

# Snapshot evaluation of acute and chronic heart failure in real-life in Turkey: A follow-up data for mortality

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## ABSTRACT

**Objective:** Heart failure (HF) is a progressive clinical syndrome. SELFIE-TR is a registry illustrating the overall HF patient profile of Turkey. Herein, all-cause mortality (ACM) data during follow-up were provided.

**Methods:** This is a prospective outcome analysis of SELFIE-TR. Patients were classified as acute HF (AHF) versus chronic HF (CHF) and HF with reduced ejection fraction (HFrEF), HF with mid-range ejection fraction, and HF with preserved ejection fraction and were followed up for ACM.

**Results:** There were 1054 patients with a mean age of 63.3±13.3 years and with a median follow-up period of 16 (7–17) months. Survival data within 1 year were available in 1022 patients. Crude ACM was 19.9% for 1 year in the whole group. ACM within 1 year was 13.7% versus 32.6% in patients with CHF and AHF, respectively (p<0.001). Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, beta blocker, and mineralocorticoid receptor antagonist were present in 70.6%, 88.2%, and 50.7%, respectively. In the whole cohort, survival curves were graded according to guideline-directed medical therapy (GDMT) scores ≤1 versus 2 versus 3 as 28% versus 20.2% versus 12.2%, respectively (p<0.001). Multivariate analysis of the whole cohort yielded age (p=0.009) and AHF (p=0.028) as independent predictors of mortality in 1 year.

**Conclusion:** One-year mortality is high in Turkish patients with HF compared with contemporary cohorts with AHF and CHF. Of note, GDMT score is influential on 1-year mortality being the most striking one on chronic HFrEF. On the other hand, in the whole cohort, age and AHF were the only independent predictors of death in 1 year. (*Anatol J Cardiol* 2020; 23: 160-8)

**Keywords:** heart failure, all-cause mortality, prognosis

## Introduction

Heart failure (HF) is a growing problem of the 21<sup>st</sup> century. A recent country-wide study demonstrated that the prevalence

of HF in Turkey is 2.9%, affecting 1.5 million people along with 3 million people under contiguous risk in the near future (1). Therefore, disease burden is high. HF is a common and a growing problem, with rates exceeding many other countries. There are

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several hypothetical reasons for that. It is assumed that cardiovascular disease begins at an earlier age, and hence, secondary complications including HF occur at an earlier age (2).

There are registries in different cardiovascular diseases including one recent registry evaluating the overall HF patient profile, representative of Turkey (3). With regard to the management of HF, observational and retrospective data from tertiary care centers in Turkey designated that overall prescription rates for beta blockers (BBs) and renin–angiotensin–aldosterone system (RAAS) blockers were acceptable; however, target dose was rarely achieved among patients with HF (4). In Turkey, the “National Heart Health Policy” has been available since 2007; however, complete implementation is yet to be achieved. In the policy paper, HF is mentioned as one of the potential growing future targets. In the 2025 program of the World Health Organization, HF disease burden is mentioned in the potential targets to be reduced. Despite these facts, HF, hypothetically, is regarded as a disease of the elderly, though previous figures designate younger profile, and is also considered as a benign disease, and hence, it is not taken into consideration by many stakeholders as seriously as it deserves in the absence of national mortality data.

Hence, the aim of the present study was to evaluate the prognosis of patients with HF in a cohort representative of the country.

## Methods

This analysis is a prospective outcome analysis of a national registry, named SELFIE-TR, conducted at 23 sites representing 12 NUTS-1 regions of Turkey. The design and methodology of SELFIE-TR was published in the baseline characteristics paper (3). Patients were classified into two as acute (AHF) versus chronic HF (CHF) per protocol. Patients were also classified into three groups as HF with reduced ejection fraction (HFrEF), HF with mid-range ejection fraction (HFmrEF), and HF with preserved ejection fraction (HFpEF) as described in the previous article. Chronic guideline-directed medical therapy (GDMT) score was calculated when data regarding the presence or absence of angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB), BB, and mineralocorticoid receptor antagonist (MRA) were available either in the discharge prescription records of patients with AHF or in chronic medication list of patients with CHF. This score is used to demonstrate the relationship between the use of drugs recommended by the guidelines and mortality. GDMT score was graded as  $\leq 1$  GDMT versus 2 GDMT versus 3 GDMT according to the presence of these three groups of drugs (5-7). Patients were followed up for all-cause mortality (ACM), which was evaluated according to predefined subgroups.

This study is a project of the Heart Failure Working Group of the Turkish Society of Cardiology. Local Ethics Committee approval was obtained (decision registration no.: B.10.4.ISM.4.06.68.49

on July 8, 2015, protocol code no.: 288-AU/003), and also each center confirmed participation according to local regulations. To be qualified as an author in this paper, participants were informed to provide both clean baseline data, exceeding the minimum number of required enrollment, and 1-year outcome data. Participants who do not fulfill these criteria were acknowledged as collaborators in the previously published manuscript.

## Statistical analysis

All statistics were analyzed via SPSS 23.0 software (SPSS Inc., Chicago, IL, USA). Categorical variables are presented as percentages, whereas continuous variables are presented as mean  $\pm$  standard deviation or median (interquartile range). Baseline characteristics were classified according to predefined subgroups in Table 1 and evaluated via appropriate statistical tests including independent samples t-test for continuous variables with normal distribution, Mann–Whitney U test for continuous variables with non-normal distribution, and appropriate chi-square test for categorical variables. The regression analysis was performed on the statistically significant parameters obtained from the univariate analysis, and independent predictors of 1-year mortality were investigated. The effect of GDMT on 1-year mortality in the whole cohort in patients with CHF, patients with chronic HFrEF, and patients with acute HFrEF was investigated by using Kaplan–Meier analysis. A p value  $\leq 0.05$  was considered significant.

## Results

As presented previously, there were 1054 patients with a mean age of  $63.3 \pm 13.3$  years (M/F:751/353, 71.3%/28.7%); 712 versus 342 patients with CHF versus AHF; 801 versus 176 versus 77 (76% vs. 16.7% vs. 7.3%) patients with HFrEF versus HFmrEF versus HFpEF and with a median follow-up period of 16–26 (7–17) months by submission of this document. The mean age of patients with CHF had been reported to be younger than that of patients with AHF ( $61.1 \pm 13.3$  vs.  $67.9 \pm 12.1$  years,  $p < 0.001$ ), and the mean age of different HF phenotypes had also been significantly different (61.1 vs. 67.8 years,  $p < 0.001$ ).

ACM data within 1 year and also after 1 year were available in 1022 patients (32 missing, 2 signing informed consent only for baseline characteristics, and 30 lost to follow-up). Baseline characteristics of patients who died versus alive at 1-year follow-up are presented in Table 1.

Crude ACM was 19.9% for 1 year (25.4% for follow-up until 26 months) in the whole group. ACM within 1 year was 13.7% versus 32.6% in patients with CHF and AHF, respectively ( $p < 0.001$ ). One-year ACM in patients with different CHF phenotypes was similar and 13.7% versus 14.2% versus 11.9% in chronic HFrEF versus chronic HFmrEF versus chronic HFpEF, respectively ( $p = 0.934$ ). One-year ACM in patients with different AHF phenotypes was not significantly different from each other as 32.7% versus 28%

**Table 1. Baseline characteristics of patients who died versus alive at 1-year follow-up**

Variables	Dead (n=203)	Alive (n=819)	P
Age (year)	69 (60-77)	61 (54-72)	<0.001
Gender (male, %)	145 (71.4)	578 (71.7)	0.945
HT (n, %)	94 (46.3)	373 (45.9)	0.913
DM (n, %)	59 (29.1)	221 (27.3)	0.605
COPD (n, %)	32 (15.8)	100 (12.2)	0.177
Previous MI (n, %)	78 (38.4)	384 (46.9)	<b>0.030</b>
PCI (n, %)	63 (30.5)	305 (37.2)	0.075
CABG (n, %)	33 (16.3)	183 (22.3)	0.057
ICD (n, %)	28 (13.8)	147 (17.9)	0.160
CRT (n, %)	13 (3.4)	40 (4.9)	0.382
Smoking (n, %)	106 (60.2)	404 (55.2)	0.192
Heart rate (bpm)	79.3 (72-92)	77.8 (69-89)	<b>0.014</b>
Sinus rhythm (n, %)	109 (62.3)	488 (68)	0.264
LA size (mm)	45.7 (42-50)	45.1 (40-50)	<b>0.027</b>
sPAP (mm Hg)	45.7 (35-56)	40.8 (30-50)	<0.001
EF (%)	30.5 (25-40)	30.3 (25-40)	0.135
LVEDD (mm)	59.4 (52-66)	58.2 (52-64)	0.324
ACEI (n, %)	102 (50)	461 (53.3)	0.672
ARB (n, %)	27 (13.4)	127 (15.5)	0.546
BB (n, %)	165 (81.4)	731(89.3)	0.500
MRA (n, %)	78 (38.4)	431 (52.6)	0.005
Ivabradine (n, %)	27 (13.4)	129 (15.7)	0.526
Digoxin (n, %)	20 (9.9)	91 (11.1)	0.629
Median GDMT score	1 (1-3)	2 (2-3)	<0.001
Fully accomplished GDMT (n, %)	42 (20.5)	289 (35.3)	<b>0.002</b>
Type of HF (%)			
HF <sub>r</sub> EF	155 (76.4)	625 (76.3)	0.916
HF <sub>m</sub> rEF	31 (15.3)	139 (17)	
HF <sub>p</sub> EF	17 (8.4)	55(6.7)	
Acute HF (n, %)	109/203 (53.7%)	227/819 (27.5%)	<0.001
Hb (g/dL)	12.5 (11-14)	13.2 (11.7-14.6)	<0.001
Htc (%)	38.7 (33.9-42.9)	40.2 (36.3-44.3)	<b>0.001</b>
WBC (10 <sup>3</sup> /μL)	8.34 (6.81-10.97)	7.94 (6.59-9.49)	<b>0.006</b>
BNP (pg/mL)	54.6 (24.9-85.1)	46.25 (29.25-80.50)	0.909
NTproBNP (pg/mL)	2495 (368-4850)	1402.50 (552.25-4165)	0.631
Na (mmol/L)	137 (133-140)	138 (136-140)	<0.001
K (mmol/L)	4.46 (4.00-4.89)	4.47 (4.08-4.89)	0.658
Creatinine (mg/dL)	1.29 (0.93-1.72)	1.02 (0.82-1.30)	<0.001
Glucose (mg/dL)	115 (94-16)	111 (96-146)	0.555
ALT (U/L)	20 (13-40)	19 (14-29)	0.615
Total cholesterol (mg/dL)	155 (124-185)	169 (134-201)	<b>0.041</b>
TG (mg/dL)	92 (71-129)	123 (84-182)	<0.001

**Table 1. Cont.**

Variables	Dead (n=203)	Alive (n=819)	P
HDL (mg/dL)	35 (29-42)	38 (30-45)	0.127
LDL (mg/dL)	100 (76-121)	105 (83-133)	0.233

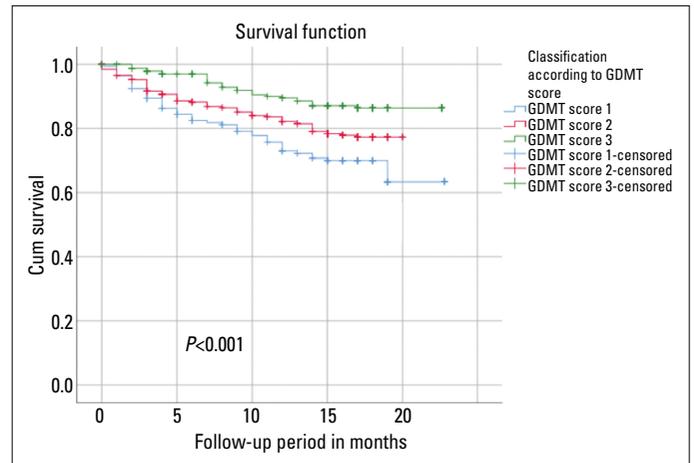
HT - hypertension; DM - diabetes mellitus; COPD - chronic obstructive pulmonary disease; MI - myocardial infarction; PCI - percutaneous coronary intervention; CABG - coronary artery bypass grafting; ICD - implantable cardioverter defibrillator; CRT - cardiac resynchronization therapy; LA - left atrium; sPAP - systolic pulmonary artery pressure; EF - ejection fraction; LVEDD - left ventricular end diastolic diameter; ACEI - angiotensin-converting enzyme inhibitor; ARB - angiotensin receptor blocker; BB - beta blocker; MRA - mineralocorticoid receptor antagonist; GDMT - guideline-directed medical therapy; HF - heart failure; HFrEF - heart failure with reduced ejection fraction; HFmrEF - heart failure with mid-range ejection fraction; HFpEF - heart failure with preserved ejection fraction; Hb - hemoglobin; Htc - hematocrit; WBC - white blood cell; Plt - platelet; BNP - brain natriuretic peptide; NTproBNP - N-terminal probrain natriuretic peptide; Na - sodium; K - potassium; AST - aspartate aminotransferase; ALT - alanine aminotransferase; TG - triglycerides; HDL - high-density lipoprotein; LDL - low-density lipoprotein

versus 40% in acute HFrEF versus acute HFmrEF versus acute HFpEF, respectively, though there were numerical differences (p=0.541).

Information regarding chronic medications was available in 769 patients and was lacking in 269 patients by the time of preparation of this document. ACE inhibitor or ARB was present in 70.6% (71.5% vs. 68.4% in CHF vs. AHF, p=387), BB was present in 88.2% (89.3% vs. 85.5% in CHF vs. AHF, p=0.141), and MRA was present in 50.7% (54.5% vs. 41.7% in CHF vs. AHF, p=0.001) of all patients. ACEI/ARB, BB, and MRA were present in 74.7%, 89.7%, and 60.9% of patients with chronic HFrEF phenotypes.

Multivariate analysis of the whole cohort including patients with HFrEF, HFmrEF, and HFpEF together yielded age (p=0.009) and having AHF (p=0.028) as independent predictors of mortality in 1 year (Table 2).

In the whole cohort, survival curves were graded according to GDMT scores ≤1 versus 2 versus 3 as 28% versus 20.2% versus 12.2%, respectively (p<0.001, Fig. 1). In patients with CHF with available mortality and available GDMT score (n=520), 1-year mor-



**Figure 1.** Whole cohort survival curves according to GDMT score. Mortality was 14.9% versus 12.3% versus 5.6% for GDMT scores ≤1 versus 2 versus 3, respectively (p=0.002 for Kaplan–Meier, Fig. 2).

In patients with chronic HFrEF, 1-year mortality was 14.3% versus 14% versus 5.8% for GDMT scores ≤1 versus 2 versus

**Table 2. Multivariate analysis for mortality in 1 year**

Variables	Univariate OR, 95% CI	P	Multivariate OR, 95% CI	P
Age	1.03 (1.01-1.04)	<0.001	1.06 (1.01-1.12)	0.009
Hb	0.83 (0.77-0.91)	<0.001	1.21 (0.88-1.68)	0.227
WBC	1.03 (0.99-1.06)	0.11	1.09 (0.88-1.34)	0.411
Na	0.93 (0.90-0.96)	<0.001	0.92 (0.82-1.04)	0.198
Creatinine	1.01 (0.97-1.05)	<0.001	1.51 (0.64-3.55)	0.336
TG	0.99 (0.98-0.99)	0.003	0.99 (0.98-1.00)	0.089
Previous MI	1.41 (1.03-1.93)	0.030	1.93 (0.73-5.05)	0.181
Acute HF	3.06 (2.23-4.19)	<0.001	3.21 (1.13-9.09)	0.028
LA size	1.02 (1.01-1.05)	0.027	0.99 (0.92-1.08)	0.973
sPAP	1.02 (1.01-1.04)	<0.001	0.99 (0.92-1.02)	0.667
Heart rate	1.01 (1.00-1.02)	0.014	1.01 (0.98-1.04)	0.439
Median GDMT score	0.59 (0.45-0.78)	<0.001	1.80 (0.88-3.68)	0.102

Hb - hemoglobin; Na - sodium; WBC - white blood cell; TG - triglycerides; MI - myocardial infarction; HF - heart failure; LA - left atrium; sPAP - systolic pulmonary artery pressure; GDMT - guideline-directed medical therapy

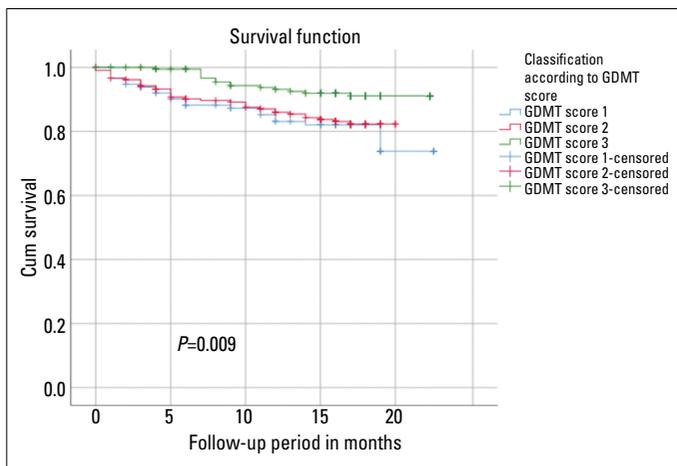


Figure 2. Chronic HF survival according to GDMT score

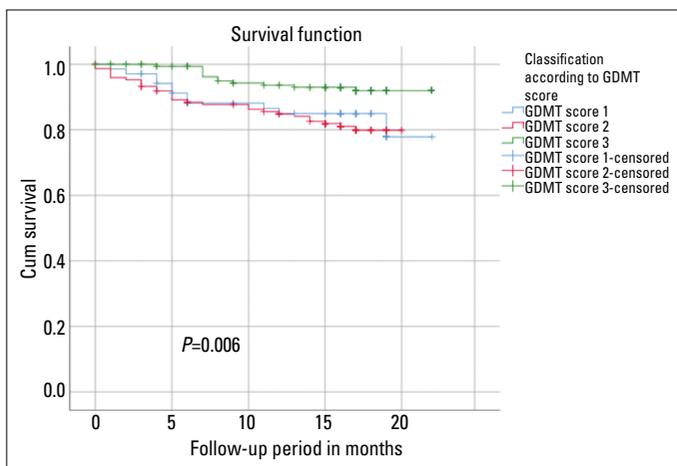


Figure 3. Chronic HFrEF survival according to GDMT score

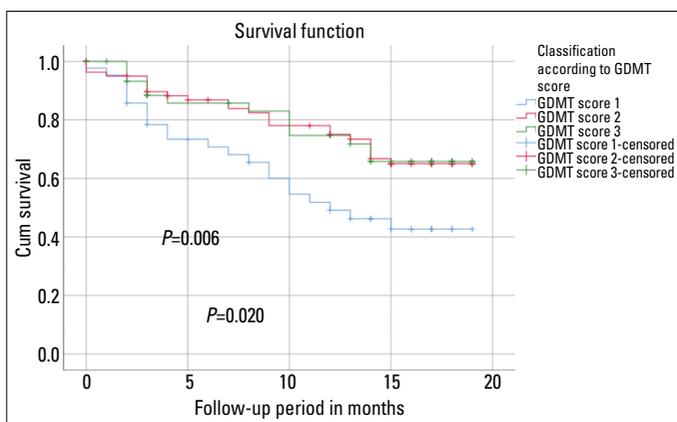


Figure 4. Acute HFrEF survival according to GDMT score

3, respectively ( $p=0.011$ , Fig. 3). In patients with chronic HFmrEF, there was a nonsignificant graded decrease of ACM by increasing GDMT scores (15.6% vs. 11.4% vs. 4.8% for GDMT scores  $\leq 1$  vs. 2 vs. 3, respectively,  $p=0.475$ ).

In patients with AHF with available mortality and available GDMT score ( $n=221$ ), 1-year ACM was 37.7% versus 20.9% versus 24% for GDMT scores  $\leq 1$  versus 2 versus 3, respectively

( $p=0.053$ ). Furthermore, in patients with acute HFrEF phenotype and with available GDMT score ( $n=170$ ), 1-year ACM was 44.2% versus 19.8% versus 23.9% for GDMT scores  $\leq 1$  versus 2 versus 3, respectively ( $p=0.024$ , Fig. 4).

## Discussion

In this analysis, evaluating the data from SELFIE-TR registry, the mortality rates, mortality predictors, GDMT utilization, and associated mortality rates according to GDMT score were investigated. The main results of our study could be summarized as follows:

1. Patients with HF in Turkey were relatively younger than patients with HF in the other contemporary cohorts, and the mortality rate was high despite young age. Studies have demonstrated that the average age of patients with HF is different between countries (8-12). In the ESC-HF pilot study, the mean age of patients with CHF was 67 years, similar to this study, whereas the mean age of patients with AHF was 70 years, and it was 61 years in the SELFIE-TR study (13). ACM rate was 19.9% in all cohort.
2. GDMT including ACEI or ARB plus BB plus MRA, traditionally known to improve the prognosis of HF, yielded graded survival curves in the whole cohort (in the analysis including all phenotypes). Of note, in further subgroup analysis, fully administered GDMT significantly decreased mortality rates in patients with HF down to the numerical levels, expressed in the contemporary registries (14).
3. In this analysis, when the whole cohort, i.e., all phenotypes of HF, was considered, age and having AHF were shown to be independent predictors of 1-year mortality.

HF is a clinical syndrome secondary to incapacities of one or both ventricles to fill with or eject blood. Significant improvements were obtained in the diagnosis and treatment of some HF phenotypes along with improved technology. The goals of treatment in patients with HF should be based on relieving symptoms and findings, preventing recurrent hospitalizations, and improving survival.

Traditionally, the left ventricular ejection fraction is used in the definition of HF. In the recent European Society of Cardiology (ESC) guidelines (15), HF was classified into three phenotypic groups based on EF as follows: 1) patients with EF  $>50\%$  as Group HFpEF, 2) patients with EF  $<40\%$  as Group HFrEF, and 3) patients with EF 40%–49% as Group HFmrEF. This classification might be important since there are different underlying etiologies, demographic characteristics, comorbidities, and response to treatments. HFrEF is the most commonly studied subgroup of HF. There are treatments proven to be effective in this phenotype. ACEIs/ARBs (or angiotensin receptor neprilysin inhibitor (ARNI) recently), BBs, and MRAs, whose effects were established repeatedly in observational and randomized controlled studies (16-33), are definitely recommended as evidence-based

treatments by the ESC (15) and American Heart Association/American College of Cardiology Foundation (AHA/ACC3) (34, 35) yielding a reduction in mortality and morbidity, and hence, are collectively called GDMT. Therefore, GDMT including ACEIs/ARBs (or ARNI according to most recent guidelines), BBs, and MRAs has become a cornerstone therapy for the prevention of disease progression in HFrEF. Since these drugs exert their effects on the RAAS and the sympathetic nervous system through different pathways, combination appears to exert synergistic benefits. It has been shown that BBs and MRAs initiated in addition to ACEI/ARB not only caused a reduction in hospitalizations but also yielded additional mortality benefits in patients (36). Hence, the drugs should be initiated as soon as possible, and they should be titrated up to the highest dose according to patient tolerability.

Since the whole patient population included patients from each of three HF phenotypes, age and having AHF were found to be independently associated with mortality in the multivariate regression analysis consistent with the literature data (23, 37-42). Of note, GDMT or aforementioned drugs were not independent predictors of mortality in 1 year. The absence of the independent prognostic role of GDMT may also be consistent with the literature since no pharmacological agent specifically yielded mortality benefit in HFpEF and HFmrEF phenotypes contrary to HFrEF. Relative inefficiency of components of GDMT in HFpEF and HFmrEF phenotypes might have reduced the statistical power of GDMT-HFrEF relationship relative to the whole group. It should also be kept in mind that the study did not consider de novo GDMT, rather made a snapshot prevalence of GDMT; hence, incident GDMT might have yielded positive outcomes (43-50). Furthermore, the duration of GDMT might not be sufficient to yield prognostic benefit in 1 year, even in incident GDMT cases, and might have already yielded positive outcomes in prevalent GDMT cases (particularly those enrolled as patients with CHF were those who survived via already initiated GDMT). Last but not the least, survival benefit of ACEIs/ARBs, BBs, and MRAs usually is known to appear after 1 year in the majority of clinical trials.

On the other hand, overlapping curves of GDMT 1 and GDMT 2 in Kaplan-Meier analysis of patients with HFrEF might be due to small patient population, not on BBs among patients with chronic HFrEF in the cohort. Marked superiority of GDMT 3 over GDMT 1 and 2 can support the notion that triple blockade including the sympathetic nervous system, angiotensin pathway, and aldosterone pathway is compared with dual blockade. It was shown that blocking all of these mechanisms was superior to other dual combinations particularly in HFrEF (36, 51). This finding strongly supports the paradigm that triple therapy should not be delayed in suitable patients with chronic HFrEF.

The use of GDMT in patients hospitalized due to AHF is also worth mentioning herein. Prior to hospital discharge, both the American and European guidelines recommend to initiate these therapies, which are known to improve survival (15, 34, 35, 52,

53). Hence, it has been recommended to continue and/or initiate GDMT during AHF episode (preferably just after the initial stabilization) and definitely before discharge (54-58). In our study, it was shown that as GDMT score increased, 1-year mortality rate decreased not only in chronic HFrEF but also in patients with acute HFrEF. However, different from GDMT-mortality relationship in chronic HFrEF, double and triple GDMT (i.e., GDMT scores 2 and 3) were statistically better than GDMT 1, but triple GDMT was not better than dual GDMT in the first year outcome analysis. This issue might be driven by continuing prescription practice that MRAs are reserved for relatively more advanced stages of HF, particularly after decompensation, and hence potentially yielding poorer prognosis despite triple GDMT (after the addition of MRA) in the first year.

In our study, 1-year mortality rates of patients with AHF were higher than those of patients with CHF. Our finding was confirmatory to the findings of OPTIMIZE-HF (56), ADHERE (40), EHFS II (41), and EUROHEART (42), in which mortality rates of patients with AHF were reported to be higher than those of patients with CHF.

In mortality analysis according to phenotypes, while there were numerical differences, no statistically significant difference was observed in 1-year mortality. There is divergence of survival analysis in the literature according to HF phenotypes. In a meta-analysis including 31 studies (Meta-analysis Global Group in Chronic Heart Failure) (38), HFrEF and HFpEF were compared in patients with CHF, and the mortality of patients with HFrEF was higher. In the ESC Heart Failure registry (59), three phenotypes of CHF were compared, and ACM rates in patients with HFrEF versus HFmrEF versus HFpEF were found to be 8.8% versus 7.6% versus 6.3%, respectively, with a statistically significant difference. Higher mortality rates were noted in our cohort as 13.7% versus 14.2% versus 11.9% in respective phenotypes. In the subgroup analysis of the CHARM study, ACM rates in patients with HFrEF versus HFmrEF versus HFpEF were found to be 10.7% versus 5.4% versus 5.7%, respectively (60). These differences can be explained by geographical difference, different demographic characteristics of the patients, and lower GDMT use or even the dose of GDMT. Of note, fully accomplished GDMT resulted in mortality rates, compatible with contemporary registries. Similar to the ESC Heart Failure registry, it was observed that the demographic data of the ESC pilot study differed with our SELFIE-TR study (13). These differences and their interpretations are mentioned in our first article where baseline characteristics are presented (3).

GDMT rates vary according to the development level of the countries and the socioeconomic level of the patients (61, 62). In a US study, the GDMT score was 2.31 and increased to 2.74 in the follow-up (6).

One-year mortality rates in HFrEF versus HFmrEF versus HFpEF AHF phenotypes were 32.7% versus 28% versus 40%, respectively. These rates are comparable to those by Coles et al. (63) reported mortality data in patients with AHF intermittently

from 1994 to 2004. According to these temporal records, 1-year mortalities of acutely decompensated HF<sub>r</sub>EF, HF<sub>m</sub>rEF, and HF<sub>p</sub>EF in 1995 and 2004 were 40.4% and 32.6%, 25.4% and 28.7%, and 35% and 29.1%, respectively. Hence, improvement in mortality trends is noted in AHF, similar to CHF.

### Study limitations

There are several limitations worthwhile mentioning. First, the snapshot nature of the present study was a significant limiting factor since temporal trends in GDMT utilization and risk factor modification could potentially have significantly impacted outcomes. Second, the number of patients with HF<sub>p</sub>EF in the cohort was limited (and also HF<sub>m</sub>rEF to some extent), and hence, these findings should be interpreted with a word of caution. Third, the doses of GDMT including ACEIs or ARBs and BBs were not separately recorded in the case report forms; hence, the doses of GDMTs were unknown until the conduct of this analysis. Of note, high doses of some GDMTs were previously shown to impact outcomes in HF<sub>r</sub>EF population. On the other hand, during the plan and conduct of the registry, phenotypic classifications had to be based on the existing 2013 ACC/AHA HF guidelines of that time. Such phenotypic definitions were updated during the data analysis period for the sake of uniformity of definitions, particularly HF with borderline ejection fraction was updated as HF<sub>m</sub>rEF. Although, many previous publications utilized these assumptions and transitional nomenclature updates, this might potentially end up with some deficits in the interpretation of the results. Moreover, adherence and compliance to GDMT remain as important confounders in the study since those issues were not taken into consideration in this analysis.

### Conclusion

Overall, in this country-representative snapshot, patients with HF in Turkey were relatively younger than those in many other cohorts, particularly patients with chronic HF<sub>r</sub>EF. One-year mortality in Turkish patients with HF was high despite young age, and this might potentially be related to lower rates of GDMT. However, fully accomplished GDMT as indicated by GDMT score appears to decrease ACM in all HF phenotypes in a year, but dramatically in patients with HF<sub>r</sub>EF, and hence appears to lower high mortality rate to average numbers of contemporary HF registries. Age and having AHF remained as the independent predictors of mortality in 1 year irrespective of HF phenotype.

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