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Long-Term Prognosis of Patients with Heart Failure: Follow-Up Results of Journey HF-TR Study Population

ABSTRACT

Background: Despite advances in therapeutic management of patients with heart failure, there is still an increasing morbidity and mortality all over the world. In this study, we aimed to present the 3-year follow-up outcomes of patients included in the Journey HF-TR study in 2016 that has evaluated the clinical characteristics and management of patients with acute heart failure admitted to the hospital and present a national registry data.

Methods: The study was designed retrospectively between November 2016 and December 2019. Patient data included in the previously published Journey HF-TR study were used. Among 1606 patients, 1484 patients were included due to dropout of 122 patients due to inhospital death and due to exclusion of 173 due to incomplete data. The study included 1311 patients. Age, gender, concomitant chronic conditions, precipitating factors, New York Heart Association, and left ventricular ejection fraction factors were adjusted in the Cox regression analysis.

Results: During the 3-year follow-up period, the ratio of hospitalization and mortality was 70.5% and 52.1%, respectively. Common causes of mortality were acute decompensation of heart failure and acute coronary syndrome. Angiotensin receptor blockers, beta-blockers, statin, and sacubitril/valsartan were found to reduce mortality. Hospitalization due to acute decompensated heart failure, acute coronary syndrome, lung diseases, oncological diseases, and cerebrovascular diseases was associated with the increased risk of mortality. Implantation of cardiac devices also reduced the mortality.

Conclusions: Despite advances in therapeutic management of patients with heart failure, our study demonstrated that the long-term mortality still is high. Much more efforts are needed to improve the inhospital and long-term survival of patients with chronic heart failure.

Keywords: Heart failure, hospitalization, mortality, prognosis, Turkey/national database

INTRODUCTION

Heart failure (HF) is a cardiovascular disease with rapidly increasing morbidity and mortality around the world.[1] There were 5.7 million patients with HF in the United States by 2016, and this number is estimated to increase to about 8 million in 2030.[2] The cost of HF was 30 billion dollars in the United States in 2012, and this cost is anticipated to reach approximately 70 billion dollars in 2030.[3] The prevalence of HF in Turkey is 3%-7%.[4] Despite following the recommendations of HF guidelines, significant inconsistencies in adherence to pharmacological and device therapy practice continue.[5,6] Heart failure may start with the appearance of mild symptoms and progress to loss of labor power, frequent hospitalization, and becoming bedridden. All of these factors have led to the necessity of further studies to investigate the pathophysiology of HF, discover new treatment options, and develop preventive approaches.

Wide and comprehensive studies were planned worldwide on the diagnosis, follow-up, and clinical outcomes of patients with HF. The European Society of Cardiology's HF Long-Term (ESC-HF) pilot study by the European Cardiology Association reviewed the epidemiology, clinical demographic findings, and

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clinical outcomes of patients with HF in 12 European countries based on a 1-year follow-up period.[7] The Rotterdam Study reviewed the incidence, prevalence, lifelong risk, and prognosis of patients with HF in the Netherlands.[8] Similarly, numerous studies were conducted on the prevalence, hospitalization status, long-term follow-up, and clinical outcomes of patients with HF in the United States.[3,9-12] However, we have not found any large-scale studies on the long-term follow-up of patients with HF in Turkey.

The Journey Heart Failure-Turkey (HF-TR) study in 2016 evaluated the clinical characteristics, management, and inhospital outcomes of hospitalized acute HF patients in the Turkish population.[5] In this study, we aimed to present the 3-year follow-up outcomes of patients included in the Journey HF-TR study that has evaluated the clinical characteristics and management of patients with acute HF admitted to the hospital and present a national registry data.

METHODS

Study Population

The design and the primary outcomes of the Journey HF-TR study have been previously published.[5] Briefly, the Journey HF-TR study reviewed the general clinical characteristics, inhospital management, and short-term outcomes (inhospital) of a large patient population with acute HF in Turkey. In the present study, the 3-year follow-up results of the cases from the Journey HF-TR study are evaluated.

Briefly, this multicenter and noninvasive study was conducted with a retrospective design between November 1, 2016, and December 31, 2019. Among 1606 patients enrolled in the Journey HF-TR study, 1484 patients were evaluated in this analysis due to dropout of 122 patients (13 patients with *de novo* acute HF and 109 patients with acute decompensated chronic HF) with inhospital death. However, 173 patients (21 patients with de novo acute HF and 152 patients with acute decompensated chronic HF) were excluded since they did not have any 3-year follow-up data. Therefore, the present study was carried out with 1311 patients (Figure 1). Follow-up data of 239 patients diagnosed with *de novo* acute HF were complete and were followed up in the clinic with the diagnosis of HF or hospitalized at least once with the diagnosis of chronic HF or decompensated HF.

Baseline demographic findings in the intensive care unit, co-morbidities, precipitating factors, referral symptoms, physical exam findings, current medications, and New York Heart Association (NYHA) scores at referral and discharge were obtained from the data of the HF-TR study. Heart failure subtypes were defined as follows: HF with preserved ejection fraction (HFpEF) ≥ 50%, HF with mildly reduced EF (HFmrEF) 40%-49%, and HF with reduced EF (HFrEF) < 40%. The medications used by the patients, number of hospitalizations, causes for hospitalization, previous cardiovascular events, and clinical outcomes during the 3-year follow-up period were obtained from the hospital patient files or hospital health information systems, the e-Nabiz personal health system (https://enabiz.gov.tr), the death notification system (https://obs.saglik.gov.tr), and telephone conversations with patients or their relatives.

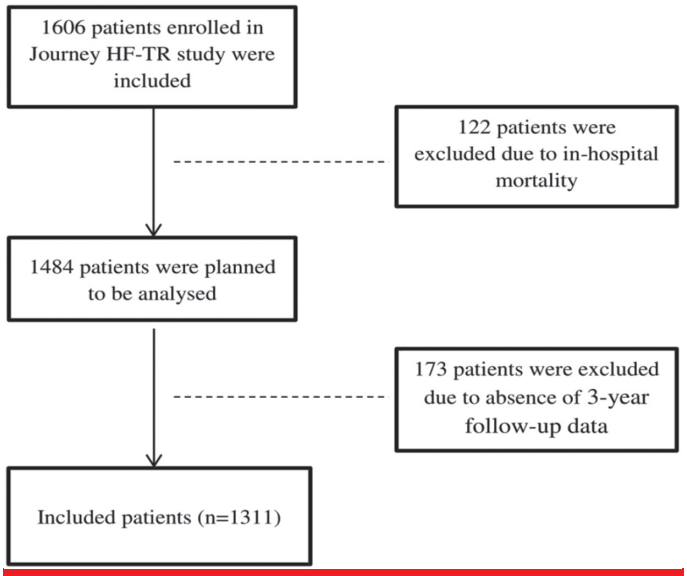

Figure 1. Flowchart of the study.

The HF-TR study followed the Declaration of Helsinki and the recommendations of the International Council on Harmonization's Good Clinical Practices. The study protocol was approved by the Local Ethics Committee with a new referral (decision date: 12.12.2019, decision no: E.155537), and written informed consent was obtained from all patients. The study is consistent with the latest version of Declaration of Helsinki that was revised in 2013.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics 22.0 for Windows (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to test the normal distribution of variables. Continuous variables with normal distribution were expressed as mean ± SD, and continuous variables without normal distribution were expressed as median (min–max). Categorical variables were presented as numbers and percentages. The differences between the medication rates used at discharge and post-discharge during the 3-year follow-up period were estimated by the McNemar's test. Cox regression analysis was performed to identify risk determinants of mortality. Age, gender, concomitant chronic conditions, precipitating factors, and NYHA and LVEF factors

HIGHLIGHTS

- Long-term mortality rates are high in patients with acute heart failure (HF).
- Hospitalization for acute decompensated HF, acute coronary syndrome, lung diseases, oncological diseases, and cerebrovascular diseases is associated with an increased risk of mortality.
- Angiotensin receptor blockers, beta-blockers, and statin treatments are associated with reduced mortality in their therapeutic management.

were adjusted in the Cox regression analysis (Adjusted Model I). A regression model was also created in which the drug effects were adjusted for the relationship between hospitalization after discharge, cardiovascular events, and mortality (Adjusted Model II). Values of $P < .05$ were considered significant for statistical analyses.

RESULTS

Table 1 shows the baseline demographic findings, co-morbidities, precipitating factors, referral symptoms, physical examination findings, EF, and NHYA scores at referral and discharge from the Journey HF-TR study records in detail.

The medications used at discharge and post-discharge during the 3-year follow-up are presented in Table 2. The usage rates of angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), and beta-blockers (BBs) tended to decrease during follow-up after discharge compared with the time at discharge. No statistical difference was found in other drug use rates.

The inhospital mortality rate was 7.6% (n = 122). The number of patients who could not be followed after discharge was 173 (11.7%). During the 3-year follow-up, 70.5% (66.1% cardiac and 4.4% non-cardiac reasons) of the patients were hospitalized at least once and the median hospitalization count was 1 (range 1-14). The cardiac reasons for hospitalization were as follows: acute decompensation of chronic HF in 51.3% of cases of hospitalization (n = 673), acute coronary syndrome in 13.5% (n = 177), fatal arrhythmias in 1.1% (n = 14), sudden cardiac death or cardiac arrest (out of hospital) in 0.2% (n = 3), dysfunctions of a pacemaker or an implantable cardioverter-defibrillator (ICD) shock in 0.2% (n = 3), medication overdose or intoxication in 0.2% (n = 2), and electrolyte imbalance, valvular diseases, and complications each in 0.1% (n = 1). The non-cardiac reasons for hospitalization were as follows: lung diseases in 1.3% (n = 17), oncological diseases in 0.8% (n = 11), cerebrovascular events in 0.6% (n = 8), cardiac or non-cardiac percutaneous or surgical procedures in 0.5% (n = 7), renal dysfunction in 0.4% (n = 5), diabetes and complications in 0.2% (n = 3), bleeding in 0.2% (n = 2), other causes in 0.3% (n = 4), and organ or tissue infections, orthopedic causes, other acute internal or surgical diseases, and thromboembolic events each in 0.1% (n = 1).

In patients who survived after discharge, the mean EF was 33.9% ± 13.1% and the ratios of HFrEF, HFmrEF, and HFpEF were 62.2%, 18.2%, and 19.6%, respectively. The mortality rate during the 3-year follow-up was 52.1% (n = 683). The risk of 1-year and 3-year mortality was higher in the HFrEF group compared to the HFmrEF and HFpEF groups (Figure 2). All causes of mortality are presented in Table 3. The effects of confounding factors were adjusted in the Cox regression analysis. The use of ARBs [hazard ratio (HR): 0.73; $P < .001$], BBs (HR: 0.68; $P < .001$), valsartan or sacubitril (HR: 0.18; $P = .015$), and statin (HR: 0.85; $P = .006$) was found to be associated with the reduced risk of mortality. There was no significant association between other medications and mortality (Table 4).

Table 1. Demographic Findings, Concomitant Conditions, Precipitating Factors, and Clinical Presentation at ICU Admission

	All Population
Variables	**n = 1606**
Age, years	67.8 ± 13.2
Male, n (%)	918 (57.2)
Concomitant chronic conditions, n (%)	
Coronary artery disease	957 (59.6)
Hypertension	1076 (67.0)
Diabetes mellitus	673 (41.9)
Atrial fibrillation	626 (39.0)
Previous stroke or TIA	177 (11.0)
Renal failure	453 (28.2)
Anemia	772 (48.1)
Venous thromboembolism	74 (4.6)
Peripheral artery diseases	103 (6.4)
Depression	273 (17.0)
Cancer	156 (9.7)
Precipitating factors, n (%)	
Acute coronary syndrome	236 (14.7)
Arrhythmia	403 (25.1)
Infection	471 (29.3)
Non-compliance with therapy	382 (23.8)
Major symptoms, n (%)	
Dyspnea on rest	1135 (70.7)
Dyspnea on exercise	1501 (93.5)
Orthopnea	1236 (77.0)
Paroxysmal nocturnal dyspnea	978 (60.9)
Angina	419 (26.1)
Anxiety	775 (48.3)
Fatigue	1353 (84.3)
Physical examination, n (%)	
Crackles on lung auscultation	1143 (71.2)
S3 gallop	772 (48.1)
Elevated jugular venous pressure	565 (35.2)
Abdominal distention and ascites	457 (28.5)
Hepatojugular reflux	504 (31.4)
Peripheral edema	1061 (66.1)
Systolic blood pressure, mm Hg	127.6 ± 30.8
Heart rate, bpm	93.9 ± 23.6
Oxygen saturation, %	90.0 ± 9.1
Baseline NYHA, n (%)	
I-II	340 (21.2)
II-IV	1266 (78.8)
Discharge NYHA, n (%)	
I-II	1362 (84.8)
II-IV	244 (15.2)
LVEF, %	32.7 ± 14.1
HFpEF	273 (17)
HFmrEF	305 (19)
HFrEF	1028 (64)

Categorical variables are shown as n (%). Numerical variables are shown as mean ± SD or median (min–max).
HFmrEF, heart failure with moderate ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICU, intensive care unit; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; TIA, transient ischemic attack.

Table 2. Drug Use at Discharge and Follow-Up

Drugs	Discharge n = 1484	At the 3-Year Follow-Up After Discharge n = 1311	*P*
ACEi, n (%)	1158 (78.0)	793 (60.5)	<.001*
ARB, n (%)	1202 (81.0)	785 (59.9)	<.001*
Beta-blockers, n (%)	1291 (87.0)	1035 (78.9)	<.001*
Calcium channel blockers, n (%)	208 (14.1)	172 (13.1)	.675
Diuretics, n (%)	1202 (81.0)	1023 (78.0)	.126
MRA, n (%)	890 (60.0)	754 (57.5)	.083
Amiodarone, n (%)	32 (2.2)	28 (2.1)	.999
Digoxin, n (%)	283 (19.1)	249 (19.0)	.999
Ivabradine, n (%)	142 (9.6)	133 (10.1)	.862
Valsartan/sacubitril, n (%)	–	17 (1.3)	–
Insulin, n (%)	310 (20.8)	270 (20.6)	.983
Statin, n (%)	321 (21.6)	285 (21.7)	.999
Oral antidiabetics, n (%)	298 (20.1)	290 (22.1)	.104
Oral nitrate, n (%)	270 (18.2)	248 (18.9)	.998
Other, n (%)	621 (41.8)	625 (47.7)	.075

Categorical variables are shown as n (%).
*$P < .05$ shows statistical significance.
ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; MRA, mineralocorticoid receptor antagonists.

Table 3. Survival Findings After Discharge

Survival Findings	At the 3-Year Follow-Up After Discharge n = 1311
Alive, n (%)	628 (47.9)
Exitus, n (%)	683 (52.1)
Cardiac	577 (44.0)
Acute decompensation of CHF	290 (22.1)
Acute coronary syndrome	270 (20.6)
Fatal arrhythmias	12 (0.9)
Sudden cardiac death or cardiac arrest	5 (0.4)
Non-cardiac	106 (8.1)
Multiorgan insufficiency	59 (4.5)
Kidney dysfunction	10 (0.8)
Oncological diseases	11 (0.8)
Cerebrovascular events	11 (0.8)
Cardiac or non-cardiac percutaneous or surgical procedure	1 (0.07)
Thromboembolic events	1 (0.07)
Lung diseases	9 (0.7)
Diabetes and complications	2 (0.2)
Bleeding	2 (0.2)

Categorical variables are shown as n (%).
CHF, chronic heart failure.

Since no deaths were detected among non-hospitalized patients, other causes (routine checks etc.) for hospitalized and non-hospitalized patients were combined, and a reference group was created. The risk factors that increased the risk of mortality were acute decompensation of chronic HF (HR: 42.8; $P < .001$; 95% CI: 24.1-75.8), hospitalization due to acute coronary syndrome (HR: 71.8; $P < .001$; 95% CI: 39.9-129.6), hospitalization due to lung diseases (HR: 14.1; $P < .001$; 95% CI: 5.3-37.7), hospitalization due to oncological diseases (HR: 54.2; $P < .001$; 95% CI: 23.4-125.6), and hospitalization due to cerebrovascular events (HR: 24.3; $P < .001$; 95% CI: 7.8-75.3) (Table 5).

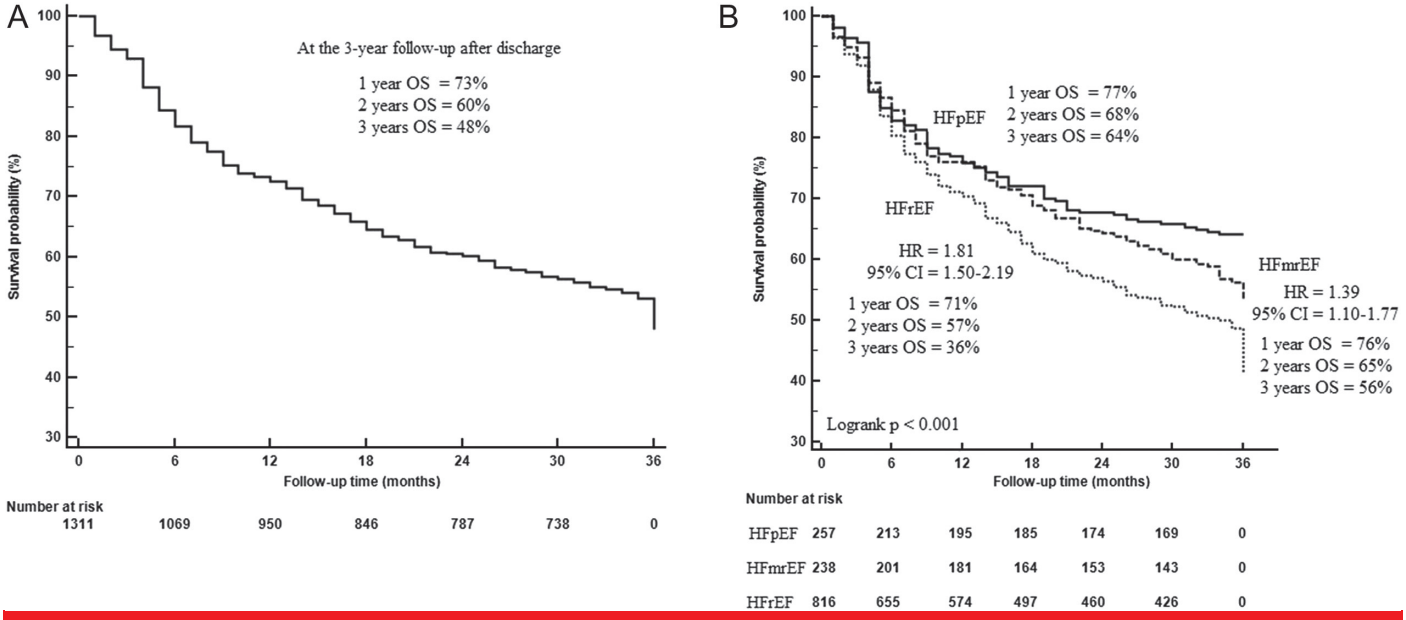

Figure 2. Probability of survival at 3-year follow-up (A) and mortality risk in HF subtypes (B) in patients who survived discharge.

Table 4. Effects of Medication Use on Survival at the 3-Year Follow-Up After Discharge

	Alive	Exitus	Adjusted Cox Regression	
Drugs	**n = 628**	**n = 683**	**HR (95% CI)**	***P***
ACEi, n (%)	387 (61.6)	406 (59.4)	0.91 (0.78-1.06)	.226
ARB, n (%)	498 (79.2)	287 (42.0)	0.73 (0.63-0.85)	<.001*
Beta-blockers, n (%)	521 (83.0)	514 (75.3)	0.68 (0.58-0.81)	<.001*
Calcium channel blockers, n (%)	87 (13.8)	85 (12.4)	0.95 (0.81-1.10)	.825
Diuretics, n (%)	484 (77.1)	539 (78.9)	1.02 (0.82-1.19)	.909
MRA, n (%)	394 (62.7)	360 (52.7)	0.92 (0.85-1.03)	.658
Amiodarone, n (%)	17 (2.7)	11 (1.6)	0.96 (0.87-1.06)	.915
Digoxin, n (%)	106 (16.9)	143 (20.9)	1.15 (0.96-1.38)	.138
Ivabradine, n (%)	72 (11.5)	61 (8.9)	0.83 (0.64-1.08)	.173
Valsartan/sacubitril, n (%)	16 (2.5)	1 (0.1)	0.18 (0.05-0.72)	.015*
Insulin, n (%)	146 (23.2)	124 (18.1)	0.88 (0.72-1.05)	.320
Statin, n (%)	158 (25.2)	127 (18.5)	0.85 (0.74-0.98)	.006*
Oral antidiabetics, n (%)	159 (25.3)	131 (19.1)	0.93 (0.82-1.05)	.218
Oral nitrate, n (%)	115 (18.3)	133 (19.5)	1.18 (0.92-1.46)	.567
Others, n (%)	310 (49.4)	344 (50.4)	0.96 (0.83-1.12)	.645

Age, gender, concomitant chronic conditions, precipitating factors, NYHA, and LVEF factors were adjusted in the Cox regression analysis.
Categorical variables are shown as n (%).
*$P < .05$ shows statistical significance.
ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; HR, hazard ratio; MRA, mineralocorticoid receptor antagonists; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Table 5. Relationship Between Hospitalization After Discharge and Cardiovascular Events and Mortality

	At the 3-Year Follow-Up After Discharge			Adjusted Model I		Adjusted Model II	
	All Population	Alive	Exitus				
Variables	**n = 1311**	**n = 628**	**n = 683**	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Hospitalization, n (%)							
No	387 (29.5)	387 (61.6)	–	Reference		Reference	
Yes	924 (70.5)	241 (38.4)	683 (100.0)	28.8 (16.8-40.1)	<.001*	31.1 (14.6-48.5)	<.001*
Number of hospitalization	1 (1-14)	2 (1-14)	1 (1-11)	0.6 (0.5-0.7)	<.001*	0.5 (0.4-0.6)	<.001*
Causes of hospitalization, n (%)							
None/other reasons	404 (30.8)	393 (62.6)	11 (1.6)	Reference		Reference	
Acute decompensation of CHF	673 (51.3)	186 (29.6)	487 (71.3)	42.8 (24.1-75.8)	<.001*	49.5 (27.2-90.1)	<.001*
Acute coronary syndrome	177 (13.5)	14 (2.2)	163 (23.9)	71.8 (39.9-129.6)	<.001*	74.1 (40.1-136.9)	<.001*
Lung diseases	17 (1.3)	11 (1.8)	6 (0.9)	14.1 (5.3-37.7)	<.001*	19.6 (7.2-53.1)	<.001*
Fatal arrhythmias	14 (1.1)	13 (2.1)	1 (0.1)	2.5 (0.3-19.4)	.373	3.8 (0.5-29.7)	.199
Oncological diseases	11 (0.8)	1 (0.2)	10 (1.5)	54.2 (23.4-125.6)	<.001*	47.7 (20.2-112.7)	<.001*
Cerebrovascular events	8 (0.6)	4 (0.6)	4 (0.6)	24.3 (7.8-75.3)	<.001*	27.2 (8.6-85.7)	<.001*
Cardiac or non-cardiac percutaneous or surgical procedure	7 (0.5)	6 (1.0)	1 (0.1)	5.0 (0.6-38.5)	.122	6.7 (0.8-51.9)	.069
Events, n (%)							
Cardiovascular events	219 (16.7)	62 (9.9)	157 (23.0)	1.8 (1.5-2.1)	<.001*	1.7 (1.4-2.1)	<.001*
Myocardial infarction	124 (9.5)	56 (8.9)	68 (10.0)	1.1 (0.8-1.4)	.654	1.1 (0.8-1.4)	.550
Stroke	47 (3.6)	23 (3.7)	24 (3.5)	0.9 (0.6-1.3)	.521	0.8 (0.6-1.2)	.364
Embolism	14 (1.1)	12 (1.9)	2 (0.3)	0.4 (0.1-1.1)	.123	0.3 (0.1-1.0)	.101
Revascularization	100 (7.6)	56 (8.9)	44 (6.4)	0.8 (0.6-1.1)	.100	0.8 (0.6-1.1)	.143
Device implantation	61 (4.7)	37 (5.9)	24 (3.5)	0.7 (0.4-0.9)	.037*	0.7 (0.5-0.9)	.045*
Heart transplant	5 (0.4)	5 (0.8)	-	0.1 (0.1-4.9)	.201	0.1 (0.1-3.3)	.450

Categorical variables are shown as n (%). Numerical variables are shown as mean ± SD or median (min–max). *$P < .05$ shows statistical significance.
Model I: Age, gender, concomitant chronic conditions, precipitating factors, NYHA factors, and LVEF were adjusted in the Cox regression analysis.
Model II: Age, gender, concomitant chronic conditions, precipitating factors, NYHA factors, LVEF, and drug (renin–angiotensin–aldosterone system inhibitors, beta-blockers, valsartan-sacubitril, and statin) factors were adjusted in the Cox regression analysis.
CHF, chronic heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

It was found that during the 3-year follow-up period after discharge, cardiovascular events increased the risk of mortality by 1.75-fold (HR: 1.75; $P < .001$; 95% CI: 1.5-2.1). Device implantation reduced the risk of mortality by 1.53-fold (1/0.65; HR: 0.65; $P = .037$; 95% CI: 0.4-0.9). There was no significant association between other cardiovascular events and mortality (Table 5).

The effect of hospitalization causes and cardiovascular events on mortality was associated regardless of mortality-reducing drugs (Adjusted Model II) (Table 5).

DISCUSSION

We reviewed the patients who were hospitalized due to acute HF with a longer follow-up period of 3 years in Turkey for the first time. We found that 70.5% of patients were re-hospitalized. The overall mortality rate was 52.1% and cardiovascular mortality rate was 44%. The most common causes of mortality were acute decompensation of chronic HF and acute coronary syndrome. The use of ARBs, BBs, valsartan/sacubitril, and statin reduced the risk of mortality. However, hospitalization due to acute decompensation of chronic HF, acute coronary syndrome, lung diseases, oncological diseases, and cerebrovascular diseases increased the risk of mortality. Furthermore, implantation of a cardiac device reduced the mortality risk.

In the ESC-HF-LT study, a total of 12 440 patients with acute and chronic HF from 21 European and Mediterranean countries were followed for 1 year. The mortality rate was 36% in cases of acute HF and 14.5% in cases of chronic HF during the 1-year follow-up period.[13] In the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with HF (OPTIMIZE-HF) study, which enrolled 41 267 patients, the patients with HF were examined in 3 different groups (HFrEF, HFpEF, and HFmrEF) within a follow-up period of 60-90 days. The mortality rate in the HFrEF and HFpEF groups was 9.8% and 9.5%, while the re-hospitalization rate was 29.5% and 29.2%, respectively.[14] Similarly, in the Get with the Guidelines (GWTG) study that enrolled 15 716 patients with HFrEF, 5626 patients with HFmrEF, and 18 897 patients with HFpEF, mortality rates within a 1-year follow-up period were 37.5%, 35.1%, and 35.6%, respectively. The re-hospitalization rates due to 1-year HF in the HFrEF, HFmrEF, and HFpEF groups were 30.9%, 28.4%, and 24.3%, respectively.[15] In the Canadian Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study, 1570 patients with HFrEF and 880 patients with HFpEF were examined; 30-day mortality rates were 7.1% and 5.3%, whereas 1-year mortality rates were 25.5% and 22.2%, respectively. The 1-year re-hospitalization rates were 16.1% and 13.5%, respectively.[16] The Euro HF Survey study reviewed 3148 patients with HF; 90-day mortality rates for patients with HFrEF and HFpEF were 12% and 10%, while the re-hospitalization rate was 21% and 22%, respectively.[17] In a study conducted in Singapore, Malaysian, Indian, and Chinese patients with HF were followed for 2 years. Mortality rates were 27.0%, 14.3%, and 18.6%, respectively.[18] In a study conducted on cases of HF in South America, mortality rates in 3-, 6-, 12-, and 24- to 60-month follow-up periods were 33%, 28%, 31%, and 35%, respectively.[19] In the present study, the 1-year mortality rate was 27% in patients who survived after discharge, while it was 52% at 3-year follow-up. This rate was higher than that reported in studies conducted in the Americas, Europe, and other Asian countries, as mentioned above. This may be due to a few reasons. The most important reason is the longer follow-up period of the present study. The studies described above had follow-up periods of 60-90 days or 2 years maximum; our follow-up period was 3 years. The aforementioned study conducted in South America[19] and the latest study[18] mentioned support our hypothesis. The mortality rates were higher in 24- to 60-month follow-up periods when compared with 3-, 6-, and 12-month follow-ups.[19] In addition, 1-year mortality rates according to LVEF groups are similar to the literature but higher in 3-year follow-up. Other reasons for higher mortality rates in our hospital may be that the patients enrolled in our study had acute decompensated HF, acute coronary syndrome, lung disease, oncological diseases, and cerebrovascular diseases, which frequently require re-hospitalization. When our findings were reviewed, the re-hospitalization rate in the entire population was 70.5%. However, congestive HF, acute coronary syndrome, lung diseases, oncological diseases, and cerebrovascular diseases were detected as risk factors for mortality.

Overactivation of the renin–angiotensin aldosterone system (RAAS) is one of the pathophysiological mechanisms of HF. Therefore, blockade of the RAAS is one of the key therapeutic targets in HF. Current guidelines recommend the use of ARBs when ACEi is not tolerated.[20] A recent meta-analysis showed that ACEi are not superior to ARBs in all-cause and cardiovascular mortality.[21] Few studies have suggested a reduced risk of cardiovascular events in patients using ARBs compared to ACEi.[22-24] Current findings showed a lower risk of mortality in ARB users, despite similar rates of ARB and ACEi use at 3-year follow-up. Moreover, ACEi did not show a significant effect on mortality. These results were not a head-to-head comparison analysis. Therefore, more prospective studies are needed to evaluate the efficacy of ARB and ACEi. In the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) study, a positive effect of ARBs on mortality was revealed.[25] Similarly, in the Prospective Comparison of angiotensin receptor neprilysin inhibitor (ARNI) with ACEi to Determine Impact on Global Mortality and Morbidity in HF (PARADIGM-HF) study, valsartan/sacubitril was reported as a mortality-reducing medication.[26] In studies conducted with BBs, mortality-reducing effects as well as positive effects on cardiac functions were revealed.[27,28] In a meta-analysis of 17 studies performed by Bielecka-Dabrowa et al.[29] statins were detected to have positive effects on all-cause mortality in patients with HF. Similar to the studies cited here, the usage of ARBs, valsa rtan/sacubitril, BBs, or statins was detected as a factor reducing mortality. However, the number of patients using valsartan/sacubitril was very low.

Goldstein et al[30] also showed a decrease in mortality and hospitalization rates with cardiac device implantation in

patients with HF. Similarly, cardiac device implantation was found to decrease mortality in our study.

Although this study benefits from analyses of a large dataset of a well-characterized and broad patient cohort, several limitations, including the study's exploratory nature, should be recognized. The most important limitation is the retrospective design of the study. Another limitation is the inability to follow and enroll 11.7% of the original patients. Furthermore, risk factors associated with mortality were not evaluated in the HFrEF, HFmrEF and HFpEF subgroups and their clinical outcomes were not determined according to such groups. Finally, there were no data available on the time of HF.

CONCLUSION

We have evaluated the 3-year follow-up data of the cases in the HF-TR study. In the present study, the mortality rate was detected as 52.1% in a 3-year follow-up period, while the re-hospitalization rate was 70.9%. Community-based and prospective studies are needed to determine the clinical outcomes of patients with HF in Turkey.

Ethics Committee Approval: The study was performed in accordance with the Declaration of Helsinki and approved by Ethics Committee of the Gazi University Faculty of Medicine, on 12 December 2019, under Decision No: E.155537.

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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