Patient and Spousal Health and Outcomes in Heart Failure

BACKGROUND: A diagnosis of heart failure (HF) often requires a comprehensive lifestyle change to maintain disease stability. When patients with HF are married, the spouse frequently assumes the caregiving role. Our objectives were to describe the health of spouses of married patients with HF, and examine whether the health of a spouse impacts patient outcomes.

METHODS AND RESULTS: We identified 905 patients that were married at the time of incident HF diagnosis in Olmsted County, MN, from 2000 to 2012. Using Rochester Epidemiology Project resources, the patient and their spouse's comprehensive longitudinal health histories were linked. Spousal health at patient HF diagnosis was assessed by comorbidity burden, self-reported difficulty with activities of daily living and prior hospitalizations. The associations of spousal health with patient outcomes and patient death with spousal outcomes were examined using Cox and Andersen–Gill models. Spouses of patients with HF were elderly (mean age, 71 years), often had comorbid conditions, and 16% had difficulty with ≥1 activities of daily living. After adjustment for patient age, sex, and comorbidity, there were no independent associations of spousal health and patient risk of death or hospitalization after HF diagnosis. However, the risk of hospitalization (adjusted hazard ratio, 1.34; 95% confidence interval, 1.11–1.60; P=0.002) and death (hazard ratio, 2.10; 95% confidence interval, 1.60–2.75; P<0.001) increased in the surviving spouse after patient death.

CONCLUSIONS: We found no evidence that the health of a spouse impacts patient outcomes after HF diagnosis. However, after a patient with HF dies, their surviving spouse's risk of hospitalization and death increases.

Shannon M. Dunlay, MD, MS
Véronique L. Roger, MD, MPH
Susan A. Weston, MS
Lauren R. Bangerter, PhD
Jill M. Killian, BS
Joan M. Griffin, PhD

Correspondence to: Shannon M. Dunlay, MD, MS, Department of Cardiovascular Diseases, Mayo Clinic, 200 First St SW, Rochester, MN 55905. E-mail dunlay.shannon@mayo.edu

Key Words: activities of daily living ■ comorbidity ■ heart failure ■ hospitalization ■ spouses

Heart failure (HF) is a chronic life-limiting syndrome that negatively impacts health and places a huge burden on society, patients, and families. Though advances in medical therapy have improved survival after diagnosis, the 5-year mortality is still ≈50%,[1,2] and HF contributes to 1 in 9 deaths each year.[3] In addition, patients continue to experience morbidity included repeated hospitalizations that are estimated to total ≥1 million annually in the United States.[4]

Efforts to improve outcomes and manage symptoms in HF have focused on prescribing medications, dietary modifications, and exercise to improve hemodynamics and relieve congestion. However, the ability to comply with recommendations and maintain clinical stability relies on a supportive social environment. A key component of this social environment is the patient's family and friends who are involved with their daily care. Because a diagnosis of HF requires a comprehensive lifestyle change, including taking multiple daily medications, making dietary changes such as restricting sodium and fluid, exercising, and attending frequent clinical appointments, this primarily elderly population routinely require help with these tasks.[5] For individuals who are married, their spouse often assumes the caregiving role[6–8]; as such, marital status has been associated with differences in outcomes in patients with cardiovascular disease.[9–12] However, among married individuals with HF, we know little about the health of their spouses, and whether the health of a spouse affects patient outcomes. Furthermore, although the increased likelihood for a recently widowed person to die, the so-called widowhood effect, has been documented,[13–15] whether the widow's hospitalization risk increases after the death of a spouse with HF remains to be rigorously studied.

Leveraging our existing epidemiological cohort of patients with incident HF, we developed a novel method to electronically link patient data with their spouse's comprehensive longitudinal health history to test the hypotheses that (1) worse spousal health is associated with worse outcomes in patients with HF, (2) the widow's risk of both hospitalization and death increases after the patient with HF dies, and (3) the patient's risk of death and hospitalization increases after their spouse dies.

METHODS

Study Design and Setting

This study was conducted in Olmsted County, MN. Population-based research is possible because there are few healthcare providers, the largest of which is Mayo Clinic. Medical records from all sources of care for residents are indexed and linked via the Rochester Epidemiology Project,[16] enabling longitudinal capture of care for the county's residents. This is a retrospective cohort study of patients with incident HF and their spouses. Patients and spouses were excluded if they declined to provide Minnesota Research Authorization. This study was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards.

Identification of Patients With Incident HF

Olmsted County residents with a possible HF diagnosis from 2000 to 2012 were identified using *International Classification of Diseases*, Ninth Revision, code 428. Codes are assigned based on physician diagnoses during outpatient visits or at hospital discharge. A 50% random sample of patients with an *International Classification of Diseases*, Ninth Revision, code 428 during 2000 to 2006 and all patients with an *International Classification of Diseases*, Ninth Revision, code 428 during 2007 to 2012 underwent case validation and data abstraction. A sample was used from 2000 to 2006 because of budget and time constraints. Nurse abstractors reviewed medical records to validate the HF episode using Framingham criteria.[2,17] The HF index date was defined as the date they first met Framingham criteria. The interabstractor agreement was 100%, indicating these methods are highly reproducible.[2]

Identification of Spouses of Patients With HF

Spouses of patients with HF were identified using a multistep approach. First, we identified patients with incident HF that were married or had a life partner at diagnosis using information in the electronic medical record. For simplification, all couples are referred to as married. Next, the spouse's name was identified using patient contact information in the medical record and death certificate. Then, Rochester Epidemiology Project resources were used to identify the spouse's medical records. The accuracy of the identified spouse was verified using address matching and manual record review. For spouses whose names could not be located electronically, the patient's medical records were manually reviewed. When a potential spouse was identified, their medical records were manually reviewed to ensure that they were married to the patient.

In 43 cases, the patient and their spouse both had HF. If both developed HF in the study period, the partner that developed HF earlier was designated as the patient, and their partner as the spouse. When the spouse had HF diagnosed before the study period or before they were married to the patient, they were retained as the spouse.

Patient and Spouse Characteristics

Patient and spouse baseline characteristics were obtained from the medical record. The Charlson comorbidity index was used to assess comorbidity.[18] Difficulty with activities of daily living (ADL) and instrumental ADLs (IADLs) was assessed using responses from a Mayo Clinic survey that all patients are asked to complete annually and with each hospitalization.[19] Patient left ventricular ejection fraction was obtained from echocardiograms closest to HF diagnosis and within 1 year in all cases. For laboratory data (hemoglobin, sodium,

and creatinine), the value closest to the date of HF diagnosis was used up to ±1 year. Anemia was defined using World Health Organization criteria.[20] Estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease equation.[21]

Study Outcomes

Data on all-cause hospitalizations occurring in Olmsted County were obtained using Rochester Epidemiology Project resources. For patients hospitalized at HF diagnosis, only subsequent hospitalizations were analyzed. In-hospital transfers or transfers between Olmsted Medical Center and Mayo Clinic hospitals, the only hospitals in the county, were considered a single hospitalization. In addition to deaths noted in clinical care, the Mayo Clinic registration office records obituaries and local death notices, and death data are obtained quarterly from the State of Minnesota Department of Vital and Health Statistics.

Statistical Analysis

Baseline characteristics for patients and spouses were compared using paired *t* tests for continuous variables, Wilcoxon signed-rank tests for ordinal variables, and McNemar tests for binary variables. Baseline spousal health at HF diagnosis was assessed using the Charlson comorbidity index, the number of hospitalizations in the 2 years before the patient's HF diagnosis, and the spouse's reported difficulty with ADLs/ IADLs. The associations of baseline spousal health and patient hospitalization and mortality risk were assessed using Andersen–Gill[17,22] and Cox proportional hazard regression models, respectively, adjusting for patient age, sex, and comorbidity. Ejection fraction (missing in 18.7% of participants) was adjusted for in a sensitivity analysis; as it made no difference in estimates, it was not included in the final models. Differences in associations by sex and age of the patient were tested by including interaction terms in the models. Patients were censored at last follow-up; in the hospitalization models, patients were also censored at death. The 4 couples that divorced during follow-up were censored at the time of divorce. We performed a sensitivity analysis where we censored patients at their spouse's last follow-up if this occurred first; results were similar and are not presented.

Rates of hospitalization in the spouse before and after patient death were calculated, and 95% Poisson confidence intervals (CIs) were estimated. The association of patient death with risk of hospitalization in the surviving spouse was examined using Andersen–Gill modeling. We modeled spouse hospitalization over time (beginning 2 years before the patient's HF diagnosis), treating patient death as a time-dependent covariate. The time scale was the age of the spouse. The association of patient death with risk of death in the surviving spouse was examined using Cox proportional hazard regression modeling. Patient death was treated as a time-dependent covariate, and the time scale was the age of the spouse. Models were adjusted for spouse sex and comorbidity. Differences in the associations by sex of the spouse were tested by including an interaction term in each of the models. The proportional hazards assumption was tested and found to be valid. A sensitivity analyses was performed excluding the 43 couples where both partners had HF, and no major differences in findings were observed (data not shown).

A similar analysis examining the impact of spousal death on patient outcomes was performed. The association of spousal death with risk of hospitalization in the surviving patient was examined using Andersen–Gill modeling. We modeled patient hospitalizations over time (beginning at incident HF date), treating spousal death as a time-dependent covariate. The association of spousal death with risk of death in the surviving patient was examined using Cox proportional hazard regression modeling, where patient death was treated as a time-dependent covariate. Models were adjusted for patient sex and comorbidity. Differences in the associations by sex of the patient were tested by including an interaction term in each of the models. Analyses were performed using SAS Version 9.4 (Cary, NC).

RESULTS

Of 2347 patients with incident HF from 2000 to 2012, 1112 (47%) were married at HF diagnosis. Of those who were unmarried, 780 (63%) were widowed, 231 (19%) were divorced, 196 (16%) were single/never married, and 28 (2%) had unknown marital status. Among the 1112 married patients, 1054 (95%) spouses were identified, of whom 905 (85.9%) met study entry criteria and were included in the analysis (Figure 1). There were 2 same-sex couples in our study. Patients with HF were older, more often male, and had more comorbidities than the spouses (Table 1). However, spouses were also elderly (mean age, 71.4 years) and comorbidities including hypertension, diabetes mellitus, depression, and malignancy were common. One in 6 spouses reported difficulty with at least 1 ADL/IADL.

Associations of Spousal Health and Patient Outcomes

After a mean (SD) follow-up of 7.3 (3.6) years, 534 (59%) patients had died. In unadjusted analyses, the

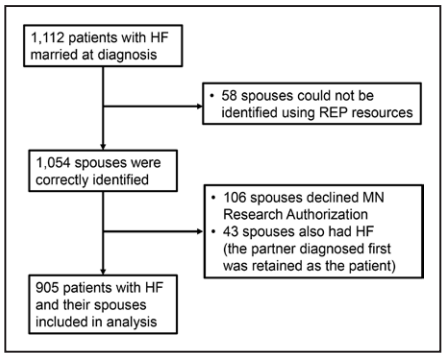

Figure 1. Study population.
Individuals that decline Minnesota (MN) research authorization in Olmsted County cannot be included in retrospective research studies. HF indicates heart failure; and REP, Rochester Epidemiology Project.

Table 1. Baseline Characteristics of Patients With Heart Failure and Spouses

	Spouses (n=905)	HF Patients (n=905)	*P* Value
Sociodemographics			
Female, n (%)	584 (65)	319 (35)	<0.001*
Age at index, mean (SD)	71.4 (12.7)	73.3 (12.1)	<0.001†
White, n (%)	865 (96)	872 (96)	0.16*
Hispanic, n (%)	19 (2)	11 (1)	0.13*
Education at index, n (%)			0.005‡
Did not graduate high school	62 (10)	155 (17)	
High school graduate	180 (30)	317 (35)	
Some college	189 (32)	200 (22)	
College graduate	73 (12)	97 (11)	
Postgraduate studies	90 (15)	127 (14)	
Unknown	311	9	
Insurance at index, n (%)			<0.001§
Private	164 (24)	143 (20)	
Government	520 (75)	554 (79)	
None	14 (2)	3 (0.4)	
Unknown	207	205	
Residence at index, n (%)			
House/apartment		672 (93)	
Assisted living/nursing home		28 (4)	
Other		21 (3)	
Unknown		184	
Comorbidities			
Charlson comorbidity index, n (%)			<0.001‡
0	513 (57)	216 (24)	
1	169 (19)	198 (22)	
2+	223 (25)	491 (54)	
Prior myocardial infarction, n (%)	40 (4)	181 (20)	<0.001*
Peripheral vascular disease, n (%)	36 (4)	106 (12)	<0.001*
Cerebrovascular disease, n (%)	79 (9)	183 (20)	<0.001*
Dementia, n (%)	36 (4)	53 (6)	0.065*
COPD, n (%)	64 (7)	175 (19)	<0.001*
Rheumatologic disease, n (%)	38 (4)	37 (4)	0.91*
Peptic ulcer disease, n (%)	66 (7)	106 (12)	0.001*
Diabetes mellitus, n (%)	133 (15)	316 (35)	<0.001*
Hemiplegia/paraplegia, n (%)	12 (1)	23 (3)	0.056*
Renal disease, n (%)	19 (2)	92 (10)	<0.001*
Malignancy, n (%)	97 (11)	191 (21)	<0.001*
Liver disease, n (%)	6 (1)	19 (2)	0.009*
Hypertension, n (%)	517 (57)	706 (78)	<0.001*
Depression, n (%)	129 (14)	171 (19)	0.005*
ADLs			
Missing within ±1 y of index, n (%)	309 (34)	111 (12)	<0.001*
Difficulty bathing, n (%)	26 (4)	105 (13)	<0.001‖
Difficulty dressing, n (%)	22 (4)	96 (12)	<0.001‖
Difficulty eating, n (%)	10 (2)	26 (3)	0.010‖
Difficulty housekeeping, n (%)	56 (9)	145 (18)	<0.001‖
Difficulty using toilet, n (%)	14 (2)	54 (7)	<0.001‖
Difficulty walking, n (%)	65 (11)	199 (25)	<0.001‖
Number of ADL difficulties, n (%)			<0.001‖
0	499 (84)	530 (67)	
1	51 (9)	117 (15)	
2	24 (4)	53 (7)	
3	8 (1)	29 (4)	
4	4 (1)	23 (3)	
5	6 (1)	29 (4)	
6	4 (1)	13 (2)	
Heart failure baseline EF and laboratories			
EF at index, mean (SD)		47.7 (16.1)	
Preserved EF (≥50%), n (%)		388 (53)	
Anemia, n(%)		467 (52)	
Sodium, mean (SD)		138.7 (4.3)	
eGFR, mean (SD)		63.0 (25.0)	
Hospitalizations in 2 y before HF diagnosis			
0	701 (77)		
1	131 (14)		
2+	73 (8)		

(*Continued*)

Table 1. Continued

ADL indicates activity of daily living; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; eGFR, estimated glomerular filtration rate; and HF, heart failure.

**P* value from McNemar test.

†*P* value from paired *t* test.

‡*P* value from Wilcoxon signed-rank test on paired differences.

§*P* value from McNemar test comparing private vs government insurance among couples in whom both patient and spouse had private or government insurance (562 couples included).

‖*P* value from McNemar test among couples in whom both patient and spouse had known ADL status (539 couples included).

presence of comorbidities in the spouse was associated with increased risk of death after HF diagnosis in patients with HF (Table 2; Figure 2A). However, after adjustment for patient age, sex, and comorbidity, associations were no longer statistically significant. The associations of spousal hospitalizations and difficulty with ADLs with patient death both followed a similar pattern (Figure 2B). Although patients whose spouses had ≥2 hospitalizations in the 2 years before HF were at increased risk for death (hazard ratio [HR], 1.56; 95% CI, 1.18–2.07; *P*=0.008), this association was no longer statistically significant after adjusting for patient age, sex, and comorbidity (adjusted HR, 1.11; 95% CI, 0.83–1.48; *P*=0.20). Similarly, patients whose spouses

Table 2. Risk of Death and Hospitalization in Patients With Heart Failure According to the Health of the Spouse

	No. of Spouses	No. of Patient Events	Unadjusted HR (95% CI)	Model 1* HR (95% CI)	Model 2† HR (95% CI)
Death					
Spouse Charlson comorbidity index					
0	513	281	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
1	169	106	1.37 (1.09–1.71)	1.13 (0.90–1.42)	1.12 (0.89–1.41)
2+	223	147	1.36 (1.12–1.67)	1.05 (0.86–1.29)	0.99 (0.80–1.21)
P value‡			0.002	0.55	0.32
Spouse number of hospitalizations					
0	701	401	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
1	131	78	1.00 (0.78–1.27)	0.83 (0.65–1.06)	0.82 (0.65–1.05)
2+	73	55	1.56 (1.18–2.07)	1.24 (0.93–1.64)	1.11 (0.83–1.48)
P value‡			0.008	0.081	0.20
Number of ADLs/IADLs where spouse reported having difficulty					
0	499	285	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
1+	97	65	1.31 (1.00–1.72)	1.00 (0.76–1.32)	1.06 (0.80–1.39)
P value‡			0.048	0.99	0.69
Hospitalization					
Spouse Charlson comorbidity index					
0	506	2034	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
1	164	637	1.12 (0.92–1.36)	1.13 (0.92–1.38)	1.11 (0.92–1.35)
2+	215	871	1.10 (0.93–1.30)	1.11 (0.93–1.33)	1.05 (0.89–1.24)
P value‡			0.39	0.35	0.54
Spouse number of hospitalizations					
0	685	2649	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
1	129	590	1.16 (0.97–1.39)	1.15 (0.96–1.37)	1.12 (0.93–1.35)
2+	71	303	1.31 (1.03–1.65)	1.28 (1.01–1.62)	1.17 (0.94–1.47)
P value‡			0.041	0.065	0.25
Number of ADLs/IADLs where spouse reported having difficulty					
0	490	1938	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
1+	92	360	1.07 (0.86–1.33)	1.05 (0.85–1.30)	1.09 (0.89–1.34)
P value‡			0.55	0.62	0.40

ADL indicates activity of daily living; CI, confidence interval; HR, hazard ratio; and IADL, instrumental activity of daily living.

*Adjusted for patient age and sex.

†Adjusted for patient age, sex, and Charlson comorbidity index.

‡*P* values are from χ^2 tests with 2 degrees of freedom for Charlson comorbidity index and number of hospitalizations and 1 degree of freedom for ADLs/IADLs.

reported difficulty with ADL/IADLs were at increased risk for death after HF diagnosis (HR, 1.31; 95% CI, 1.00–1.72; *P*=0.048), but this was no longer statistically significant after adjusting for differences in patient age, sex, and comorbidity (adjusted HR, 1.06; 95% CI, 0.80–1.39; *P*=0.70). There were no statistically significant differences in the associations of spousal health and patient risk of death by age or sex of the patient (*P* values for interactions >0.05).

There was a stepwise increase in patient hospitalization risk after diagnosis associated with increasing number of prior hospitalizations in spouses (Table 2). However, after adjustment for patient age, sex, and comorbidity, the HR for hospitalization was near 1, regardless of the number of prior hospitalizations in the spouse. We found no statistically significant association of comorbidity or reported ADL/IADL difficulty in the spouse with risk of hospitalization in the patient after HF diagnosis. There were no statistically significant differences in the associations of spousal health and patient risk of hospitalization by age or sex of the patient (*P* values for interactions >0.05).

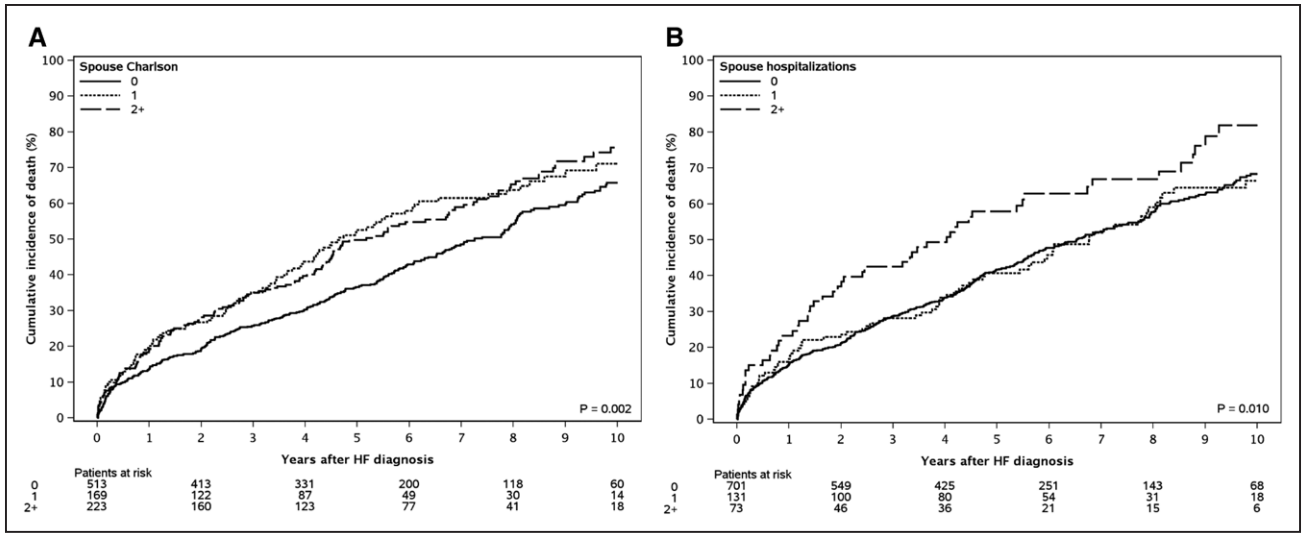

Figure 2. Cumulative incidence of death in patients with heart failure (HF) by health of the spouse.
The cumulative incidence of death (*y*-axis) in patients with heart failure over time (*x*-axis) is shown, stratified by comorbidity burden (**A**) and number of hospitalizations (**B**) of the spouse.

Impact of Patient Death on Risk of Death and Hospitalization in the Surviving Spouse

The impact of patient death on the risks of death and all-cause hospitalization in the spouse is shown in Table 3. In total, 251 (28%) spouses died during the study period, including 103 spouses that died whereas their partner with HF was still alive, and 148 spouses that died after their partner. After patient death, the risk of death in the surviving spouse markedly increased (adjusted HR, 2.10; 95% CI, 1.60–2.75; *P*<0.001). This association did not differ by sex of the spouse (*P* value for interaction=0.37).

When the patient was alive, the mean rate of hospitalization in the spouse per 100 person-years of follow-up was 21.5 (95% CI, 20.4–22.7). After patient death, the rate of hospitalization in the surviving spouse increased to 33.3 per 100 person-years of follow-up (95% CI, 30.9–35.8). Among all patient-spouse couples in this study (n=905), the risk of hospitalization in the surviving spouse increased by 21% (adjusted HR, 1.21; 95% CI, 1.01–1.45; *P*=0.038) after death of the patient. However, not all patients in this study died during the study period or when their spouse was still alive. When we restricted the analysis to couples where the patient died before spousal death or last follow-up (n=468 couples), the association of patient death with hospitalization risk in the surviving spouse was even stronger. Adjusting for spouse sex and comorbidity, the risk of hospitalization in the surviving spouse increased by 34% (HR, 1.34; 95% CI, 1.11–1.60; *P*=0.002) after patient death. However, the increased risk of hospitalization in the spouse after patient death differed by sex of the spouse (*P* value for interaction=0.010; Figure 3). After a female patient with HF died, the surviving spouse's risk of hospitalization increased (HR, 1.82; 95% CI, 1.37–2.41). However, after a male patient died, their spouse's hospitalization risk did not increase (HR, 1.14; 95% CI, 0.91–1.42).

Table 3. Associations of Patient Death With Risks of Hospitalization and Death in the Surviving Spouse

	Unadjusted		Adjusted*	
	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
Risk of death in spouse†				
All couples (n=905, 251 spouse deaths)	1.86 (1.43–2.41)	<0.001	2.10 (1.60–2.75)	<0.001
Hospitalization risk in spouse†				
All couples (n=905, 2055 spouse hospitalizations)	1.14 (0.96–1.36)	0.14	1.21 (1.01–1.45)	0.038
Couples where patient died with surviving spouse (n=468, 1289 spouse hospitalizations)	1.28 (1.07–1.53)	0.007	1.34 (1.11–1.60)	0.002

CI indicates confidence interval.
*Adjusted for spouse sex and Charlson comorbidity index.
†Patient death is a time-dependent covariate.

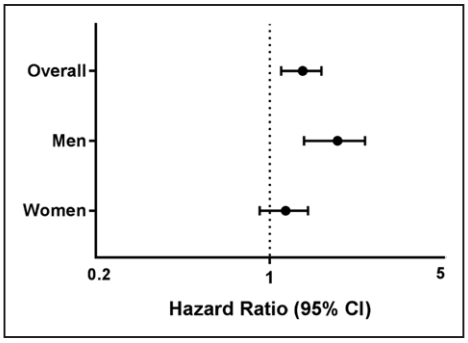

Figure 3. Risk of hospitalization after patient death in male and female widows.
The hazard ratios and 95% confidence intervals (CIs) for risk of all-cause hospitalization after compared with before patient death, overall, and stratified by sex, are shown. This analysis includes the 468 couples in whom the patient died before the spouse. The *P* value for the interaction of patient death*sex=0.010.

Impact of Spousal Death on Risk of Death and Hospitalization in the Surviving Patient

The impact of spousal death on the risks of death and all-cause hospitalization in the patient is shown in Table 4. After spousal death, the risk of death in the surviving patient increased (adjusted HR, 1.44; 95% CI, 1.08–1.92; *P*=0.014). The association did not differ by sex of the patient (*P* value for interaction=0.36). After spousal death, the risk of hospitalization in the surviving patient did not change (adjusted HR, 0.88; 95% CI, 0.67–1.16; *P*=0.37). This association did not differ by sex of the patient (*P* value for interaction=0.87). When we restricted the analysis to couples where the spouse died before patient death or last follow-up (n=103 couples), there was still no association of spousal death with patient hospitalization risk (HR, 1.19; 95% CI, 0.91–1.56; *P*=0.20).

DISCUSSION

In this community cohort, the health of a spouse, measured 3 separate ways, had no independent association with patient outcomes after HF diagnosis. In contrast, the spouse's risks of death and hospitalization increased after the death of the patient with HF. While the risk of death increased in widowed men and women, the increased risk of hospitalization occurred only in male widowers. Finally, the patient's risk of death, but not hospitalization, increased after the death of their spouse.

Informal caregivers are essential to the health and care of individuals living with chronic conditions such as HF. Prior studies of patient-caregiver dyads in HF have described caregivers as being older,[23,24] and often measured quality of life and depression,[8] but details of their medical histories and chronic conditions were unknown. We found that spouses of patients with newly diagnosed HF were, on average, much healthier than the patients. They had fewer chronic conditions, less difficulty with ADL/IADLs, and most had not been hospitalized in the past 2 years. However, they were still elderly (mean age, 71 years), and ≈1 in 6 reported difficulty with mobility and other ADL/ IADLs, and some had been hospitalized multiple times. Understanding the health history and functional status of spouses of patients with HF is important to consider when planning for the care of patients with HF, as some married patients may require assistance with daily tasks that their spouses cannot physically provide. Although there has been increased recognition of the importance of identifying and clearly communicating care responsibilities with informal caregivers,[25] it is also essential to assess the health and well-being of those caregivers so that potential gaps in care can be addressed.

Although numerous studies have reported deleterious effects of caregiving on psychological and physical heath,[7,26–28] we knew little about how the physical health of informal caregivers impacts the health and outcomes of patients with a chronic life-limiting condition such as HF. A 2016 meta-analysis summarized existing evidence on the associations of caregiver health with patient outcomes in HF.[29] Four studies reported that increased caregiver strain and psychologi-

Table 4. Associations of Spouse Death With Risks of Hospitalization and Death in the Surviving Patient

	Unadjusted		Adjusted*	
	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
Risk of death in patient†				
All couples (n=905, 534 patient deaths)	1.32 (0.99–1.76)	0.058	1.44 (1.08–1.92)	0.014
Hospitalization risk in patient†				
All couples (n=905, 3957 patient hospitalizations)	0.83 (0.64–1.09)	0.18	0.88 (0.67–1.16)	0.37
Couples where spouse died with surviving patient (n=103, 464 patient hospitalizations)	1.22 (0.92–1.61)	0.17	1.19 (0.91–1.56)	0.20

CI indicates confidence interval.
*Adjusted for patient sex and Charlson comorbidity index.
†Spouse death is a time-dependent covariate.

cal distress were associated with increased risk of short-term clinical events in patients with HF. However, caregiver health was limited to measures of psychological health, and did not assess measures of physical health that require access to medical record information. In this analysis, after assessing spousal health in 3 ways (prior hospitalizations, comorbidities, and difficulty with ADLs/ IADLs), we found no independent associations of spousal health with patient outcomes after diagnosis. Although we observed increased risks of hospitalization and death in patients with sicker spouses before adjustment, these associations were eliminated by adjustment for age, sex, and comorbidity. An explanation of this could be that patients who are older and sicker tend to have spouses who are older and sicker, but the physical health of the spouse does not directly impact patient outcomes. Although spousal health at baseline was not associated with differences in subsequent patient outcomes, the patient's risk of death did increase after the death of their spouse. These findings in the context of prior research demonstrating that marriage is protective against some adverse outcomes,[9,10] suggest that being in a committed relationship may be more important than a partner's physical health. However, as we only assessed spousal health at the time of HF diagnosis, it could also be that changes in spousal health over time can impact patient outcomes, and this could be explored in future studies.

The increased risk of death in a recently widowed individual—the so-called widowhood effect has been reported for spouses of patients with a variety of chronic conditions across the world.[13–15,30] An analysis of married Medicare fee-for-service beneficiaries found that the risk of death in the widow increased >10% after death of a spouse with HF.[14] We found an even greater association in this study, as the risk of death in the widow more than doubled after death of the patient. Furthermore, we extended prior findings by examining the effects of widowhood on hospitalization risk. We found that, in addition to suffering excess mortality, widows are also more likely to be hospitalized. The excess risk of hospitalization was limited to men after death of their wife with HF. This is consistent with prior studies suggesting that sex differences in the widowhood effect exist and are stronger for male widows.[31] This may be because men are less likely than women to have social networks and struggle more to adapt to the loss of help with tasks at home.[32] Although the increase in risk of death was not as great for patients with HF that survived their spouse, they still experienced a 44% increased risk of death after their spouse died, demonstrating that the widowhood effect also impacts patients with HF.

Because >6 million Americans are living with HF, a condition with a median survival of only 5 years,[1,2] the increased risk of mortality and hospitalization imposed by widowhood is not trivial. Previous studies have suggested that the increased mortality associated with bereavement may not be a direct result of new or worsening physical disease,[33] though adverse psychological responses associated with acute grief[34] and cumulative wear and tear associated with caregiving of a dying spouse are likely contributing factors.[32] Further work is needed to delineate the pathways by which widowhood impacts health and outcomes. Recognition of this phenomenon would grant us an important opportunity to intervene with enhanced bereavement care and skill building to promote positive coping and independent functioning in the absence of a spouse.

Limitations and Strengths

There are limitations to acknowledge to aid in interpretation of these findings. First, we could not identify or include caregivers other than spouses in our analysis. Second, we do not have information on the burden of care that spouses experience, which may impact the associations observed. In addition, this reflects the experience of a single community, and findings in other populations may differ. Finally, hospitalizations occurring outside of Olmsted County were not captured. However, in Medicare-eligible Olmsted County residents, only 5% of all hospitalizations in 2005 were to hospitals outside of Olmsted County. There are also important strengths. We were able to link the comprehensive health histories of patients with their spouses. The lack of longitudinal health history of caregivers before an important diagnosis such as HF and throughout the course of care is considered a significant gap in the caregiving literature.[29,35] This novel method of linkage could be utilized in future community-based epidemiological studies to explore the associations of patient and spousal health in HF and other chronic conditions.

Conclusions

This longitudinal community study of nearly 1000 couples demonstrates that the health of a spouse does not impact patient outcomes in HF. However, death of the patient with HF has a tremendous impact on the risk of hospitalization and death in their surviving spouse, and represents an important opportunity for enhanced bereavement care.

ACKNOWLEDGMENTS

All authors participated in conception and design and analysis and interpretation of data. Dr Dunlay, Dr Roger, J.M. Killian, and S.A. Weston acquired subjects and data. Dr Dunlay prepared the article and all other authors have been involved in critical revision of the article.

SOURCES OF FUNDING

This study was funded by the National Institutes of Health (R03HL 135225, Principal Investigator Dunlay and R01 HL120957, Principal Investigator Roger) and made possible by the Rochester Epidemiology Project (R01 AG034676 from the National Institute on Aging). Dr Dunlay's time is funded by the National Institutes of Health (K23 HL 116643).

DISCLOSURES

None.

AFFILIATIONS

From the Department of Cardiovascular Diseases (S.M.D., V.L.R.) and Department of Health Sciences Research (S.M.D., V.L.R., S.A.W., L.R.B., J.M.G., J.M.K.), Mayo Clinic, Rochester, MN.

FOOTNOTES

Received March 28, 2017; accepted September 12, 2017.

Circ Heart Fail is available at http://circheartfailure.ahajournals.org.

REFERENCES

1. Gerber Y, Weston SA, Redfield MM, Chamberlain AM, Manemann SM, Jiang R, Killian JM, Roger VL. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. *JAMA Intern Med*. 2015;175:996–1004. doi: 10.1001/jamainternmed.2015.0924.
2. Roger VL, Weston SA, Redfield MM, Hellermann-Homan JP, Killian J, Yawn BP, Jacobsen SJ. Trends in heart failure incidence and survival in a community-based population. *JAMA*. 2004;292:344–350. doi: 10.1001/jama.292.3.344.
3. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jimenez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER, 3rd, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation*. 2016;133:e38–360.
4. Blecker S, Paul M, Taksler G, Ogedegbe G, Katz S. Heart failure–associated hospitalizations in the United States. *J Am Coll Cardiol*. 2013;61:1259–1267. doi: 10.1016/j.jacc.2012.12.038.
5. Buck HG, Harkness K, Wion R, Carroll SL, Cosman T, Kaasalainen S, Kryworuchko J, McGillion M, O'Keefe-McCarthy S, Sherifali D, Strachan PH, Arthur HM. Caregivers' contributions to heart failure self-care: a systematic review. *Eur J Cardiovasc Nurs*. 2015;14:79–89. doi: 10.1177/1474515113518434.
6. Reinhard SC. Family Caregivers Providing Complex Chronic Care to their Spouses. AARP Public Policy Institute, 2014. http://www.aarp.org/home-family/caregiving/info-04-2014/family-caregivers-providing-complex-chronic-care-to-spouses-AARP-ppi-health.html. Accessed September 12, 2017.
7. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *JAMA*. 1999;282:2215–2219.
8. Whittingham K, Barnes S, Gardiner C. Tools to measure quality of life and carer burden in informal carers of heart failure patients: a narrative review. *Palliat Med*. 2013;27:596–607. doi: 10.1177/0269216313477179.
9. Floud S, Balkwill A, Canoy D, Wright FL, Reeves GK, Green J, Beral V, Cairns BJ; Million Women Study Collaborators. Marital status and ischemic heart disease incidence and mortality in women: a large prospective study. *BMC Med*. 2014;12:42. doi: 10.1186/1741-7015-12-42.
10. Luttik ML, Jaarsma T, Veeger N, van Veldhuisen DJ. Marital status, quality of life, and clinical outcome in patients with heart failure. *Heart Lung*. 2006;35:3–8. doi: 10.1016/j.hrtlng.2005.08.001.
11. Maselko J, Bates LM, Avendaño M, Glymour MM. The intersection of sex, marital status, and cardiovascular risk factors in shaping stroke incidence: results from the health and retirement study. *J Am Geriatr Soc*. 2009;57:2293–2299. doi: 10.1111/j.1532-5415.2009.02555.x.
12. Quinones PA, Kirchberger I, Heier M, Kuch B, Trentinaglia I, Mielck A, Peters A, von Scheidt W, Meisinger C. Marital status shows a strong protective effect on long-term mortality among first acute myocardial infarction-survivors with diagnosed hyperlipidemia–findings from the MONICA/KORA myocardial infarction registry. *BMC Public Health*. 2014;14:98. doi: 10.1186/1471-2458-14-98.
13. Boyle PJ, Feng Z, Raab GM. Does widowhood increase mortality risk?: testing for selection effects by comparing causes of spousal death. *Epidemiology*. 2011;22:1–5. doi: 10.1097/EDE.0b013e3181fdcc0b.
14. Elwert F, Christakis NA. The effect of widowhood on mortality by the causes of death of both spouses. *Am J Public Health*. 2008;98:2092–2098. doi: 10.2105/AJPH.2007.114348.
15. Martikainen P, Valkonen T. Mortality after death of spouse in relation to duration of bereavement in Finland. *J Epidemiol Community Health*. 1996;50:264–268.
16. Melton LJ III. History of the Rochester Epidemiology Project. *Mayo Clin Proc*. 1996;71:266–274. doi: 10.1016/S0025-6196(11)63966-9.
17. Dunlay SM, Redfield MM, Weston SA, Therneau TM, Hall Long K, Shah ND, Roger VL. Hospitalizations after heart failure diagnosis a community perspective. *J Am Coll Cardiol*. 2009;54:1695–1702. doi: 10.1016/j.jacc.2009.08.019.
18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373–383.
19. Dunlay SM, Manemann SM, Chamberlain AM, Cheville AL, Jiang R, Weston SA, Roger VL. Activities of daily living and outcomes in heart failure. *Circ Heart Fail*. 2015;8:261–267. doi: 10.1161/CIRCHEARTFAILURE.114.001542.
20. Blanc B, Finch CA, Hallberg L, Herbert V, Lawkowicz W, Layrisee M, Mollin DL, Rachmilewitz M, Ramalingaswami V, Sanchez-Medal L, Wintrobe MM. *Nutritional Anemia: report of a WHO Scientific Group*. Geneva, Switzerland: World Health Organization; 1968.
21. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, Kusek JW, Van Lente F; Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med*. 2006;145:247–254.
22. Andersen PK, Gill RD. Cox's regression model for counting processes: a large sample study. *Ann Stat*. 1982;10:1100–1120.
23. Pressler SJ, Gradus-Pizlo I, Chubinski SD, Smith G, Wheeler S, Wu J, Sloan R. Family caregiver outcomes in heart failure. *Am J Crit Care*. 2009;18:149–159. doi: 10.4037/ajcc2009300.
24. Hwang B, Fleischmann KE, Howie-Esquivel J, Stotts NA, Dracup K. Caregiving for patients with heart failure: impact on patients' families. *Am J Crit Care*. 2011;20:431–441; quiz 442. doi: 10.4037/ajcc2011472.
25. Coleman EA. Family caregivers as partners in care transitions: the caregiver advise record and enable act. *J Hosp Med*. 2016;11:883–885. doi: 10.1002/jhm.2637.
26. Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS. Caregiver burden: a clinical review. *JAMA*. 2014;311:1052–1060. doi: 10.1001/jama.2014.304.
27. Pinquart M, Sörensen S. Gender differences in caregiver stressors, social resources, and health: an updated meta-analysis. *J Gerontol B Psychol Sci Soc Sci*. 2006;61:P33–P45.
28. Cameron JI, Chu LM, Matte A, Tomlinson G, Chan L, Thomas C, Friedrich JO, Mehta S, Lamontagne F, Levasseur M, Ferguson ND, Adhikari NK, Rudkowski JC, Meggison H, Skrobik Y, Flannery J, Bayley M, Batt J, dos Santos C, Abbey SE, Tan A, Lo V, Mathur S, Parotto M, Morris D, Flockhart L, Fan E, Lee CM, Wilcox ME, Ayas N, Choong K, Fowler R, Scales DC, Sinuff T, Cuthbertson BH, Rose L, Robles P, Burns S, Cypel M, Singer L, Chaparro C, Chow CW, Keshavjee S, Brochard L, Hébert P, Slutsky AS, Marshall JC, Cook D, Herridge MS; RECOVER Program Investigators (Phase 1: towards RECOVER); Canadian

Critical Care Trials Group. One-year outcomes in caregivers of critically ill patients. *N Engl J Med*. 2016;374:1831–1841. doi: 10.1056/NEJMoa1511160.
29. Bidwell JT, Lyons KS, Lee CS. Caregiver well-being and patient outcomes in heart failure: a meta-analysis. *J Cardiovasc Nurs*. 2017;32:372–382. doi: 10.1097/JCN.0000000000000350.
30. Christakis NA, Allison PD. Mortality after the hospitalization of a spouse. *N Engl J Med*. 2006;354:719–730. doi: 10.1056/NEJMsa050196.
31. Moon JR, Kondo N, Glymour MM, Subramanian SV. Widowhood and mortality: a meta-analysis. *PLoS One*. 2011;6:e23465. doi: 10.1371/journal.pone.0023465.
32. Sullivan AR, Fenelon A. Patterns of widowhood mortality. *J Gerontol B Psychol Sci Soc Sci*. 2014;69:53–62. doi: 10.1093/geronb/gbt079.
33. Shah SM, Carey IM, Harris T, DeWilde S, Victor CR, Cook DG. Do good health and material circumstances protect older people from the increased risk of death after bereavement? *Am J Epidemiol*. 2012;176:689–698. doi: 10.1093/aje/kws162.
34. Carey IM, Shah SM, DeWilde S, Harris T, Victor CR, Cook DG. Increased risk of acute cardiovascular events after partner bereavement: a matched cohort study. *JAMA Intern Med*. 2014;174:598–605. doi: 10.1001/jamainternmed.2013.14558.
35. Steinhauser KE, Clipp EC, Hays JC, Olsen M, Arnold R, Christakis NA, Lindquist JH, Tulsky JA. Identifying, recruiting, and retaining seriously-ill patients and their caregivers in longitudinal research. *Palliat Med*. 2006;20:745–754. doi: 10.1177/0269216306073112.

Patient and Spousal Health and Outcomes in Heart Failure

Shannon M. Dunlay, Véronique L. Roger, Susan A. Weston, Lauren R. Bangerter, Jill M. Killian and Joan M. Griffin

Circ Heart Fail. 2017;10:
doi: 10.1161/CIRCHEARTFAILURE.117.004088
Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-3289. Online ISSN: 1941-3297