Single living predicts a higher mortality in both women and men with chronic heart failure

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Single living predicts a higher mortality in both women and men with chronic heart failure

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ABSTRACT

INTRODUCTION: We examined the impact of single living on all-cause mortality in patients with chronic heart failure and determined if this association was modified by gender.

METHODS: This historical cohort study included 637 patients who were admitted to the Department of Cardiology, Herlev Hospital, Denmark, between 1 July 2005 and 30 June 2007. Baseline clinical data were obtained from patient records. Data on survival rates were obtained from the Danish Civil Registration System. Cox proportional hazard analysis was used to compute the hazard ratio (HR) of all-cause mortality, controlling for confounding factors.

RESULTS: The median follow-up time was 2.8 years. A total of 323 (50.7%) patients died during the follow-up period. After adjustment for confounding factors, risk of death was associated with being single (HR = 1.53 (95% confidence interval: 1.19-1.96)). In a gender-stratified analysis, the risk of death did not differ among single-living women and men.

CONCLUSION: Single living is a prognostic determinant of all-cause mortality in men and women with chronic heart failure.

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Approximately 1-2% of the adult population has heart failure (HF) [1]. Almost 50% of patients with HF die within four years [1].

Several prognostic determinants have been identified in patients with HF [1]. Social support has a significant impact on health and well-being in general [2], and it has been associated with better self-care and good treatment adherence among patients with HF [3]. Single living is an easy-to-measure proxy for a low level of social support in a wide variety of patient populations, and several studies have shown a negative impact of single living on survival [4, 5]. Although studies suggest an association between social support and outcome among patients with HF, there are conflicting results [6-9]. Furthermore, there are also conflicting data regarding differences in relative risk between genders [5, 10-12].

Hence, we examined the prognostic impact of single living on all-cause long-term mortality among patients with chronic HF and whether the association between single living and mortality varied by gender.

METHODS

Patients referred to the outpatient clinic (OPC) and HF clinic (HFC) or admitted to the ward of the Department of Cardiology, Herlev Hospital, Denmark, during the period from 1 July 2005 to 30 June 2007 and discharged with a HF diagnosis were identified through the Danish National Registry of Patients (DNRP). The first hospital contact for HF within that period was registered as the index hospital contact. The positive predictive value of the HF diagnosis in the DNRP is relatively high [13]. Information about the diagnoses was coded according to the International Classification of Diseases, tenth edition (ICD-10). The codes used for identification of patients with HF were I11.0, I13.0, I13.2, I42.0, I42.6-9, I50.0-1 and I50.9.

Medical records were reviewed during the period from 1 October 2009 to 23 March 2010. We obtained information on age, gender, single living or living with a partner, weight, height, tobacco use and alcohol consumption, results of laboratory tests, whether the patients fulfilled the HF criteria [14], New York Heart Association functional class, history of ischaemic heart disease, history of valve disease and other co-morbidities at the time of the index hospital contact. All descriptions of the first echocardiographic examination performed either in the ward, the OPC or the HFC at the index hospital contact were reviewed for information on left ventricular ejection fraction (LVEF) and severity of valve diseases. LVEF was usually assessed visually by the operators. Mitral valve regurgitation (MVR) was most often measured semi-quantitatively by assessing the regurgitation jet area by colour Doppler and was classified as either absent or as one of the three progressive degrees of severity of mild, moderate or severe MVR. The degree of aortic stenosis (AS) was classified as absent, mild, moderate or severe depending on the reported figures for the maximum transaortic pressure gradient and the aortic valve area. Pulmonary hypertension was suspected when the maximum velocity of the tricuspid regurgitation jet exceeded 36 mmHg.

Information on pulmonary congestion was obtained from the descriptions of the chest X-ray. From records we obtained information on medical treatment, whether the patients were referred to the HFC or the OPC after discharge, and readmissions during the follow-

ORIGINAL ARTICLE

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TABLE 1

Baseline characteristics of patients with chronic heart failure, by living arrangements.

Variable	Single living (n = 303)	Living with a partner (n = 334)	p-value
Age, yrs, mean (± SD)	76.9 (± 11.9)	70.8 (± 10.8)	< 0.001
Female, %	54.1	26.4	< 0.001
Smoking, %	31.4	31.7	0.932
Drinking alcohol every day, %	5.6	9.0	0.129
Diabetes, %	18.5	18.9	0.919
Hypertension, %	48.2	43.1	0.204
Stroke, %	15.5	12.9	0.363
Ischaemic heart disease, %	55.5	58.7	0.424
COPD, %	16.2	15.0	0.743
ICD, %	4.0	6.9	0.119
Atrial fibrillation, %	48.5	46.7	0.691
Pulmonary congestion, %	48.6	39.2	0.039
Echocardiography, %			
Performed	92.4	97.6	0.003
LVEF, mean (± SD)	36.7 (± 14.7)	35.8 (± 14.0)	0.228
Valvular disease, %			
Valve prosthesis	1.3	5.1	0.008
Mitral valve regurgitation:	0.112		
Absent	38.9	48.1	
Mild	38.9	35.1	
Moderate	17.2	13.4	
Severe	5.0	3.4	
Aortic stenosis:			0.051
Absent	89.3	94.4	
Mild or moderate	3.2	2.2	
Severe	7.5	3.4	
Pulmonary hypertension	25.4	15.9	0.003
Creatinine concentration[a], µmol/l, median (IQR; range)	107 (85-142; 45-1,417)	104 (83.5-139; 26-969)	0.670
Body mass index[b], kg/m^2, mean (± SD)	25.9 (± 5.9)	26.5 (± 5.1)	0.858
OPC/HFC, %	45.9	65.6	< 0.001
Medical treatment among patients with LVEF ≤ 40%, %			
ACEI or ARB	90.9	92.7	0.579
Beta-blocker	71.4	79.4	0.076
Aldosterone antagonist	37.7	40.8	0.535
Hospitalisation within 12 mo. of initial contact at hospital, %			
Hospitalisation (all-cause)	58.1	51.5	0.111
Heart failure	13.9	13.8	1.00
Acute myocardial infarction	4.0	3.0	0.523
Angina pectoris	5.0	5.1	1.000
Atrial fibrillation	3.6	1.8	0.218
Stroke	2.0	3.3	0.336

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; HFC = heart failure clinic; ICD = implantable cardioverter defibrillator; IQR = interquartile range; LVEF = left ventricular ejection fraction; OPC = outpatient clinic; SD = standard deviation.
a) Data available for 471 patients.
b) Data available for 480 patients.

ing year. The patients were registered as having been treated with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers or aldosterone antagonists if they were treated with at least one of the agents at the index hospital contact or if the treatment was initiated within a period of three months after their index hospital contact. Data on death during the follow-up period were obtained from the Danish Civil Registration System. The study was performed as a part of a quality assurance HF project [13], and was registered and approved by the Danish Data Protection Agency (2008-41-2889).

Statistics

Data were analysed using Stata 13.1 (StataCorp, College Station, Texas, USA).

All patients were observed from the date of index hospital contact until death or end of

follow-up, whichever came first. End of follow-up was the day patients' records were reviewed. The assumption of normality of continuous data was evaluated by normal probability plots. Normally distributed data were summarised as mean and standard deviation (SD); others were summarised as median, interquartile range (IQR) and range. Categorical variables were reported as frequencies and percentages. Differences in baseline variables were estimated by Fisher's test (categorical variables), Wilcoxon rank-sum test (non-normally distributed variables) and t-test (normally distributed variables). The relation between the hazard function and the covariates was modelled by Cox proportional-hazard regression. Selection of the variables in the models was based on an a priori decision of important variables in combination with the results of the crude associations between the variables and death. Initially, a model containing all baseline variables associated with death at the 25% level in the crude analyses was fitted. The model selection procedure also allowed for variable selection based on hypothesised importance, e.g., gender. Various models were compared by examining changes produced in the value of minus twice the logarithm of the maximised likelihood, –2logL, by adding or deleting variables in the model. The smaller the value of –2logL, the better the model. Schoenfeld and Cox-Snell residuals were used to check the assumptions and the overall model fit. A plot of Martingale residuals against covariates was used to detect nonlinearity.

Trial registration: not relevant.

RESULTS

Of 758 patients treated during the study period, 637 (84%) fulfilled the HF criteria [14]. There were 385 (60.4%) men with a mean age of 72.1 years (SD: ± 11.5), and 252 (39.6%) women with a mean age of 76.0 years (SD: ± 11.7) ($p < 0.001$). A total of 364 (57.1%) patients had a history of ischaemic heart disease, and 303 (47.6%) patients lived alone.

Differences in patient characteristics by single living are provided in **Table 1**. Single-living patients were older, were more likely to be female and were more likely to have pulmonary congestion. Less single-living patients were examined by echocardiography. However, there were no differences in LVEF. Single-living patients were more likely to have pulmonary hypertension and less likely to be referred to the OPC or the HFC. There were no significant differences in medical treatments. All-cause hospitalisation during the first 12 months after discharge was more frequent among single-living patients; however, this difference was not significant (Table 1). The median follow-up time was 2.8 years (IQR: 1.1-3.7 years, range: 1 day to 4.7 years).

Unadjusted analyses

A total of 323 (50.7%) patients died during the follow-up period. Survival was significantly decreased among single-living patients (**Figure 1**).

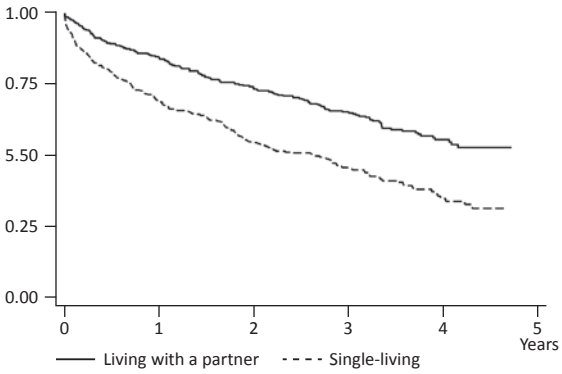
The unadjusted hazard ratios (HR) are given in **Table 2**. After stratification of living arrangements by gender, it was found that both single-living men and women had a significantly increased risk of death with either men living with a partner (model I) or women living with a partner (model II) as reference (**Table 3**). Other variables associated with shorter survival in unadjusted analyses were old age, diabetes, hypertension, stroke, atrial fibrillation, pulmonary congestion, reduced LVEF, moderate and severe MVR, AS, pulmonary hypertension and increasing creatinine (Table 2). Follow-up in the OPC or the HFC clinics, increasing values of body mass index and treatment with angiotensin-converting enzyme inhibitors and angiotensin receptor II blockers were associated with better post-discharge survival (Table 2).

Adjusted analyses

After controlling for potential confounders, single living was found to be associated with all-cause mortality (HR = 1.53 (95% CI: 1.19-1.96)). A Cox proportional model (Table 3) that included living arrangements, stratified by gender, as well as age, diabetes, stroke, LVEF and b was found to be the best model. The risk of death in single-living patients was increased in both men and women. In a model with men living with a partner as reference, it

FIGURE 1

The unadjusted survival curves of patients with chronic heart failure, by living arrangements, $p < 0.001$.



was found that for both women and men, living alone were associated with mortality (Table 3). For women, living alone was associated with mortality in a model with women living with a partner as reference. The interaction between single living and gender was not significant (p = 0.661) and was therefore not included in the model.

DISCUSSION

We found that single living, used as a proxy for lack of social support, was associated with increased long-term all-cause mortality among patients with HF. Furthermore, single living was a predictive factor for mortality in both sexes.

TABLE 2

Unadjusted predictors of long-term all-cause mortality among patients with chronic heart failure.

Variable	HR (95% CI)	p-value
Single living	1.81 (1.46- 2.27)	< 0.001
Age[a]	1.05 (1.03-1.06)	< 0.001
Male	1.04 (0.83-1.30)	0.714
Smoking	0.80 (0.62-1.01)	0.066
Alcohol	0.84 (0.55-1.30)	0.446
Diabetes	1.36 (1.06-1.77)	0.022
Hypertension	1.34 (1.08-1.68)	0.008
Stroke	1.87 (1.42-2.47)	< 0.001
Ischaemic heart disease	1.08 (0.87-1.36)	0.472
COPD	1.14 (0.86-1.53)	0.364
ICD	0.98 (0.61-1.59)	0.955
Atrial fibrillation	1.30 (1.04-1.61)	0.020
Pulmonary congestion	1.62 (1.28-2.05)	< 0.001
LVEF[b]	0.96 (0.93-1.00)	0.084
Valvular disease		
Mitral valve regurgitation:		
None	Reference	–
Mild	1.16 (0.89-1.50)	0.271
Moderate	1.51 (1.10-2.07)	0.011
Severe	2.04 (1.24-3.35)	0.005
Aortic stenosis:		
None	Reference	–
Mild or moderate	2.47 (1.41-4.31)	0.002
Severe	2.19 (1.45-3.31)	0.000
Pulmonary hypertension	1.53 (1.19-1.98)	0.001
Creatinine concentration[a]	1.001 (1.000-1.002)	0.001
Body mass index	0.94 (0.92-0.97)	< 0.001
OPC/HFC	0.61 (0.49-0.76)	< 0.001
Medical treatment among patients with LVEF ≤ 40%		
ACEI or ARB	0.45 (0.29-0.69)	< 0.001
Beta-blocker	0.73 (0.54-0.99)	0.043
Aldosterone antagonist	0.98 (0.74-1.30)	0.882

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CI = confidence interval; COPD = chronic obstructive pulmonary disease; HFC = heart failure clinic; HR = hazard ratio; ICD = implantable cardioverter defibrillator; LVEF = left ventricular ejection fraction; OPC = outpatient clinic.
a) HR is for 1-unit change of the variable.
b) HR is per 5-unit change of the variable.

Other studies

Evidence on the role of social support in the prognosis among patients with HF is conflicting [6-9, 15-17]. This may be explained by the different methods used to measure social support and missing consensus on the best definition of social support [4, 6, 18]. In a review of the role of social support on prognosis in HF, two of six studies showed a relation between social support constructs (social isolation, a lower degree of interaction with relatives, friends and community) and mortality among inpatients. The relation was independent of potential confounders [6]. Among outpatients, constructs related to social support were related to mortality in two out of four studies, independently of biomedical factors [6].

Our finding that single living was associated with a greater risk of death among patients with HF is in accordance with the literature describing the association between social support, marital status, living arrangements and outcome among patients with ischaemic heart disease [4, 10-11], and other conditions such as cancer, chronic pulmonary disease, stroke and alcohol consumption [19]. Living with a partner has been associated with longer survival in patients with diastolic HF [9], and in a smaller study of patients with HF recruited from an outpatient clinic [20]. In contrast hereto, marital status was not a significant variable for in-hospital death or for time to readmission for HF in one study of HF [8].

The hazard ratios for women and men were relatively imprecise in our study. Therefore, we could not conclude if the association between single living and mortality was stronger for one of the sexes. However, recent meta-analyses of the mortality for singles have shown that the risk of death has become approximately equal for men and women and that the historical gender difference in risk has decreased slightly because the risk for women has increased at a faster rate than the risk for men [5].

Pathophysiological mechanisms

Mechanisms whereby social support and single living can influence the outcome in patients with HF are not well defined. Potential biological and psychosocial pathophysiological mechanisms described in the literature include cardiovascular, immune and endocrine processes, psychological distress and inappropriate health behaviour [6]. A poor social network may generate anxiety and stress, which stimulates the sympathetic nervous, hypothalamus-pituitary-adrenal and renin-angiotensin-aldosterone systems and causes damage to the arterial wall and to the myocardium [6]. A poor social network and poor social support are also associated with a higher frequency of depression, leading to a poorer prognosis in HF, and influences access to health

TABLE 3

Unadjusted and adjusted hazard ratios for all-cause mortality in relation to living arrangements stratified by gender[a].

	Unadjusted		Adjusted	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Model I				
Men living with a partner	Reference	–	Reference	-
Women living with a partner	1.74 (1.13-2.66)	0.011	1.48 (0.95-2.30)	0.079
Women living alone	2.85 (1.83-4.42)	0.000	2.25 (1.42-3.54)	0.001
Men living alone	2.71 (1.76-4.18)	0.000	1.71 (1.08-2.70)	0.023
Model II				
Women living with a partner	Reference	–	Reference	–
Men living with a partner	0.58 (0.38-0.88)	0.011	0.67 (0.43-1.05)	0.079
Women living alone	1.64 (1.24-2.17)	0.001	1.51 (1.13-2.03)	0.005
Men living alone	1.56 (1.19-2.05)	0.001	1.15 (0.85-1.56)	0.359

CI = confidence interval; HR = hazard ratio.
a) Other significant variables in the final Cox proportional hazard models (HR (95% CI)) were: age[b] (1.05 (1.03-1.06)), diabetes (1.69 (1.28-2.24)), left ventricular ejection fraction[c] (0.95 (0.91-0.99)), stroke (1.73 (1.30-2.33)), and severe mitral valve regurgitation (2.24 (1.33-3.79)).
b) HR is for a 1-unit change of the variable.
c) HR is per 5-unit change of the variable.

services and treatment compliance and thereby influences progression of the disease [6]. Social support has impact on self-care and behaviours among patients with HF, which in turn has an impact on prognosis [3, 6].

Clinical implications

Our findings have potentially important clinical implications. Living arrangement is a simple measure that can identify patients with HF who have a higher risk of mortality. Although there are no interventions for living arrangements with a documented effect on adverse outcomes among patients with HF, we emphasise the importance of assessing living arrangements as a part of risk stratification. More research is needed to identify interventions that might minimise the negative effects of single living. Identification of those at increased risk of worsening outcomes may lead to improved intervention strategies, thereby reducing the negative effects of single living on outcome.

Limitations

This study has several limitations. Due to the historical cohort design, we have no control over the quality of the baseline measurements. The control for confounding might therefore have been incomplete. We have not measured socioeconomic status or depressive symptoms, which are common in patients with HF [4, 6]. Both factors are potential causal pathways and mediating factors with potential confounding properties. The duration of single living was not known in our study. The living arrangements of patients could have changed during the follow-up period, causing misclassification of the social status. In addition, the quality of the living arrangements and social support were not studied and could have contributed to the risk of cardiovascular disease. Finally, the small sample size increased the risk of limited precision of the estimates. Despite these limitations, the results of the present study strongly indicated that social isolation, defined as single living, was a risk for death in patients with HF.

CONCLUSION

Single living is associated with increased mortality in male and female patients with chronic HF. Further studies should confirm our findings and define the underlying mechanisms responsible for this association.

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