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# High 30-day readmission rates in hospitalized patients with heart failure: Strengthening the need for a multidisciplinary and integrated approach

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ABSTRACT

Background: Heart failure (HF) is a common disease which is one of the most common causes of hospitalization. Although mortality rates are decreasing, readmission rates are still quite high.

Objectives: We aimed to investigate the risk factors for readmission and death in patients who were hospitalized due to HF.

Design and Setting: Retrospective study, Hacettepe University, Ankara, Turkey

Methods: Patients hospitalized between 1 January 2014 to 31 December 2018 with the primary diagnosis of HF were included. Outcome variables were risk factors for 30-day all- caused readmission, 30-day HF related readmission, mortality.

Results: All-cause 30-day readmission rate was 34.8% and HF-related 30-day readmission rate was 21.2%. The factors associated with increased all-caused 30-day readmission were male gender, hyperlipidemia, chronic liver disease, malignancy. The factors associated with increased HF-related 30-day readmission were hyperlipidemia, chronic liver disease, inflammatory rheumatologic diseases, malignancy. Use of ACE-i was found to be protective against all-cause and HF-related 30-day readmission. Factors associated with mortality were ejection fraction <30%, chronic liver disease, acute kidney injury, hypoalbuminemia at the time of admission.

Conclusions: Nearly one third of patients in this cohort who were hospitalized with a primary diagnosis of HF were readmitted in the following 30 days. Having certain chronic diseases and conditions were associated with an increased risk for readmission and mortality. These findings point out to the special needs of HF patients, who require a proactive, integrated and multidisciplinary management strategy to control the risk factors and to improve the inpatient and transitional stages in the hospital.

Keywords: heart failure, hospital readmission, mortality, transitional care.

## INTRODUCTION

Heart failure (HF) is a common clinical condition which affects millions of people worldwide with increasing numbers of new diagnoses each year [1]. It is a chronic, complex disease greatly despairing the quality of life of the patients, having psychological, social and financial impact on the families and putting a huge burden on the healthcare systems. Heart failure is one of the most common causes of hospitalization both in Europe and in the United States [2]. One million hospitalization due to heart failure annually was estimated and the number is expected to increase significantly [3]. Unfortunately, 2%-17% of patients who are admitted to hospital because of HF die in the hospital in that particular episode [4]. While mortality decreased with new treatments over the years, there was no change in the rate of hospitalization [5]. Although numbers are very different among studies, 20%-33% of patients hospitalized due to heart failure are readmitted to the hospital within the first 30 days after discharge and almost 70% are readmitted within one year [6-10]. Age, chronic obstructive pulmonary disease (COPD), liver diseases, diabetes mellitus (DM), peripheral vascular disease, stroke, renal dysfunction, malnutrition, hyponatremia, hypokalemia, anemia, high brain natriuretic peptide (BNP) levels, number HF hospitalization within one year were defined as risk factors for heart failure related readmission in previous studies [5,11-13]. On the other hand, the use of certain medications, such as angiotensin converting enzyme inhibitors (ACE-i), aldosterone receptors blockers (ARB), beta-blockers and sacubitril-valsartan in the treatment of HF not only reduce the mortality but also the readmission rates [11,14]. Twenty-seven percent of these readmissions can be prevented by optimization of medical care [15]. Identifying risk factors for readmission is crucial to define the interventions required and to provide the optimal care. Reducing hospital readmission rates increases the quality of health care and decreases the cost of hospitalization. In this study, we aimed to investigate the risk factors for 30 days readmission and mortality for HF in hospitalized adult patients in a tertiary care university hospital in Turkey.

## METHODS

### 2.1. Patients and Protocol

This is a retrospective study that analyzes the hospitalization data of patients treated with the primary diagnosis of HF. Adult patients who were hospitalized in the internal medicine wards of a tertiary care university hospital between 1 January 2014 to 31 December 2018 due to HF were enrolled. Firstly; patients with relevant ICD-10 codes I50.0, I50.1, I50.2, I50.3, I50.4, I50.8, I50.9, I11.0, I13.0, I13.2, I25.0, I25.1 or the key word (heart failure) in the medical records were identified through the hospital information management system. Among these patients, those who have transthoracic echocardiography (TTE) with the reporting of the ejection fraction (EF) at the time of or before the admission were detected and screened. Patients who were admitted for the first time with the primary diagnosis of HF and whose ejection fraction was <50% on TTE were included in the study. Exclusion criteria were not having a HF-related diagnosis, having any hospitalization episode due to HF before 1 January 2014, not having a TTE before or at the time of that particular admission and having an EF of ≥50% on TTE.

Sociodemographic characteristic, comorbidities, laboratory findings and medical treatments were recorded for each episode, retrospectively.

This study complies with the principles of Declaration of Helsinki. This study has been approved by the University Ethics Commission (Approval number: GO 19/349).

### End-points and Definitions

Since definitive causes of some patients' deaths were not known, the end point for survival analysis was determined as all-cause mortality until 31 December 2018. Since some patients died during hospitalization, only the variables at the admission were used in the mortality analysis. Second end-point was determined as 30-day readmission, which was defined as unplanned admission to the hospital within 30 days of discharge. Unplanned admission to the hospital with the primary

 

diagnosis of HF was accepted as HF-related 30-day readmission. Each hospitalization period was accepted as an episode and the episodes which end up with mortality were excluded from 30-day readmission analysis. Mortality analysis was done case based and readmission analysis was done episode based.

Hyperlipidemia was defined as a low-density lipoprotein (LDL) level above the target level according to European Society of Cardiology (ESC) 2019 Guidelines on dyslipidemias [16]. Overt hypo- or hyperthyroidism or usage of L- thyroxine or any antithyroid drug was considered as thyroid disease. Increase in serum creatinine by ≥ 0.3 mg/dl within 48 hours of hospital admission was accepted as acute kidney injury (AKI) [17]. Glomerular filtration rate < 60 ml/min/1.73 $m^2$ and history of renal transplantation were accepted as chronic renal disease. DM defined as use of any antidiabetic drug or meeting American Diabetes Association criteria for the diagnosis of diabetes [18]. Cirrhosis or any other liver dysfunction more than 6 months which caused by any pathology were considered as chronic liver disease. Other chronic diseases were recorded based on the medical records of the patients. Anemia was defined as hemoglobin (Hb) level of <13.0 g/dl for men and <12.0 g/ dl for women. Serum albumin level <3.5 g/dL was considered as hypoalbuminemia. Because no generally excepted cut-off level for brain natriuretic peptide (BNP) exists, BNP cut-off level which was used in Kaplan-Meier survival analysis was identified as 1000 pg/mL by receiver operating curve (ROC) analysis with a positive predictive value of 66%, and negative predictive value of %53.

### Statistical Analysis

All statistical analyses were done with IBM SPSS Statistics 24.0 statistical package program. Continuous variables were described as median (inter- quartile range, IQR) and categorical variables as percentages. Chi- square test was used to compare categorical variables and Mann–Whitney U test/Student's T-test/ Kruskal Wallis/ one-way ANOVA test were used to compare continuous variables. Logistic regression method was applied to calculate odds ratios (OR) to comprise the occurrence of event. Hosmer-Lemeshow goodness of fit statistics were used to assess model fit. Kaplan-Meier survival estimates were calculated. Possible factors identified with univariate analyses were further entered into the Cox regression analysis, with backward selection, to determine independent predictors of survival. P- values of <0.05 were considered as significant.

## RESULTS

A total of 30228 patients were determined in the hospital information management system based on relevant ICD codes and "heart failure" key-word, and among them 2523 eligible patients were found to be hospitalized in Internal Medicine wards between 1 January 2014 to 31 December 2018 (Figure 1). Those who did not have TTE imaging before or at the time of admission, who were hospitalized with a primary diagnosis other than HF or who had previous hospitalization episodes due to HF before 1 January 2014 were excluded. Finally, 404 hospitalization episodes of 303 patients were included in the final analysis. One hundred ninety-one (36.9%) patients were male, median age was 72 (IQR=14) years and median EF was 35 (IQR = 18). The most common comorbidities accompanying HF were coronary artery disease (CAD) (74.9%), hypertension (HT) (67.7%) and hyperlipidemia (63%). Sociodemographic characteristics of patients are demonstrated in Table 1.

### 30-day readmissions

Since 63 out of 404 episodes ended with mortality, these episodes were not included in the readmission analysis and 339 hospitalization episodes were evaluated for 30-day readmission. All-cause 30-day readmission rate was 34.8% (118 episodes) and HF-related 30-day readmission rate was 21.2% (72 episodes). Atrial fibrillation (AF) (48.3%), hyperlipidemia (78.3%), thyroid dysfunction (22.2%), chronic liver disease (9.3%) and malignancy (26.3%) were more prevalent in patients who were hospitalized within 30-days compared to those patients who weren't. On the other hand, hyperlipidemia (80%), thyroid diseases (25%), chronic liver disease (9.7%), inflammatory rheumatologic diseases (18.1%) and malignancy (27.8%) were found to be more prevalent in patients who were admitted due to HF within 30-days of discharge compared to those who were

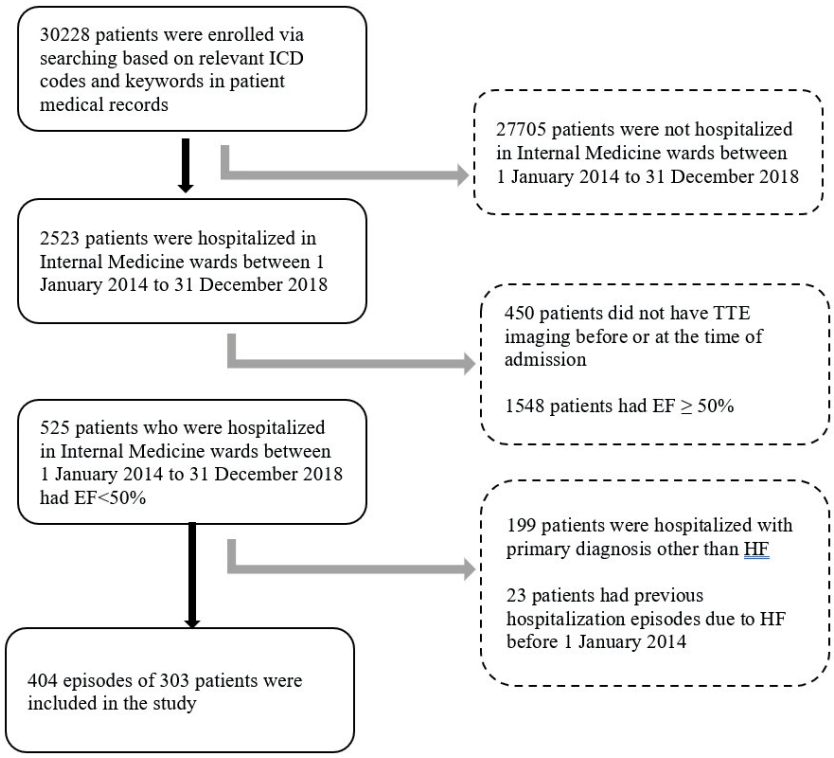


**Figure 1.** Study flow chart.

Abbreviations= HF= Heart failure, TTE= transthoracic echocardiography

**Table 1.** Baseline characteristics of patients.

| | | All patients (N=303) |
|---|---|---|
| Gender, Male | | 191 (63.7%) |
| Age, year (Median, IQR) | | 72 (14) |
| EF, % (Median, IQR) | | 35 (18) |
| EF range | EF <40% | 178 (58.7%) |
| | EF 40-49% | 125 (41.3%) |
| COPD | | 91 (30%) |
| DM | | 141 (46.5%) |
| AF | | 120 (39.6%) |
| CAD | | 227 (74.9%) |
| HT | | 205 (67.7%) |
| Chronic renal disease | | 154 (50.8%) |
| Hyperlipidemia | | 191 (63%) |
| Thyroid diseases | | 50 (16.5%) |
| PTE history | | 14 (4.6%) |
| Chronic liver disease | | 21 (6.9%) |
| Inflammatory rheumatologic diseases | | 28 (9.2%) |
| Malignancy[¥] | | 48 (15.8%) |

Abbreviations: AF= Atrial fibrillation, COPD= Chronic obstructive pulmonary disease, CAD= Coronary artery disease, DM= Diabetes mellitus, EF= Ejection fraction, HT= Hypertension, IQR= Interquartile range, PTE = Pulmonary thromboembolism

[¥] Other malignancies than non-melanoma skin cancer

not re-hospitalized because of HF within 30 days (including patients either not re-hospitalized at all or hospitalized due to another reason except for HF). Median time for HF related readmission was 13.3 (IQR=15.5) days after discharge and the highest number of readmissions was on the 8th day after discharge. Patients who were re-admitted due to any cause or HF had lower rates of ACE-i use. General features of patients based on 30-day readmission were given in Table 2.

On multivariate analysis, factors determined to be independently associated with increased all-cause 30-day readmission rates included male gender (OR 1.816; 95% CI,1.022-3.226), hyperlipidemia (OR 2.845; 95% CI, 1.570-5.152), chronic liver disease (OR 4.717; 95% CI, 1.282-17.353) and malignancy (OR 1.988; 95% CI, 1.037-3.811) (Table 3a). Factors determined to be independently associated with increased HF-related 30-day readmission rates included hyperlipidemia (OR 2.771; 95% CI, 1.346-5.707), chronic liver disease (OR 6.496; 95% CI, 1.849-22.830), inflammatory rheumatologic diseases (OR 2.996; 95% CI, 1.263-7.110) and malignancy (OR 2.124; 95% CI, 1.041-4.332) (Table 3b). Use of ACE-i was found to be protective against both all-cause and HF-related 30-day readmission. Each 1 day increase in length of stay was associated with 4.6% decrease in HF-related 30-day readmission.

 

**Table 2.** Comparison of features of patients based on 30-day readmission.

| | | All episodes (N=339) | All-cause 30-day readmission (+) (N=118) | All-cause 30-day readmission (-) (N=221) | p | HF-related 30-day readmission (+) (N=72) | HF-related 30-day readmission (-) (N=267) | p |
|---|---|---|---|---|---|---|---|---|
| Gender, Male | | 209 (61.7%) | 78 (66.1%) | 131 (59.3%) | 0.24 | 48 (66.7%) | 161 (30.3%) | 0.24 |
| Age, year (Median, IQR) | | 73.50 (15) | 74 (14) | 72 (14) | 0.20 | 74 (12) | 72.50 (15) | 0.55 |
| EF, % (Median, IQR) | | 35 (15.5) | 35 (15) | 33 (17) | 0.23 | 35 (13.7) | 35 (17.5) | 0.60 |
| EF range | EF <40% | 193 (56.9%) | 69 (58.5%) | 124 (56.1%) | 0.67 | 45 (62.5%) | 148 (55.4%) | 0.28 |
| | EF 40-49 | 146 (%43.1) | 49 (41.5%) | 97 (43.9%) | | 27 (37.5%) | 119 (44.6%) | |
| **COPD** | | 106 (31.3%) | 37 (31.4%) | 69 (31.2%) | 1 | 23(31.9%) | 83 (31.1%) | 0.89 |
| DM | | 164 (48.4%) | **48 (40.7%)** | **116 (52.5%)** | 0.04 | 31 (43.1%) | 133 (49.8%) | 0.35 |
| AF | | 137 (40.4%) | **57 (48.3%)** | **80 (36.2%)** | 0.03 | 32 (%44.4) | 105 (39.3%) | 0.50 |
| CAD | | 259 (76.4%) | 94 (79.7%) | 165(74.7%) | 0.35 | 58 (80.6%) | 201(75.3%) | 0.43 |
| HT | | 253 (74.6%) | 94 (79.7%) | 159 (71.9%) | 0.15 | 59 (81.9%) | 194 (72.7%) | 0.13 |
| Chronic renal disease | | 189 (55.8%) | 68 (57.6%) | 121 (54.8%) | 0.65 | 41(56.9%) | 148 (55.4%) | 0.89 |
| Hyperlipidemia | | 228 (68.5%) | **90 (78.3%)** | **138 (63.3%)** | **0.006** | **57 (80.3%)** | **171 (65.3%)** | **0.02** |
| Thyroid diseases | | 56 (16.6%) | **26 (22.2%)** | **30 (13.6%)** | **0.04** | **18 (25%)** | **38 (14.3%)** | **0.04** |
| PTE history | | 15 (4.4%) | 6 (5.1%) | 9 (4.1%) | 0.78 | 3(4.2%) | 12 (4.5%) | 0.90 |
| Chronic liver disease | | 17 (5%) | **11 (9.3%)** | **6 (2.7%)** | **0.01** | **7 (9.7%)** | **10 (3.7%)** | **0.04** |
| Inflammatory rheumatologic diseases | | 36 (10.6%) | 17 (14.4%) | 19 (8.6%) | 0.14 | **13 (18.1%)** | **23 (8.6%)** | **0.03** |
| Malignancy | | 60 (17.7%) | **31 (26.3%)** | **29 (13.1%)** | **0.004** | **29 (27.8%)** | **40 (15%)** | **0.01** |
| AKI | | 144 (43.5%) | 55 (47%) | 89 (41.6%) | 0.36 | 32 (45.1%) | 112 (43.1%) | 0.79 |
| BNP admission, pg/mL (Median, IQR) | | 1517.50 (2011) | 1422 (1473) | 1544 (2442) | 0.43 | 1422 (1433) | 1544 (2168) | 0.99 |
| BNP discharge, pg/mL (Median, IQR) | | 732.5 (1266) | 789.5 (810) | 694.0 (1774) | 0.23 | 880.5 (797) | 657.5 (1541) | 0.21 |
| Hemoglobin admission, g/dl (Mean, SD) | | 11.32 (2.1) | 10.97 (2.1) | 11.5 (2.1) | 0.78 | 10.18 (1.7) | 11.59 (2.0) | 0.45 |
| Hemoglobin discharge, g/dl (Mean, SD) | | 10.93 (1.7) | 10.62 (1.5) | 11.09 (1.8) | 0.22 | 10.16 (1.1) | 11.11 (1.8) | 0.26 |
| Hematocrit admission, % (Mean, SD) | | 35.58 (6.4) | 34.02 (6.4) | 36.11 (6.3) | 0.37 | 31.57 (5.5) | 36.32 (6.3) | 0.36 |
| Hematocrit discharge, % (Mean, SD) | | 33.93 (5.1) | 32.88 (4.6) | 34.49 (5.2) | 0.18 | 31.81 (3.6) | 34.4 (5.2) | 0.46 |
| Creatinine admission, mg/dl (Median, IQR) | | 1.40 (1.1) | 1.36 (0.9) | 1.40 (1.2) | 0.26 | 1.46 (0.8) | 1.49 (1.1) | 0.60 |
| Creatinine discharge, mg/dl (Median, IQR) | | 1.27 (1.1) | 1.29 (1.1) | 1.27 (1.1) | 0.97 | 1.33 (1.3) | 1.26 (1.3) | 0.62 |
| Sodium admission, mEq/L (Median, IQR) | | 135 (6) | 135 (5) | 135 (7) | 0.32 | 135 (6) | 135 (6) | 0.95 |
| Sodium discharge, mEq/L (Median, IQR) | | 136 (5) | 137 (5) | 136 (5) | 0.18 | 136 (5) | 136 (5) | 0.26 |
| Albumin admission, g/dL (Mean, SD) | | 3.39 (0.7) | 3.41 (0.7) | 3.38 (0.6) | 0.52 | 3.39 (0.8) | 3.39 (0.8) | 0.96 |
| Albumin discharge, g/dL (Mean, SD) | | 3.20 (0.4) | 3.17 (0.6) | 3.25 (0.7) | 0.13 | 3.16 (0.5) | 3.24 (0.7) | 0.26 |
| Potassium admission, mEq/L (Median, IQR) | | 4.30 (0.9) | 4.20 (0.8) | 4.40 (1) | 0.14 | 4.20 (0.8) | 4.30 (1) | 0.15 |
| Potassium, discharge, mEq/L (Median, IQR) | | 4.30 (0.7) | **4.18 (0.7)** | **4.30 (0.9)** | **0.005** | 4.18 (0.7) | 4.32 (0.8) | 0.06 |
| IV diuretic treatment in the hospital | | 286 (85.4%) | 101 (85.6%) | 185 (85.3%) | 1 | 63 (87.5%) | 223 (84.8%) | 0.71 |
| Follow-on appointment at discharge | | 281 (83.9%) | 101 (85.6%) | 180 (82.9%) | 0.64 | 62 (86.1%) | 219 (83.3%) | 0.72 |
| Length of hospital stay, days (median, IQR) | | 13 (13) | 13 (12) | 14 (13.5) | 0.54 | **10 (10.25)** | **14 (13)** | **0.001** |
| **Drugs prescribed at discharge** | | | | | | | | |
| Beta blocker | | 273 (83.7%) | 98 (83.8%) | 175 (83.7%) | 1 | 63 (87.5%) | 210 (82.7%) | 0.37 |
| ACE-i | | 78 (24.1%) | **18 (15.5%)** | **60 (28.8%)** | **0.007** | **8 (11.3%)** | **70 (27.7%)** | **0.004** |
| ARB | | 40 (12.3%) | 16 (13.7%) | 24 (11.5%) | 0.60 | 13 (18.1%) | 27 (10.6%) | 0.10 |
| MRA | | 124 (38.3%) | 40 (34.5%) | 84 (40.4%) | 0.34 | 23 (32.4%) | 101 (39.9%) | 0.27 |
| Digoxin | | 81 (25%) | 30 (25.6%) | 51 (24.6%) | 0.89 | 17 (23.6%) | 64 (25.4%) | 0.88 |
| Statin | | 153 (47.7%) | 61 (53%) | 92 (44.2%) | 0.13 | 40 (57.1%) | 113 (44.7%) | 0.08 |

Abbreviations: ACE-i= Angiotensin converting enzyme inhibitors, AF= Atrial fibrillation, AKI = Acute kidney injury, ARB= Aldosterone receptor blockers, BNP= Brain natriuretic peptide, COPD= Chronic obstructive pulmonary disease, CAD= Coronary artery disease, DM= Diabetes mellitus, EF= Ejection fraction, HF= Heart failure, HT= Hypertension, IQR= Interquartile range, IV= Intravenous, MRA= Mineralocorticoid receptor antagonists, PTE = Pulmonary thromboembolism, SD= Standard deviation

**Table 3.** Independent predictors for 30-day readmission in multivariate logistic analysis.

| 3a. Independent predictors for all-cause 30-day readmission in multivariate logistic analysis. | | | 3b. Independent predictors for HF-related 30-day readmission in multivariate logistic analysis. | | |
|---|---|---|---|---|---|
| **Variables** | **Odds ratio (95% CI)** | **P-value** | **Variables** | **Odds ratio (95% CI)** | **P-value** |
| **Gender, male** | **1.816 (1.022-3.226)** | **0.042** | Gender, male | 1.776 (0.898-3.512) | 0.099 |
| Age, year | 1.021 (0.996-1.046) | 0.100 | Age, year | 1.017 (0.987-1.048) | 0.269 |
| DM | 0.755 (0.444-1.285) | 0.300 | **Hyperlipidemia** | **2.771 (1.346-5.707)** | **0.006** |
| AF | 1.582 (0.938-2.667) | 0.085 | Thyroid diseases | 2.072 (0.961-4.466) | 0.063 |
| **Hyperlipidemia** | **2.845 (1.570-5.152)** | **0.001** | **Chronic liver disease** | **6.496 (1.849-22.830)** | **0.004** |
| Thyroid diseases | 1.696 (0.850-3.380) | 0.134 | **Inflammatory rheumatologic diseases** | **2.996 (1.263-7.110)** | **0.013** |
| **Chronic liver disease** | **4.717(1.282-17.353)** | **0.020** | | | |
| **Malignancy** | **1.988 (1.037-3.811)** | **0.039** | **Malignancy** | **2.124 (1.041-4.332)** | **0.038** |
| **Serum potassium level** | **0.587 (0.376-0.937)** | **0.025** | **ACE-i** | **0.331 (0.143-0.770)** | **0.010** |
| **ACE-i** | **0.480 (0.252-0.911)** | **0.025** | **Length of stay** | **0.954 (0.922-0.987)** | **0.007** |

### Mortality

Three hundred-three patients were included in the mortality analysis. Median follow-up time was 25 (IOR= 42.1) months. Kaplan-Meier analysis estimated that gender (p=0.021), EF range (p<0.001), chronic liver disease (p=0.002), AKI at the admission (p<0.001), serum BNP at the admission (p<0.001), hyponatremia at admission (p=0.048), hypoalbuminemia at admission (p<0.001) were risk factors for mortality. In addition to these variables; age, COPD, DM, AF, CAD, chronic renal disease, hyperlipidemia, thyroid dysfunction, inflammatory rheumatologic diseases, malignancy, anemia at admission were also evaluated in the Kaplan-Meier analysis, but no effect on mortality could be shown. Cox regression analysis model was constructed for the variables that were significant in the Kaplan-Meier analysis (Table-4). Factors associated with mortality in Cox regression analysis model were determined as EF<30% (OR 2.120; 95% CI, 0.431-3.088), chronic liver disease (OR 1.857; 95% CI,1.089-3.165), AKI (OR 1.584; 95% CI, 1.157-2.169) and hypoalbuminemia at admission (OR 1.576; 95% CI, 1.142-2.175). Kaplan-Meier analysis of these variables were given in Figure 2.

**Table 4.** Independent predictors for mortality in Cox regression analysis.

| Variables | Odds ratio (95% CI) | P-value |
|---|---|---|
| EF 40-49% (reference) | | |
| EF 30-39% | 1.225 (0.804-1.867) | 0.334 |
| **EF <30%** | **2.102 (0.431-3.088)** | **<0.0001** |
| **Chronic liver disease** | **1.857 (1.089-3.165)** | **0.023** |
| **AKI** | **1.584 (1.157-2.169)** | **0.004** |
| **Hypoalbuminemia** | **1.576 (1.142-2.175)** | **0.006** |

Abbreviations: AKI= Acute kidney injury, CI= Confidence interval, EF= Ejection fraction

## DISCUSSION

Although the definition of HF has changed over the years, the current definition of the European Society of Cardiology (ESC) categorizes HF with regards to the EF range: EF ≥ 50% as HF with preserved EF (HFpEF), EF = 40-49% as HF with mid-range EF (HFmrEF) and EF<40% as HF with reduced EF (HFrEF) [19]. Signs of HF are generally related to volume overload and/or hypoperfusion. There is no specific test to diagnose HF, yet diagnosis mainly depends on history and physical examination together with certain laboratory and imaging tests. Although there is slight decrease in mortality rates with new treatments, HF related mortality rate, readmission rate and cost are still high [20,21].

In this study, we investigated the risk factors for 30-day readmission and mortality in adult patients hospitalized with a primary diagnosis of HF in a tertiary care university hospital in Turkey. All-cause 30-day readmission rate was 34.8% and HF-related 30-day readmission rate was 21.2%. Although all cause 30-day readmission rates reported in different studies are variable, they range between 20%-33% [7-10]. The rate of all-cause 30-day readmission was close to previous studies, but among them, the proportion of HF related 30-day readmission was higher than other studies. Among the heart failure patient with 30-day readmissions, less than 40% are admitted with a primary diagnosis of heart failure [6,22,23]. Hyperlipidemia, chronic liver disease, inflammatory rheumatologic diseases, malignancy, shorter length of stay and not being discharged on an ACE-i were found to be independent risk factors for HF related 30-day readmission.

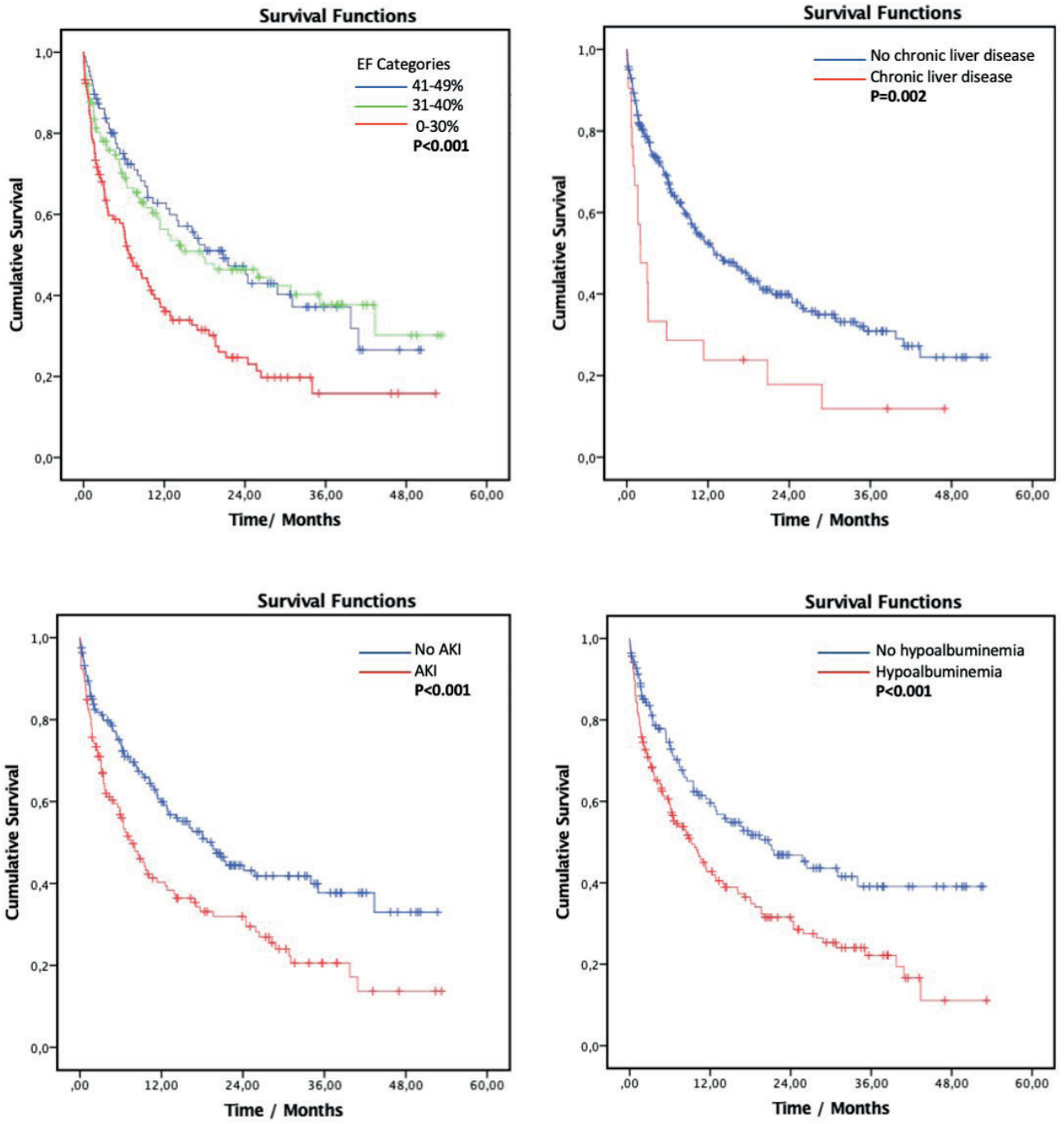


**Figure 2.** Kaplan-Meier curves for mortality.
Abbreviations: AKI= Acute kidney injury, EF= Ejection fraction

Having an EF<30%, chronic liver disease, AKI and hypoalbuminemia were associated with increased mortality. It's well known that increasing number of comorbidities and higher Charlson comorbidity index score are associated with poor prognosis [9,24]. Comorbidities can lead to the development of HF, as well as result in exacerbations and complications of the disease. Reduced EF is also a well-known risk factor for increased HF-related mortality [21,24]. Curtis and colleagues showed that HF-related mortality correlates closely with the level of reduction in the EF [25].

The benefit of ACE-i on HF related readmission and mortality has been demonstrated in several studies [10,26]. ACE-i not only block renin-angiotensin-aldosterone system but also prevent progressive remodeling in the heart and cause changes in neurohormonal level so improve myocyte contractility and cardiac performance [27]. Statin treatment is associated with reduced mortality in HF patients, but this study did not demonstrate a positive effect of statins on mortality [28]. Hyperlipidemia was a risk factor for unplanned readmission in this study, independent of statin

use. Unlike our study, a meta-analysis has shown that hyperlipidemia is associated with decreased mortality in patients with heart failure, but further studies are needed [29].

Although the exact mechanism is unknown, hepatic dysfunction has been found to be associated with poor outcomes and increased 30-day readmission in HF patients [8,30]. Hepatic congestion due to elevated central venous pressure and impaired hepatic perfusion due to decreased cardiac output cause hepatic dysfunction in HF patients. On the other hand, hepatic diseases such as non-alcoholic fatty liver disease are associated with development of HF and also with poor prognosis in established HF [30,31]. Functional hypovolemia despite the volume expansion and reduced systemic vascular resistance, which causes a hyperdynamic state in cirrhosis can contribute to worsening of HF [32]. Renal dysfunction accompanies more than 60% of HF patients who are hospitalized due to HF exacerbation [33]. HF patients with impaired renal function have an approximately 50% increased relative mortality risk compared to patients with normal renal function and renal dysfunction is important for risk stratification [34].

Patients with inflammatory rheumatologic diseases have higher cardiovascular disease burden than general population and most common cause of mortality in inflammatory rheumatologic diseases is cardiac diseases [35]. Inflammation is deemed to be the main contributor for the increased cardiovascular mortality, however drugs such as steroids, non-steroidal anti-inflammatory drugs and tumor necrosis factor inhibitors which target inflammation also have undesired effects on the heart [36]. In addition to these shared risk factors, patients with malignancies have other risk factors for cardiotoxicity namely therapeutic agents used in malignancies (e.g., conventional cytotoxic agents such as anthracyclines, alkylating agent; targeted therapies such as vascular endothelial growth factor inhibitors; immunotherapies) and radiotherapy [37].

Hypoalbuminemia can be a sign of cardiac cachexia, malnutrition or a consequence of chronic liver disease. Malnutrition is very commonly seen in HF patients and is found to be a prognostic risk factor for hospitalization and mortality [38]. The study from Australia was also showed that higher serum albumin levels were protective against readmission and mortality [9]. Nutritional intervention in malnourished patients have been shown to be associated with a reduced risk of HF related hospitalization and mortality [39].

Shorter length of stay was shown to be an independent risk factor for HF related 30-day readmission in our study, as Roshanghalb and colleagues also showed that longer length of stay was associated with decreased mortality and readmission rates [40]. Yet, most of the other studies demonstrated that prolonged hospitalization was associated with increased readmission rates [8,41]. Symptom severity (e.g. edema, dyspnea and poorer NYHA functional class), end organ damage (e.g. renal dysfunction and elevated troponin), comorbidities (e.g. diabetes, chronic renal disease) and social problems are the predictors of length of stay in HF patients [41-43]. Actually, prolonged length of stay can be accepted as a surrogate marker of disease severity and comorbidity burden.

As evident from our findings and from the evidence in the literature, multiple factors intervene negatively with the course of disease. The complexity of HF patients due to multiple comorbidities and polypharmacy makes it difficult to manage the patient in a fragmented healthcare system, necessitating a multidisciplinary and integrated approach [44]. Avoidable proportion of HF related 30-day readmission ranged between 5% to 79% among 16 studies, and the meta-analysis of these studies estimated that on average 23.1% of HF related 30-day readmission was avoidable [45]. Unplanned hospital readmissions, especially avoidable unplanned readmissions, are accepted as an indicator of quality of care and a hospital performance measure. Because readmissions are mainly related to previous readmission for HF, proper management of index admission is the first and most important step to prevent readmissions [46].

Pre-discharge period in the hospital, the transitional period (from hospital to home) and stable outpatient period are the main targeted time periods for interventions to reduce HF related

 

readmissions. As HF patients are more vulnerable in the transitional period, interventions in this period that aim to reduce unplanned hospital readmissions and mortality and improve the quality of life are promising [47]. Meta-analysis showed that transitional care programs provide reduction in all-cause mortality by 25% and HF related readmission by nearly half [48]. These programs have common components such as telephone follow-up, education, self-management, weight monitoring, sodium restriction or dietary advice, exercise recommendations, medication review, and social and psychological support. Development of congestion is the leading cause of HF decompensation and a strong predictor of poor outcome so monitoring and early detection of the congestion before decompensation is crucial [49]. Steps in transitional care programs like weight monitoring, dietary advice, medication review help prevent the congestion and telephone follow up help recognize the congestion in a timely manner. Medication adherence is one of the key points in HF treatment and interventions to improve medication compliance can reduce the risk for readmission and mortality in HF patients [50]. Unfortunately, less than half of the hospitals carry specific programs associated with transitional care in United States and this ratio is less in lower- and middle-income countries.

This study has several limitations. First of all, as it is a retrospective study and all data was obtained from patients' medical records, some factors that could have affected the disease prognosis such as drug compliance, nutritional status, physical therapy, Charlson comorbidity index and NYHA functional classification could not be assessed. Because some patients do not have TTE during hospitalization, the last TTE was taken into account. Therefore, EF at hospitalization might have been different (probably worse) from the previous EF evaluations. This is a single center study and readmissions which occurred to our hospital could be determined, so the readmission rate might be higher than calculated.

## CONCLUSION

Nearly one third of patients in this cohort who were hospitalized with a primary diagnosis of HF were readmitted in the following 30 days. Having certain chronic diseases and conditions as well as a shorter length of stay were associated with an increased risk for readmission and mortality in this complex patient population. These findings point out to the special needs of HF patients, who require a proactive, integrated and multidisciplinary management strategy to control the risk factors and to improve the inpatient and transitional stages in the hospital.

### Author contribution

Study conception and design: HB, MDT; data collection: HB, FC, SC; analysis and interpretation of results: HB, ECB; literature review: HB, MDT; draft manuscript preparation: HB; critical review: MDT, OAU. All authors reviewed the results and approved the final version of the manuscript.

### Ethical approval

The study was approved by the Hacettepe University Non-Interventional Clinical Researches Ethics Board (Protocol no: GO 19/349, date: 02/04/2019).

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### Conflict of interest

The authors declare that there is no conflict of interest.

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