 (19.3%)	94 (19.5%)	155 (27.4%)	0.0006
Previous stroke or PVD	1902 (0.0%)	146 (17.1%)	92 (19.0%)	111 (19.6%)	0.4541
Diabetes mellitus	1901 (0.1%)	352 (41.3%)	239 (49.4%)	281 (49.7%)	0.0016
Respiratory disease	1898 (0.2%)	168 (19.8%)	85 (17.6%)	124 (21.9%)	0.2236
Mitral regurgitation	1899 (0.2%)	281 (33.0%)	169 (34.9%)	194 (34.4%)	0.7484
History of atrial fibrillation/flutter	1888 (0.7%)	446 (52.7%)	249 (51.8%)	318 (56.7%)	0.2167
History of CHF	1902 (0.0%)	809 (95.0%)	461 (95.2%)	536 (94.7%)	0.9214
History of hypertension	1902 (0.0%)	666 (78.2%)	391 (80.8%)	457 (80.7%)	0.3776
History of hyperlipidemia	1901 (0.1%)	453 (53.2%)	247 (51.1%)	302 (53.4%)	0.7242
History of smoking	1898 (0.2%)	179 (21.1%)	98 (20.3%)	119 (21.1%)	0.9374

Length of stay [1]

Parameter	n (% missing)	Category	Short (N = 852)	Medium (N = 484)	Long (N = 566)	P-value [2]
History of CABG or PCI	1892 (0.5%)		325 (38.4%)	186 (38.5%)	217 (38.6%)	0.9957
HF hospitalization in previous year	1902 (0.0%)		397 (46.6%)	232 (47.9%)	298 (52.7%)	0.0759
NYHA class in previous month	1900 (0.1%)	None/I/II	190 (22.3%)	112 (23.1%)	118 (20.9%)	0.1453
		III	431 (50.6%)	229 (47.3%)	258 (45.7%)	
		IV	231 (27.1%)	143 (29.5%)	188 (33.3%)	
BMI, kg/m**2	1880 (1.2%)		28.36 (5.926), 27.36 (24.12 - 31.23)	28.94 (5.974), 27.91 (24.75 - 31.77)	29.44 (6.560), 28.37 (24.68 - 32.87)	0.0050
Heart rate, bpm	1900 (0.1%)		79.9 (14.58), 80.0 (70.0 - 90.0)	79.8 (15.65), 78.0 (69.0 - 90.0)	80.7 (16.47), 78.0 (69.0 - 90.0)	0.5562
Systolic blood pressure, mmHg	1902 (0.0%)		124.7 (16.71), 125.0 (110.0 - 140.0)	127.0 (17.91), 130.0 (110.0 - 140.0)	122.9 (18.02), 120.0 (110.0 - 137.0)	0.0008
Diastolic blood pressure, mmHg	1902 (0.0%)		74.2 (11.65), 73.0 (68.0 - 80.0)	74.2 (12.21), 74.0 (65.0 - 80.0)	73.2 (11.81), 72.0 (65.0 - 80.0)	0.2618
Pulse pressure, mmHg	1902 (0.0%)		50.5 (14.41), 50.0 (40.0 - 60.0)	52.8 (15.04), 50.0 (40.0 - 60.0)	49.7 (15.80), 49.0 (40.0 - 60.0)	0.0028
Mean arterial pressure, mmHg	1902 (0.0%)		91.02 (11.723), 90.00 (83.33 - 99.00)	91.79 (12.487), 91.83 (82.17 - 100.00)	89.77 (12.075), 90.00 (80.00 - 98.00)	0.0218
Respiratory rate, breaths per min	1813 (4.7%)		21.2 (4.23), 21.0 (18.0 - 24.0)	21.1 (4.01), 20.0 (18.0 - 24.0)	21.3 (4.34), 20.0 (18.0 - 24.0)	0.5655
Edema	1902 (0.0%)	0	139 (16.3%)	70 (14.5%)	66 (11.7%)	<.0001

Parameter	n (% missing)	Category	Short (N = 852)	Medium (N = 484)	Long (N = 566)	P-value [2]
		>1	189 (22.2%)	70 (14.5%)	91 (16.1%)	
		>2	358 (42.0%)	213 (44.0%)	198 (35.0%)	
		>3	166 (19.5%)	131 (27.1%)	211 (37.3%)	
JVP	1717 (9.7%)	<6 cm	89 (11.8%)	48 (10.9%)	67 (12.9%)	0.0278
		6-10 cm	390 (51.5%)	212 (48.2%)	221 (42.5%)	
		>10 cm	278 (36.7%)	180 (40.9%)	232 (44.6%)	
Orthopnea	1877 (1.3%)	None	36 (4.3%)	20 (4.2%)	20 (3.6%)	<.0001
		1 pillow	124 (14.8%)	55 (11.5%)	48 (8.5%)	
		2 pillows	365 (43.7%)	184 (38.5%)	214 (38.0%)	
		>30°	311 (37.2%)	219 (45.8%)	281 (49.9%)	
Rales	1899 (0.2%)	0	84 (9.9%)	46 (9.5%)	52 (9.2%)	0.0050
		<1/3	245 (28.8%)	160 (33.1%)	159 (28.1%)	
		1/3 to 2/3	461 (54.2%)	227 (47.0%)	282 (49.8%)	
		>2/3	60 (7.1%)	50 (10.4%)	73 (12.9%)	
Hemoglobin, g/dL	1662 (12.6%)		12.87 (1.908), 12.80 (11.50 - 14.15)	12.58 (1.967), 12.50 (11.20 - 13.90)	12.52 (2.067), 12.40 (11.00 - 13.80)	0.0045
WBC count, x10**9/L	1662 (12.6%)		7.83 (2.663), 7.44 (6.22 - 9.04)	7.90 (2.853), 7.48 (5.92 - 9.31)	8.08 (3.928), 7.41 (6.01 - 9.29)	0.3715
Sodium, mEq/L	1846 (2.9%)		139.5 (3.86), 140.0 (137.0 - 142.0)	139.5 (4.08), 140.0 (137.0 - 142.0)	139.1 (4.27), 140.0 (137.0 - 142.0)	0.1300

------ Length of stay [1] ------

------ Length of stay [1] ------

Parameter	n (% missing) Categor	y Short (N = 852)	Medium (N = 484)	Long (N = 566)	P-value [2]
Potassium, mEq/L	1750 (8.0%)	4.27 (0.573), 4.20 (3.90 - 4.60)	4.27 (0.588), 4.20 (3.90 - 4.70)	4.28 (0.564), 4.20 (3.90 - 4.60)	0.9100
Bicarbonate, mEq/L	1771 (6.9%)	24.0 (3.64), 24.0 (21.0 - 26.0)	24.1 (3.71), 24.0 (22.0 - 26.0)	23.9 (4.00), 24.0 (21.0 - 26.0)	0.6478
Creatinine, mg/dL	1843 (3.1%)	1.47 (0.547), 1.30 (1.10 - 1.70)	1.53 (0.616), 1.40 (1.10 - 1.80)	1.54 (0.577), 1.40 (1.20 - 1.80)	0.0262
eGFR, mL/min	1840 (3.3%)	50.49 (18.805), 48.64 (36.86 - 61.76)	48.15 (19.236), 45.10 (32.77 - 60.40)	46.69 (17.489), 44.29 (34.04 - 56.50)	0.0007
BUN, mg/dL	1848 (2.8%)	31.8 (15.76), 28.0 (21.0 - 38.0)	33.3 (16.53), 29.0 (22.0 - 41.5)	36.0 (18.89), 31.0 (23.0 - 43.0)	<.0001
BUN/creatinine ratio	1843 (3.1%)	21.76 (6.686), 20.61 (17.27 - 25.00)	21.88 (6.980), 20.77 (17.14 - 25.45)	23.28 (7.527), 22.00 (17.78 - 27.69)	0.0002
Uric acid, mg/dL	1771 (6.9%)	517.76 (144.986), 505.58 (422.31 - 612.64)	527.57 (151.302), 523.42 (410.41 - 630.49)	559.71 (156.333), 544.24 (452.05 - 660.23)	<.0001
Albumin, g/dL	1842 (3.2%)	3.93 (0.408), 3.90 (3.70 - 4.20)	3.79 (0.458), 3.80 (3.60 - 4.10)	3.81 (0.421), 3.80 (3.50 - 4.10)	<.0001
ALT, U/L	1721 (9.5%)	27.2 (24.71), 21.0 (15.0 - 30.0)	29.0 (27.58), 21.0 (15.0 - 33.0)	33.3 (39.15), 21.0 (15.0 - 33.0)	0.0021
Glucose, mg/dL	1787 (6.0%)	7.79 (3.168), 6.99 (5.72 - 8.88)	7.88 (3.397), 7.10 (5.61 - 9.21)	7.87 (3.195), 7.10 (5.77 - 9.10)	0.8774
Cholesterol, mg/dL	1841 (3.2%)	3.96 (1.087), 3.88 (3.19 - 4.64)	3.85 (1.178), 3.65 (3.08 - 4.43)	3.64 (1.143), 3.47 (2.80 - 4.27)	<.0001

			Length of stay [1]				
Parameter	n (% missing)	Category	Short (N = 852)	Medium (N = 484)	Long (N = 566)	P-value [2]	
Triglycerides, mg/dL	1829 (3.8%)		104.7 (53.19), 94.0 (67.0 - 128.0)	100.6 (51.96), 88.5 (65.0 - 120.0)	97.6 (49.91), 84.5 (64.0 - 119.0)	0.0423	

Notes:

ALT, alanine transferase; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; CHF, chronic heart failure; eGFR, estimated glomerular filtration rate; HF, heart failure; JVP, jugular venous pressure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; WBC, white blood cells.

[1] Results shown are mean (standard deviation), median (25th - 75th percentile) for continuous variables, or prevalence (%) for categorical variables, unless otherwise noted. Numbers may vary due to missing values.

[2] P-values from ANOVA (F-test) for continuous variables, or from Chi-squared test for categorical variables, unless otherwise noted.

Supplemental table 2a: Baseline characteristics by	rehospitalization up to 30 days after discharge

------ Any cause rehospitalization up to 30 days after discharge [1] -------

	n (%				
Parameter	missing)	Category	No (N = 1477)	Yes (N = 372)	P-value [2]
Age, y	1849 (0.0%)		69.8 (11.47), 71.0 (62.0 - 78.0)	70.5 (12.38), 73.0 (62.5 - 80.0)	0.2744
Male sex	1849 (0.0%)		988 (66.9%)	254 (68.3%)	0.6106
White race	1836 (0.7%)		1399 (95.4%)	347 (94.0%)	0.2914
Time from presentation to rand., h	1834 (0.8%)		14.9 (13.97), 17.1 (5.5 - 21.6)	14.3 (8.23), 16.5 (5.6 - 21.8)	0.4394
Ischemic heart disease	1847 (0.1%)		1005 (68.1%)	268 (72.0%)	0.1456
History of angina	1845 (0.2%)		326 (22.1%)	68 (18.4%)	0.1251
Previous stroke or PVD	1849 (0.0%)		267 (18.1%)	77 (20.7%)	0.2455
Diabetes mellitus	1848 (0.1%)		643 (43.6%)	201 (54.0%)	0.0003
Respiratory disease	1845 (0.2%)		281 (19.0%)	78 (21.1%)	0.3620
Mitral regurgitation	1846 (0.2%)		498 (33.8%)	126 (33.9%)	0.9752
History of atrial fibrillation/flutter	1836 (0.7%)		789 (53.8%)	194 (52.4%)	0.6325
History of CHF	1849 (0.0%)		1401 (94.9%)	358 (96.2%)	0.2682
History of hypertension	1849 (0.0%)		1176 (79.6%)	298 (80.1%)	0.8347
History of hyperlipidemia	1848 (0.1%)		742 (50.3%)	239 (64.2%)	<.0001
History of smoking	1845 (0.2%)		300 (20.4%)	82 (22.1%)	0.4572
History of CABG or PCI	1839 (0.5%)		531 (36.2%)	185 (49.9%)	<.0001

- .	n (%	• •			- / 61
Parameter	missing)	Category	No (N = 1477)	Yes (N = 372)	P-value [2]
HF hospitalization in previous year	1849 (0.0%)		684 (46.3%)	216 (58.1%)	<.0001
NYHA class in previous month	1847 (0.1%)	None/I/II	319 (21.6%)	89 (23.9%)	0.0002
		111	692 (46.9%)	206 (55.4%)	
		IV	464 (31.5%)	77 (20.7%)	
BMI, kg/m**2	1827 (1.2%)		28.74 (6.192), 27.64 (24.34 - 31.64)	29.08 (5.931), 28.20 (24.69 - 32.31)	0.3417
Heart rate, bpm	1847 (0.1%)		80.8 (15.68), 80.0 (70.0 - 90.0)	77.1 (13.71), 76.0 (68.0 - 85.0)	<.0001
Systolic blood pressure, mmHg	1849 (0.0%)		125.4 (17.36), 125.0 (110.0 - 140.0)	122.4 (17.46), 120.0 (110.0 - 136.0)	0.0029
Diastolic blood pressure, mmHg	1849 (0.0%)		74.6 (11.78), 75.0 (68.0 - 80.0)	71.5 (11.84), 70.0 (62.0 - 80.0)	<.0001
Pulse pressure, mmHg	1849 (0.0%)		50.8 (14.92), 50.0 (40.0 - 60.0)	50.9 (15.54), 50.0 (40.0 - 60.0)	0.9137
Mean arterial pressure, mmHg	1849 (0.0%)		91.50 (11.976), 91.67 (83.33 - 100.00)	88.43 (11.895), 87.33 (80.00 - 96.67)	<.0001
Respiratory rate, breaths per min	1766 (4.5%)		21.2 (4.22), 21.0 (18.0 - 24.0)	21.0 (4.04), 20.0 (18.0 - 24.0)	0.2999
Edema	1849 (0.0%)	0	202 (13.7%)	70 (18.8%)	0.0089
		>1	264 (17.9%)	72 (19.4%)	
		>2	603 (40.8%)	154 (41.4%)	
		>3	408 (27.6%)	76 (20.4%)	
JVP	1672 (9.6%)	<6 cm	158 (11.9%)	42 (12.4%)	0.8598
		6-10 cm	645 (48.4%)	159 (46.8%)	

------ Any cause rehospitalization up to 30 days after discharge [1] ------

	n (%				
Parameter	missing)	Category	No (N = 1477)	Yes (N = 372)	P-value [2]
		>10 cm	529 (39.7%)	139 (40.9%)	
Orthopnea	1824 (1.4%)	None	57 (3.9%)	14 (3.8%)	0.7731
		1 pillow	181 (12.4%)	39 (10.7%)	
		2 pillows	591 (40.5%)	156 (42.9%)	
		>30°	631 (43.2%)	155 (42.6%)	
Rales	1846 (0.2%)	0	144 (9.8%)	33 (8.9%)	0.7756
		<1/3	430 (29.2%)	116 (31.2%)	
		1/3 to 2/3	762 (51.7%)	185 (49.7%)	
		>2/3	138 (9.4%)	38 (10.2%)	
Hemoglobin, g/dL	1613 (12.8%)		12.79 (1.980), 12.80 (11.40 - 14.10)	12.37 (1.901), 12.20 (11.10 - 13.70)	0.0006
WBC count, x10**9/L	1613 (12.8%)		7.88 (2.923), 7.42 (6.08 - 9.15)	7.97 (3.025), 7.49 (6.11 - 9.24)	0.6390
Sodium, mEq/L	1793 (3.0%)		139.6 (3.92), 140.0 (137.0 - 142.0)	138.7 (4.30), 139.0 (136.0 - 142.0)	<.0001
Potassium, mEq/L	1702 (8.0%)		4.26 (0.580), 4.20 (3.90 - 4.60)	4.28 (0.541), 4.25 (3.90 - 4.60)	0.6735
Bicarbonate, mEq/L	1720 (7.0%)		24.0 (3.75), 24.0 (21.0 - 26.0)	24.0 (3.80), 24.0 (22.0 - 27.0)	0.8856
Creatinine, mg/dL	1790 (3.2%)		1.47 (0.557), 1.30 (1.10 - 1.70)	1.62 (0.596), 1.50 (1.20 - 1.90)	<.0001
eGFR, mL/min	1787 (3.4%)		49.72 (18.526), 48.28 (36.30 - 60.71)	45.57 (18.640), 42.92 (31.62 - 57.55)	0.0001
BUN, mg/dL	1795 (2.9%)		31.9 (15.67), 28.0 (21.0 - 38.0)	38.4 (19.80), 33.5 (24.5 - 48.0)	<.0001

------ Any cause rehospitalization up to 30 days after discharge [1] -------

------ Any cause rehospitalization up to 30 days after discharge [1] ------

Parameter	n (% missing)	Category	No (N = 1477)	Yes (N = 372)	P-value [2]
BUN/creatinine ratio	1790 (3.2%)		21.80 (6.931), 20.71 (17.00 - 25.00)	23.50 (7.210), 22.18 (18.15 - 27.89)	<.0001
Uric acid, mg/dL	1720 (7.0%)		527.18 (149.330), 517.48 (422.31 - 624.54)	549.04 (151.685), 529.37 (440.15 - 648.33)	0.0155
Albumin, g/dL	1789 (3.2%)		3.85 (0.432), 3.90 (3.60 - 4.10)	3.88 (0.422), 3.90 (3.60 - 4.10)	0.3388
ALT, U/L	1673 (9.5%)		29.6 (29.93), 21.0 (15.0 - 32.0)	28.6 (31.36), 19.0 (14.0 - 29.0)	0.5868
Glucose, mg/dL	1737 (6.1%)		7.77 (3.210), 6.99 (5.61 - 8.88)	8.00 (3.231), 7.10 (5.77 - 9.60)	0.2323
Cholesterol, mg/dL	1788 (3.3%)		3.87 (1.138), 3.73 (3.08 - 4.53)	3.70 (1.101), 3.55 (2.93 - 4.31)	0.0089
Triglycerides, mg/dL	1776 (3.9%)		100.7 (51.28), 89.0 (65.0 - 122.0)	105.7 (55.79), 95.0 (65.0 - 133.0)	0.1107

Notes:

ALT, alanine transferase; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; CHF, chronic heart failure; eGFR, estimated glomerular filtration rate; HF, heart failure; JVP, jugular venous pressure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; WBC, white blood cells.

[1] Results shown are mean (standard deviation), median (25th - 75th percentile) for continuous variables, or prevalence (%) for categorical variables, unless otherwise noted. Numbers may vary due to missing values.

[2] P-values from ANOVA (F-test) for continuous variables, or from Chi-squared test for categorical variables, unless otherwise noted.

Supplemental table 2b: Baseline characteristics by rehospitalization for heart failure up to 30 days after discharge

------ Heart failure rehospitalization up to 30 days after discharge [1] ------

	n (%				
Parameter	missing)	Category	No (N = 1667)	Yes (N = 182)	P-value [2]
Age, y	1849 (0.0%)		69.9 (11.60), 72.0 (62.0 - 78.0)	70.0 (12.21), 73.0 (62.0 - 79.0)	0.9541
Male sex	1849 (0.0%)		1116 (66.9%)	126 (69.2%)	0.5332
White race	1836 (0.7%)		1580 (95.4%)	166 (92.7%)	0.1236
Time from presentation to rand., h	1834 (0.8%)		14.8 (13.46), 17.0 (5.5 - 21.6)	14.9 (8.10), 17.0 (6.4 - 22.1)	0.9456
Ischemic heart disease	1847 (0.1%)		1144 (68.7%)	129 (70.9%)	0.5480
History of angina	1845 (0.2%)		365 (21.9%)	29 (16.1%)	0.0707
Previous stroke or PVD	1849 (0.0%)		310 (18.6%)	34 (18.7%)	0.9777
Diabetes mellitus	1848 (0.1%)		743 (44.6%)	101 (55.5%)	0.0051
Respiratory disease	1845 (0.2%)		318 (19.1%)	41 (22.9%)	0.2202
Mitral regurgitation	1846 (0.2%)		552 (33.2%)	72 (39.6%)	0.0837
History of atrial fibrillation/flutter	1836 (0.7%)		883 (53.3%)	100 (55.6%)	0.5681
History of CHF	1849 (0.0%)		1583 (95.0%)	176 (96.7%)	0.2997
History of hypertension	1849 (0.0%)		1326 (79.5%)	148 (81.3%)	0.5718
History of hyperlipidemia	1848 (0.1%)		861 (51.7%)	120 (65.9%)	0.0003
History of smoking	1845 (0.2%)		340 (20.4%)	42 (23.2%)	0.3821
History of CABG or PCI	1839 (0.5%)		626 (37.8%)	90 (49.5%)	0.0022

Parameter	n (%	Catorow	No (N = 1007)	Yes (N = 182)	Duralua [2]
HF hospitalization in previous year	<i>missing)</i> 1849 (0.0%)	Category	No (N = 1667) 778 (46.7%)	122 (67.0%)	<i>P-value</i> [2]
NYHA class in previous month	1847 (0.1%)	None/I/II	368 (22.1%)	40 (22.0%)	0.0193
		Ш	794 (47.7%)	104 (57.1%)	
		IV	503 (30.2%)	38 (20.9%)	
BMI, kg/m**2	1827 (1.2%)		28.77 (6.142), 27.68 (24.39 - 31.77)	29.09 (6.131), 28.39 (24.53 - 31.89)	0.5121
Heart rate, bpm	1847 (0.1%)		80.4 (15.56), 79.0 (70.0 - 90.0)	76.8 (13.06), 76.0 (70.0 - 83.0)	0.0029
Systolic blood pressure, mmHg	1849 (0.0%)		125.2 (17.32), 125.0 (110.0 - 140.0)	120.7 (17.78), 120.0 (107.0 - 135.0)	0.0007
Diastolic blood pressure, mmHg	1849 (0.0%)		74.3 (11.81), 75.0 (67.0 - 80.0)	71.0 (11.84), 70.0 (61.0 - 80.0)	0.0005
Pulse pressure, mmHg	1849 (0.0%)		51.0 (15.03), 50.0 (40.0 - 60.0)	49.6 (15.17), 49.0 (40.0 - 60.0)	0.2526
Mean arterial pressure, mmHg	1849 (0.0%)		91.25 (11.953), 90.67 (83.33 - 100.00)	87.56 (12.154), 86.33 (78.00 - 96.00)	<.0001
Respiratory rate, breaths per min	1766 (4.5%)		21.2 (4.18), 21.0 (18.0 - 24.0)	21.1 (4.23), 20.0 (18.0 - 24.0)	0.7683
Edema	1849 (0.0%)	0	238 (14.3%)	34 (18.7%)	0.2111
		>1	299 (17.9%)	37 (20.3%)	
		>2	685 (41.1%)	72 (39.6%)	
		>3	445 (26.7%)	39 (21.4%)	
JVP	1672 (9.6%)	<6 cm	179 (11.9%)	21 (12.5%)	0.1411
		6-10 cm	735 (48.9%)	69 (41.1%)	

------ Heart failure rehospitalization up to 30 days after discharge [1] ------

Parameter	n (% missing)	Category	No (N = 1667)	Yes (N = 182)	P-value [2]
	missing	>10 cm	590 (39.2%)	78 (46.4%)	
Orthopnea	1824 (1.4%)	None	62 (3.8%)	9 (5.1%)	0.1959
		1 pillow	207 (12.6%)	13 (7.3%)	
		2 pillows	673 (40.9%)	74 (41.8%)	
		>30°	705 (42.8%)	81 (45.8%)	
Rales	1846 (0.2%)	0	159 (9.6%)	18 (9.9%)	0.9466
		<1/3	489 (29.4%)	57 (31.3%)	
		1/3 to 2/3	857 (51.5%)	90 (49.5%)	
		>2/3	159 (9.6%)	17 (9.3%)	
Hemoglobin, g/dL	1613 (12.8%)		12.75 (1.970), 12.70 (11.30 - 14.10)	12.29 (1.940), 12.00 (10.95 - 13.60)	0.0063
WBC count, x10**9/L	1613 (12.8%)		7.87 (2.877), 7.42 (6.08 - 9.16)	8.21 (3.528), 7.56 (6.14 - 9.26)	0.1688
Sodium, mEq/L	1793 (3.0%)		139.6 (3.89), 140.0 (137.0 - 142.0)	137.8 (4.75), 138.0 (135.0 - 141.0)	<.0001
Potassium, mEq/L	1702 (8.0%)		4.26 (0.576), 4.20 (3.80 - 4.60)	4.31 (0.540), 4.30 (3.90 - 4.60)	0.3281
Bicarbonate, mEq/L	1720 (7.0%)		24.0 (3.72), 24.0 (22.0 - 26.0)	23.8 (4.12), 24.0 (21.0 - 27.0)	0.5217
Creatinine, mg/dL	1790 (3.2%)		1.48 (0.561), 1.30 (1.10 - 1.70)	1.70 (0.597), 1.60 (1.20 - 2.10)	<.0001
eGFR, mL/min	1787 (3.4%)		49.51 (18.612), 47.74 (36.09 - 60.58)	43.21 (17.752), 39.07 (29.74 - 54.05)	<.0001
BUN, mg/dL	1795 (2.9%)		32.2 (15.85), 28.0 (21.0 - 39.0)	42.3 (21.68), 36.0 (26.0 - 51.0)	<.0001

------ Heart failure rehospitalization up to 30 days after discharge [1] ------

----- Heart failure rehospitalization up to 30 days after discharge [1] -----

_	n (%				
Parameter	missing)	Category	No (N = 1667)	Yes (N = 182)	P-value [2]
BUN/creatinine ratio	1790 (3.2%)		21.86 (6.842), 20.77 (17.14 - 25.26)	24.74 (8.019), 23.00 (18.75 - 30.00)	<.0001
Uric acid, mg/dL	1720 (7.0%)		527.23 (147.803), 517.48 (422.31 - 624.54)	572.68 (164.483), 553.16 (449.07 - 689.97)	0.0002
Albumin, g/dL	1789 (3.2%)		3.85 (0.429), 3.90 (3.60 - 4.10)	3.90 (0.431), 3.90 (3.60 - 4.20)	0.1515
ALT, U/L	1673 (9.5%)		29.4 (30.16), 21.0 (15.0 - 32.0)	28.8 (30.84), 20.0 (14.0 - 30.0)	0.8068
Glucose, mg/dL	1737 (6.1%)		7.77 (3.186), 6.99 (5.66 - 8.99)	8.26 (3.438), 7.44 (5.88 - 9.88)	0.0543
Cholesterol, mg/dL	1788 (3.3%)		3.87 (1.146), 3.73 (3.08 - 4.53)	3.55 (0.958), 3.37 (2.95 - 4.14)	0.0004
Triglycerides, mg/dL	1776 (3.9%)		101.2 (51.67), 89.0 (65.0 - 124.0)	106.5 (57.06), 96.0 (67.0 - 131.0)	0.1980

Notes:

ALT, alanine transferase; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; CHF, chronic heart failure; eGFR, estimated glomerular filtration rate; HF, heart failure; JVP, jugular venous pressure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; WBC, white blood cells.

[1] Results shown are mean (standard deviation), median (25th - 75th percentile) for continuous variables, or prevalence (%) for categorical variables, unless otherwise noted. Numbers may vary due to missing values.

[2] P-values from ANOVA (F-test) for continuous variables, or from Chi-squared test for categorical variables, unless otherwise noted.

Supplemental table 3: Baseline characteristics by death up to 90 days after discharge

			Death up to 90 days after discharge [1]		
Parameter	n (% missing)	Category	No (N = 1749)	 Yes (N = 153)	P-value [2]
Age, y	1902 (0.0%)		69.8 (11.67), 72.0 (62.0 - 78.0)	71.8 (11.24), 73.0 (64.0 - 80.0)	0.0380
Male sex	1902 (0.0%)		1169 (66.8%)	106 (69.3%)	0.5376
White race	1889 (0.7%)		1653 (95.2%)	145 (95.4%)	0.8987
Time from presentation to rand., h	1885 (0.9%)		14.9 (13.24), 17.2 (5.6 - 21.7)	14.0 (8.22), 16.4 (5.2 - 21.6)	0.4084
Ischemic heart disease	1900 (0.1%)		1196 (68.5%)	115 (75.2%)	0.0856
History of angina	1898 (0.2%)		378 (21.6%)	35 (23.0%)	0.6932
Previous stroke or PVD	1902 (0.0%)		310 (17.7%)	39 (25.5%)	0.0173
Diabetes mellitus	1901 (0.1%)		797 (45.6%)	75 (49.0%)	0.4150
Respiratory disease	1898 (0.2%)		334 (19.1%)	43 (28.3%)	0.0066
Mitral regurgitation	1899 (0.2%)		583 (33.4%)	61 (39.9%)	0.1046
History of atrial fibrillation/flutter	1888 (0.7%)		933 (53.7%)	80 (53.0%)	0.8624
History of CHF	1902 (0.0%)		1661 (95.0%)	145 (94.8%)	0.9149
History of hypertension	1902 (0.0%)		1398 (79.9%)	116 (75.8%)	0.2259
History of hyperlipidemia	1901 (0.1%)		915 (52.3%)	87 (56.9%)	0.2832
History of smoking	1898 (0.2%)		362 (20.7%)	34 (22.4%)	0.6341
History of CABG or PCI	1892 (0.5%)		656 (37.7%)	72 (47.1%)	0.0229

Parameter	n (% missing)	Category	No (N = 1749)	Yes (N = 153)	P-value [2]
HF hospitalization in previous year	1902 (0.0%)		836 (47.8%)	91 (59.5%)	0.0056
NYHA class in previous month	1900 (0.1%)	None/I/II	396 (22.6%)	24 (15.9%)	0.1497
		Ш	841 (48.1%)	77 (51.0%)	
		IV	512 (29.3%)	50 (33.1%)	
BMI, kg/m**2	1880 (1.2%)		28.87 (6.132), 27.77 (24.53 - 31.91)	28.30 (6.314), 27.18 (23.89 - 30.95)	0.2716
Heart rate, bpm	1900 (0.1%)		80.1 (15.43), 78.0 (70.0 - 90.0)	80.2 (15.47), 79.0 (69.0 - 90.0)	0.9615
Systolic blood pressure, mmHg	1902 (0.0%)		125.4 (17.41), 125.0 (110.0 - 140.0)	117.5 (16.60), 115.0 (103.0 - 130.0)	<.0001
Diastolic blood pressure, mmHg	1902 (0.0%)		74.2 (11.83), 74.0 (67.0 - 80.0)	70.3 (11.45), 70.0 (60.0 - 80.0)	<.0001
Pulse pressure, mmHg	1902 (0.0%)		51.2 (15.03), 50.0 (40.0 - 60.0)	47.2 (14.70), 46.0 (38.0 - 55.0)	0.0019
Mean arterial pressure, mmHg	1902 (0.0%)		91.26 (12.007), 91.00 (83.33 - 100.00)	86.06 (11.454), 86.00 (77.67 - 93.33)	<.0001
Respiratory rate, breaths per min	1813 (4.7%)		21.3 (4.24), 21.0 (18.0 - 24.0)	20.6 (3.76), 20.0 (18.0 - 23.0)	0.0616
Edema	1902 (0.0%)	0	249 (14.2%)	26 (17.0%)	0.1192
		>1	326 (18.6%)	24 (15.7%)	
		>2	717 (41.0%)	52 (34.0%)	
		>3	457 (26.1%)	51 (33.3%)	
JVP	1717 (9.7%)	<6 cm	188 (11.9%)	16 (11.3%)	0.9793
		6-10 cm	755 (47.9%)	68 (48.2%)	

------ Death up to 90 days after discharge [1] ------

Parameter	n (% missing)	Category	No (N = 1749)	Yes (N = 153)	P-value [2]
		>10 cm	633 (40.2%)	57 (40.4%)	
Orthopnea	1877 (1.3%)	None	67 (3.9%)	9 (6.0%)	0.4445
		1 pillow	210 (12.2%)	17 (11.3%)	
		2 pillows	708 (41.0%)	55 (36.4%)	
		>30°	741 (42.9%)	70 (46.4%)	
Rales	1899 (0.2%)	0	167 (9.6%)	15 (9.8%)	0.0081
		<1/3	509 (29.2%)	55 (35.9%)	
		1/3 to 2/3	910 (52.1%)	60 (39.2%)	
		>2/3	160 (9.2%)	23 (15.0%)	
Hemoglobin, g/dL	1662 (12.6%)		12.72 (1.977), 12.60 (11.30 - 14.10)	12.41 (1.954), 12.30 (11.10 - 13.70)	0.0863
WBC count, x10**9/L	1662 (12.6%)		7.87 (2.937), 7.42 (6.04 - 9.15)	8.55 (4.826), 7.50 (6.25 - 9.89)	0.0154
Sodium, mEq/L	1846 (2.9%)		139.6 (3.96), 140.0 (137.0 - 142.0)	137.7 (4.62), 138.0 (135.0 - 141.0)	<.0001
Potassium, mEq/L	1750 (8.0%)		4.27 (0.569), 4.20 (3.90 - 4.60)	4.33 (0.626), 4.40 (3.90 - 4.70)	0.1736
Bicarbonate, mEq/L	1771 (6.9%)		24.1 (3.69), 24.0 (22.0 - 26.0)	23.2 (4.55), 23.0 (20.0 - 26.0)	0.0109
Creatinine, mg/dL	1843 (3.1%)		1.49 (0.566), 1.40 (1.10 - 1.70)	1.72 (0.638), 1.50 (1.20 - 2.20)	<.0001
eGFR, mL/min	1840 (3.3%)		49.27 (18.463), 47.32 (35.82 - 60.40)	42.81 (19.247), 39.31 (28.24 - 51.83)	<.0001
BUN, mg/dL	1848 (2.8%)		32.6 (16.41), 28.0 (21.0 - 39.0)	43.6 (20.61), 39.0 (28.0 - 54.0)	<.0001

------ Death up to 90 days after discharge [1] ------

----- Death up to 90 days after discharge [1] ------

Parameter	n (% missing) Cate	tegory	No (N = 1749)	Yes (N = 153)	P-value [2]
BUN/creatinine ratio	1843 (3.1%)		21.96 (6.864), 20.77 (17.22 - 25.45)	25.60 (8.274), 24.35 (18.89 - 31.52)	<.0001
Uric acid, mg/dL	1771 (6.9%)		527.89 (149.557), 517.48 (422.31 - 624.54)	590.95 (156.937), 582.90 (484.76 - 704.84)	<.0001
Albumin, g/dL	1842 (3.2%)		3.86 (0.434), 3.90 (3.60 - 4.20)	3.81 (0.384), 3.80 (3.60 - 4.00)	0.1873
ALT, U/L	1721 (9.5%)		29.2 (29.23), 21.0 (15.0 - 32.0)	32.9 (42.59), 20.0 (14.0 - 32.0)	0.1732
Glucose, mg/dL	1787 (6.0%)		7.85 (3.268), 6.99 (5.72 - 9.10)	7.65 (2.810), 6.94 (5.77 - 9.38)	0.4790
Cholesterol, mg/dL	1841 (3.2%)		3.86 (1.135), 3.72 (3.06 - 4.51)	3.49 (1.081), 3.37 (2.80 - 4.20)	0.0001
Triglycerides, mg/dL	1829 (3.8%)		102.3 (52.51), 90.0 (65.0 - 126.0)	92.3 (44.31), 82.0 (59.0 - 115.0)	0.0273

Notes:

ALT, alanine transferase; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass graft; CHF, chronic heart failure; eGFR, estimated glomerular filtration rate; HF, heart failure; JVP, jugular venous pressure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; WBC, white blood cells.

[1] Results shown are mean (standard deviation), median (25th - 75th percentile) for continuous variables, or prevalence (%) for categorical variables, unless otherwise noted. Numbers may vary due to missing values.

[2] P-values from ANOVA (F-test) for continuous variables, or from Chi-squared test for categorical variables, unless otherwise noted.