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Original Article CARDIOLOGY

Marital status and outcomes in chronic heart failure: Does it make a difference of being married, widow or widower?

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ABSTRACT

OBJECTIVE: We aimed to compare the outcomes of chronic heart failure (HF) patients with reduced ejection fraction (CHFrEF) in the Turkish Research Team in HF (TREAT-HF) registry according to marital status with a specific focus on being the widowed (widow/widower) versus the married.

METHODS: TREAT-HF is a network, enrolling CHFrEF with a follow up for HF-related hospitalization (HFrH) and all-cause mortality (ACM). In this cohort, the widowed patients were compared with patients who were married before and after propensity score (PS) matching analysis.

RESULTS: There were 723 cHFrEF patients with a complete dataset, including reported marital status at baseline for this analysis. Out of 723 patients with HF, 37 "never-married" and "divorced" patients were excluded from the analysis. Then, out of 686 remaining patients with HF, who had at least one reported marriage in the database, widowed patients with HF (n=124) were compared with married patients (n=562). The mean follow up period was 21±12 months up to 48 months. The widowed patients had a higher risk of HFrH (p=0.047), although ACM remained similar compared to married patients (p=0.054). After PS matching, HFrH remained more frequent among the widowed compared with the married (p=0.039) although ACM yielded similar rates. Of note, it was shown that being a widower (p=0.419) was not linked to increased risk of HFrH during follow up contrary to being a widow (p=0.037) despite similar age, ejection fraction, creatinine, NYHA functional class distribution and a similar rate of life-saving medications.

CONCLUSION: PS matching analysis yielded that the widowed had increased the risk for HFrH. Of note, widowers did not seem to have an increased risk for HFrH, contrary to widows.

Keywords: Heart failure with reduced ejection fraction; marital status; widowed.

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A leading clinical and public health problem, heart failure (HF) is responsible for putting a considerable burden on the healthcare system as well as causing a poor quality of life and poor survival [1]. Besides medical interventions, social factors may also affect the clinical outcomes of HF [2, 3]. In general, social support seems to have a considerably positive effect on health and it plays an important role in sustaining the mental and physical well-being of patients with HF [4]. In general, social support seems to have a considerably positive effect on health and it plays an important role in the sustaining mental and physical well-being of the patients with HF. There may be various sources of social support, but one of the most beneficial ones for a patient with HF is having a life-time partner or a spouse. It has been shown that marriage or living with a partner provides satisfactory improvements concerning mortality, event-free survival, and readmission rates for patients with HF [5, 6]. On the contrary, readmission and mortality rates have been higher in patients with HF with poor or no social support [7–9].

It has been reported that outcomes in HF are affected by marital status [10–12]. Although comparisons were mainly based on married versus unmarried groups (single, divorced, widowed), to our knowledge, the effects of widowhood on prognosis and its relation to gender in stable chronic heart failure patients with reduced ejection fraction (CHFrEF) had not been studied. In this study, we aimed to specifically compare the widowed (widow/widower) with the married at index admission about heart failure-related hospitalization (HFrH) and all-cause mortality (ACM) during follow-up in the Turkish Research Team in HF (TREAT-HF) network population (https://www.treat-hf.com/).

MATERIALS AND METHODS

In the TREAT-HF registry, heart failure with reduced ejection fraction (HFrEF) was diagnosed by participating investigators according to guidelines [13, 14]. Chronic HFrEF was defined as left ventricular ejection fraction (LVEF)<40% along with stable HF symptoms more than one month, absence of hospitalization in prior three months, a stable dose of diuretics more than one month, optimally titrated and stable (at least a month) doses of guideline-directed medical therapy (GDMT), including angiotensin-converting enzyme inhibitor&angiotensin receptor blocker (ACEI&ARB)s, beta-blockers (BB)s, mineralocorticoid receptor antagonists (MRA)s and ivabradine if indicated. All patients were ACC/AHA Stage C patients and patients were classified according to the New York heart association (NYHA) class at index participation time irrespective of previous status [14]. All patients were those on chronic outpatient follow-up by HF centers, and patients requiring parenteral therapy or intensification of oral diuretic and/or nitrate therapy while on admission to the outpatient department were not considered. HF-related hospitalization was noted when a patient, either admitted to Emergency Department or Cardiology, required parenteral therapy for HF symptoms and signs along with at least one-day hospitalization, along with "Acutely Decompensated Heart Failure" as a primary diagnosis. Patients were followed up for all ACM and HFrH and both events were collected annually and all events were recorded individually by local investigators. In this study, TREAT-HF consecutive prospective co-

Highlight key points

- To our knowledge, the effects of widowhood on prognosis and its relation to gender in stable chronic heart failure patients with reduced ejection fraction have not been studied.
- Among chronic HFrEF outpatients, PS matching analysis yielded that widowed patients had increased the risk for HFrH, although all-cause mortality was not different compared to married patients with HF.
- Widows, rather than widowers seemed to have increased risk for HFrH.

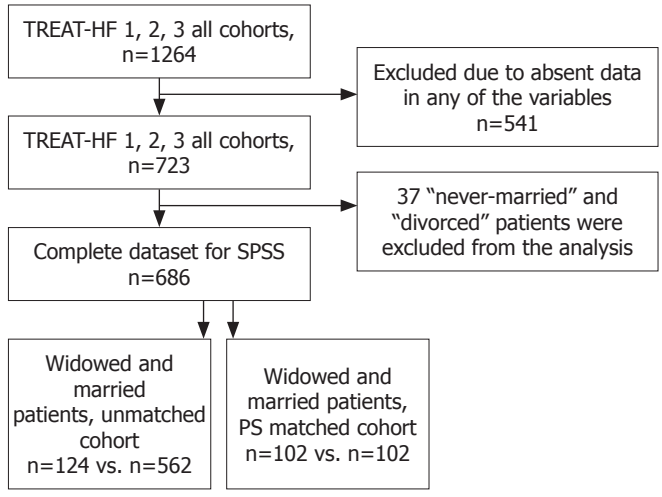

FIGURE 1. Flow-chart of this study.

Table 1. Comparison of the widowed versus married patients with heart failure before and after PS matching

Characteristics	Widowed patients (n=124)	Married patients (n=562)	p	Widowed patients after PS matching (n=102)	Married patients after PS matching (n=102)	p
Age (years)	73.5±11	61.5±11.7	<**0.001**	71.1±10.5	68.7±12.9	0.154
Gender (female) %	52.4	28.1	<**0.001**	41.2	45.1	0.572
Hypertension %	54	32.6	<**0.001**	50	43.1	0.326
Diabetes mellitus %	25	25.6	0.886	24.5	25.5	0.872
CAD %	46.8	49.1	0.638	50	46,1	0.575
NYHA Class III-IV %	56.5	44.3	**0.014**	54.9	55.9	0.888
AF %	29.8	21.7	0.052	28.4	28.4	1.0
Heart rate (bpm)	83.7±21.3	81.7±17.4	0.338	84.2±22.3	81.8±16.7	0.386
Laboratory parameters						
BUN (mg/dl)	40.5 (27.6–61.7)	38.5 (25–58)	0.173	40.5 (27.2–61.2)	42 (28.7–67.2)	0.492
Creatinine (mg/dl)	1.3±0.7	1.3±0.7	0.916	1.3±0.7	1.5±0.9	0.290
Sodium (mmol/l)	138.4±4.1	137.7±4.2	0.125	138.1±4.0	137.6±4.7	0.425
Potassium (mmol/l)	4.6±0.6	4.5±0.5	0.148	4.64±0.6	4.57±0.6	0.467
NT-proBNP (pg/ml)	2659 (705–4867)	1327 (565–3613)	0.139	2659 (713–4341)	2338 (1323–3970)	0.823
Hb (g/dl)	12±2.2	12.7±2.2	**0.003**	12±2.3	12±2.1	0.981
Hct (%)	37±6.8	39±6.3	**0.007**	37.5±7.1	37.7±6.2	0.876
Echocardiographic parameters						
LA diameter (mm)	43.6±6.2	44.9±7.4	**0.032**	43.9±6.1	44.3±7.8	0.669
EF (%)	32±7.9	31.2±8.2	0.371	31±8	32±8.5	0.403
LVEDD (mm)	54.9±6.9	58±8.7	<**0.001**	55.7±6.7	57.2±9.3	0.195
RV dilatation %	37.9	36	0.794	38.2	45.1	0.320
SPAP (mmHg)	43.3±14.3	42±12.9	0.310	43.3±14.5	41.7±13.3	0.427
Medications						
Beta blocker %	79	82.7	0.330	82.4	83.3	0.853
ACEI/ARB %	65.3	75.3	**0.023**	67.6	69.6	0.763
MRA %	41.1	52.1	**0.027**	43.1	51	0.262
Daily loop diuretics %	80.6	73	0.076	81.4	76.5	0.391
Ivabradine %	5.6	13.2	**0.028**	5.9	12.7	0.148
Digoxin %	25.8	23	0.497	27.5	29.4	0.756
Outcomes						
HF-related hospitalization %	72.6	63.2	**0.047**	72.5	58.8	**0.039**
All-cause death %	35.5	26.9	0.054	36.3	36.3	1

CAD: Coronary artery disease; NYHA: New York heart association; AF: Atrial fibrillation; Hb: Hemoglobin; Hct: Hematocrit; LA: Left atrium; EF: Left ventricular ejection fraction; LVEDD: Left ventricular end diastolic diameter; RV: Right ventricular; SPAP: Systolic pulmonary artery pressure; ACEI/ARB: Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; MRA: Mineralocorticoid receptor antagonist.

horts for the years 2013, 2014, 2015 enrolling chronic HFrEF outpatients were considered. In this analysis, "never-married" and "divorced" patients were excluded. The patients who were reported with their marital status as married were compared with the widowed (widow/widower) during follow up. Herein, a widow was defined as a female patient who had lost her spousal partner and a widower was defined as a male patient who had lost his spousal partner. This study was approved by the Cumhuriyet University Clinical Research Ethics Committee (Ethical approval number of the study is 2010-01/13).

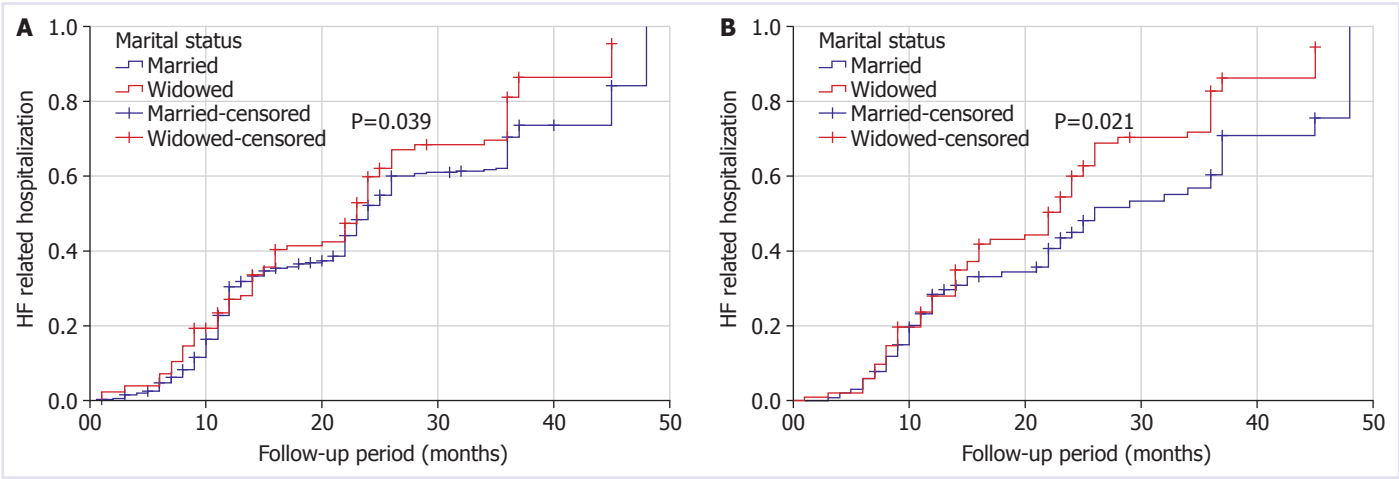

FIGURE 2. **(A)** Kaplan Meier analysis of heart failure-related hospitalization by marital status before PS matching analysis. **(B)** Kaplan Meier analysis of heart failure-related hospitalization by marital status after PS matching analysis.

Statistics

All statistical procedures were performed using SPSS software (version 25.0, SPSS Inc., Chicago, IL, institutionally registered software). The normality was assessed with the Kolmogorov-Smirnov test. Continuous variables were presented as mean±SD or median (25^{th}–75^{th} percentile) in the presence of abnormal distribution. Categorical variables were reported as numbers and percentages. Comparisons between groups were made using the appropriate chi-square (χ^2) test for categorical variables, the Student's t-test for normally distributed continuous variables, and the Mann-Whitney U test when distribution was not normal. An institutionally registered Propensity score (PS) matching extension was downloaded on top of institutional SPSS 25.0 (Thoemmes, 2012). Propensity score was matched in SPSS. arXiv:1201.6385 [stat.AP]). Propensity-based matching was used to create paired samples of patients with similar propensity score and stratified by "widowed" or "married" groups according to marital status. Along with the requirement of the completely filled dataset, the nearest neighbor matching algorithm was utilized, and covariate adjustment was obtained for age, gender, hypertension, NYHA Class (III-IV versus NYHA I-II), atrial fibrillation, hemoglobin, left atrium diameter, left ventricular end-diastolic diameter, ACEI&ARB use, MRA use, ivabradine use, daily loop diuretic (≥40 mg furosemide or equivalent) use according to data obtained from the unmatched cohort. Kaplan Meier analysis for HFrH was provided for those married versus widowed patients with cHFrEF A p-value ≤0.05 was considered statistically significant.

RESULTS

There were 723 cHFrEF patients with a complete dataset, including reported marital status at baseline for this analysis. Out of 723 patients with HF, 37 "never-married" and "divorced" patients were excluded from the analysis. Then, out of 686 remaining patients with HF who had at least one reported marriage in the database, the widowed patients with HF at baseline index admission (n=124) were compared with the married (n=562). Flow-chart of this study is presented in Figure 1. The mean follow up period was 21±12 months up to 48 months. The widowed were older, more frequently female, more frequently poor New York heart association class (NYHA III-IV), hypertension, lower hemoglobin level, larger left atria and left ventricular diastolic diameter, less frequently on ACEI&ARBs, MRAs, and ivabradine compare with the married before PS matching (Table 1, left panel). In addition, the widowed patients had a higher risk of HFrH (p=0.047), although ACM remained similar compared to married patients (p=0.054). After PS matching, adjusting for differences, HFrH remained more frequent among the widowed compared to the married (72.5% vs. 58.5%, p=0.039), although ACM yielded similar rates. Kaplan Meier analysis according to marital status provided HFrH event curves which are significantly diverging from each other not only before but also after PS matching (Long rank: p=0.039, 24 (95%CI: 22.9–25.0), (Long rank: p=0.021, 24 (95%CI: 22.0–25.9) respectively (Fig. 2A, B). Comparison was also provided for 686 patients with HF with and without HFrH during follow up and widowed patients with HF were

Table 2. Comparison of the patients with and without HF-related hospitalization

Characteristics	Patients without HF-related hospitalization (n=241)	Patients with HF-related hospitalization (n=445)	p
Age (years)	62.3±12.4	64.4±12.4	**0.034**
Gender (Female) %	32.4	32.6	0.953
Urban life			
Hypertension %	33.6	38	0.257
Diabetes mellitus %	25.3	25.6	0.930
CAD %	44.4	51	0.098
Widowed %	14.1	20.2	**0.047**
NYHA Class III-IV %	34.4	53	<**0.001**
AF %	22	23.8	0.588
Heart rate (bpm)	81.6±17.8	82.3±18.5	0.612
Laboratory parameters			
BUN (mg/dl)	40.6 (27.5–63)	36 (22–52)	**0.004**
Creatinine (mg/dl)	1.2±0.6	1.5±0.8	<**0.001**
Sodium (mmol/l)	138.3±4.4	137.6±4.1	0.047
Potassium (mmol/l)	4.51±0.5	4.53±0.5	0.555
NT-proBNP (pg/ml)	704 (368–1464)	1805 (714–4870)	<**0.001**
Hb (g/dl)	13.1±2.1	12.2±2.2	<0.001
Htc (%)	40.1±6.1	37.9±6.4	<0.001
Echocardiographic parameters			
LA diameter (mm)	44.5±7.5	44.8±7.1	0.601
LVEF (%)	32.4±8.2	30.8±8.1	**0.015**
LVEDD (mm)	57.1+8.8	57.7±8.4	0.449
RV dilatation %	36.5	37.1	0.884
SPAP (mmHg)	40.4±13.3	43.3±12.9	**0.007**
Medications			
Beta blocker %	85.5	80.2	0.087
ACEI/ARB %	75.5	72.4	0.415
MRA %	53.5	48.3	0.192
Loop diuretics %	69.7	76.9	0.041
Ivabradine %	12.4	11.5	0.702
Digoxin 5	25.3	22.5	0.402
Outcome			
All cause death %	20.7	32.6	**0.001**

CAD: Coronary artery disease; NYHA-FC: New York heart association functional capacity; AF: Atrial fibrillation; Hb: Hemoglobin; Hct: Hematocrit; LA: Left atrium; LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end diastolic diameter; RV: Right ventricular; SPAP: Systolic pulmonary artery pressure; ACEI/ARB: Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; MRA: Mineralocorticoid receptor antagonist.

more frequent in patients with HFrH during follow up compared to patients without HFrH (20.2% vs. 14.1%, p=0.047) (Table 2). The mean age of female and male patients without HFrH was 62.9±12.8, 62.0±12.2, respectively. The mean age of female and male patients with HFrH was 66.2±12.6, 63.5±12.2, respectively. However, on a gender-specific analysis, it was shown that being a widower (p=0.419) was not associated with increased risk of HFrH on follow up contrary to being a widow (p=0.037) (Table 3) although the mean age of widowers was not different from widows in the whole cohort (72±12 vs. 75±10 years, p=0.097) and lifesav-

Table 3. Relationship between marital status and heart failure-related hospitalization according to gender

	Heart failure-related hospitalization present (%)	HF-related hospitalization absent (%)	p
Male			
Widowed (n=59)	69.5	30.5	0.419
Married (n=404)	64.1	35.9	
Female			
Widowed (n=65)	75.4	24.6	**0.037**
Married (n=158)	60.8	39.2	
All patients			
Widowed (n=124)	72.6	27.4	**0.047**
Married (n=562)	63.2	36.8	

ing cHFrEF therapies were not significantly different in widowers versus widows (for beta-blockers 84.7% vs. 73.8%, p=0.205; for ACE inhibitors or ARBs 66.1% vs. 64.6%, p=0.862; for MRA 44.1% vs. 38.5%, p=0.526). Besides, distribution of NYHA Class III-IV, LVEF and creatinine levels were similar in both groups (55.9% vs. 56.9%, p=0912; 30±8% vs. 33±8%, p=0.195; 1.4±0.7 vs. 1.3±0.7 mg/dl, p=0.719 for widowers and widows respectively).

DISCUSSION

There are some previous studies evaluating marital status in HF and comparing the outcomes in the form of married versus unmarried (single, divorced, widowed) [10–12]. However, this study differs from other studies by including patients with HF who had at least one reported marriage and excluding those who did not divorce. The state of being married is in close connection with better outcomes in patients with HF concerning mortality and rehospitalization [12]. Various marital contributions can potentially result in better clinical outcomes in HF, such as social, emotional, financial support, assistance in medication adherence, and quick disease detection [15–17].

Widowhood or divorce may lead to considerable decreases in mental health [18]. However, the death of a spouse is a very important event in a person's life and it has been reported to be closely linked to mortality and other adverse results [19, 20]. Having a new partner after a divorce has been more common than having a new partner after widowhood [21]. Given these reasons, we have come to the idea that the degree of self-care and mental health in those people who have never married or who got divorced can be different from those people who lost their partners. Therefore, we classified patients as those who were married by the time of index admission versus those who were widowed.

In this study, we found that marital loss in the form of spousal death affects widows more than widowers. Widowers did not seem to have increased risk for HFrH compared with widows despite their similar ages, LVEF, creatinine levels, lifesaving cHFrEF therapies, distribution of NYHA Class III-IV class. This may be related to a social point of view that the female patients may perceive being widowed differently from males and men may not be as socially isolated as the women. Another explanation for that may be that there can be unreported partners among the widowers because it has been shown that repartnering is more common in men than women after marital dissolution [22, 23]. Furthermore, widows may be more depressive than widowers [24, 25]. In a study compatible with our results, which investigated emotional support's prognostic value in elderly patients who were admitted to hospital because of HF, the link between emotional support and cardiovascular events was strong in women, but it was absent in men [8].

Before PS matching, the widowed patients had higher risk of HFrH (p=0.047). However, after PS matching, adjusting for differences, HFrH remained more frequent among the widowed, compared to the married (72.5% vs. 58.5%, p=0.039), although ACM yielded similar rates (p=1). The higher frequency of HFrH in the widowed -especially in the widows- may be assessed as the widowed may suffer more frequently from depressive disorders [24, 25]. In a study that supports our opinion, depression has been shown to be an independent predictor of rehospitalization in patients with HF [26].

This study proposed that widowhood may have more adverse effect for widows compared to widowers. Differences in emotional status between widows and widowers may cause this result, but the underlying reasons are not completely clear.

Limitations

This study has several limitations: first of all, since only marital status at index baseline admission was considered in this study, any influence of change in marital status all

through follow-up either in the form of loss of partner or divorce in the married patients or a new partner among widowed patients might potentially influence the overall result significantly; hence, definitive conclusion about ACM cannot be withdrawn from this analysis.

Secondly, some might think of the potential influence of any "unreported" partner among "widowed" patients. Of note, all married patients were thoroughly confirmed via an electronic database. Besides, centers participating TREAT-HF cohorts were expert HF centers in Turkey and all of them were aware of their patients and potential long-term partners closely.

Marital quality is known to have a significant impact on cardiovascular health [27]. Another limitation of this study is that the lack of observational measurements and interviews to determine the marital quality and social support levels of the spouses.

In this study, we thought that widows might have suffered more frequently from depressive disorder although no scale was used to evaluate the depression status of the participants.

Increased risk of HFrH among widowed patients, not ACM, might potentially be linked to GDMT adherence, which was not considered in this study, although it is relatively a well-established entity. However, the patient cohort was made up of relatively stable and chronic outpatients with HFrEF among expert centers with a 3-month interval regular follow up schedule.

Diagnosis of HF-related hospitalization was not adjudicated independently, and some events outside the participant hospitals might have been underestimated since some HF-related events might not be properly recorded, at least as the primary diagnosis, in other hospitals. In this study, ACM was investigated; we did not report the cardiovascular mortality, which is another limitation of our study.

Conclusion

In conclusion, among relatively stable chronic HFrEF outpatients, PS matching analysis yielded that widowed patients had an increased the risk for HFrH, although all-cause mortality was not different compared to married patients with HF. Of note, widows, rather than widowers seemed to have increased risk for HFrH.

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Ethics Committee Approval: The Cumhuriyet University Clinical Research Ethics Committee granted approval for this study (date: 30.11.2010, number: 2010-01/13).

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Authorship Contributions: Concept – BS, LB, HK, AC, HG, MZ, DU, YC, MBY, AT; Design – AT, MBY, DU, YC, MZ, BS; Supervision – LB, MBY, AT, YC, DU, HG, BS; Fundings – BS, MBY, LB, HK, AC, HG, YC, MZ; Materials – MBY, BS, LB, YC, DU, AT, HG, AC; Data collection and/or processing – BS, LB, AT, DU, HG, MZ, MBY, AC; Analysis and/or interpretation – BS, MBY, YC, HG, AT; Literature review – BS, LB, MBY, AC, AT, MZ; Writing – BS, MBY, AT, DU, AC; Critical review – BS, MBY, AT, AC, DU, YC, MZ.

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