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Marital Status as an Independent Predictor of Event-Free Survival of Patients with Heart Failure

Misook L. Chung

Terry A. Lennie

Barbara Riegel
University of Pennsylvania, briegel@nursing.upenn.edu

Jia-Rong Wu

Rebecca L. Dekker

See next page for additional authors

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Abstract

Background: Depressive symptoms are a well-known predictor of mortality in patients with heart failure, and positive spousal support is associated with improved outcomes in these patients. However, in the context of depressive symptoms, the effect on survival of having a spouse is unknown.

Objective: To determine the effect of marital status on event-free survival in patients with heart failure who did or did not have depressive symptoms.

Methods: Depressive symptoms were assessed by using the Back Depression Inventory-II in patients with heart failure who were followed-up for up to 4 years to collect data on mortality and hospitalizations. Patients were grouped according to the presence and absence of depressive symptoms by using the standard cutoff score of 14 on the Beck Depression Inventory-II. Kaplan-Meier and Cox regression analyses were used to compare event-free survival for married and nonmarried patients who were stratified according to the presence or absence of depressive symptoms.

Results: Of 166 patients, 56% were married, and 33% had depressive symptoms. Levels of depressive symptoms were similar between married and nonmarried patients (10.9 vs 12.1; *P*=.39). Married patients experienced longer event-free survival than did nonmarried patients (*P*=.01).

Conclusions: Patients with a spouse had longer event-free survival than nonmarried patients did, even in the context of depressive symptoms.

Disciplines

Cardiology | Cardiovascular Diseases | Circulatory and Respiratory Physiology | Critical Care | Critical Care Nursing | Health and Medical Administration | Health Services Research | Medical Humanities | Medicine and Health Sciences | Nursing | Preventive Medicine

Author(s)

Misook L. Chung, Terry A. Lennie, Barbara Riegel, Jia-Rong Wu, Rebecca L. Dekker, and Debra K. Moser

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By Misook L. Chung, RN, PhD, Terry A. Lennie, RN, PhD, Barbara Riegel, RN, DNSc, Jia-Rong Wu, RN, PhD, Rebecca L. Dekker, RN, MSN, and Debra K. Moser, RN, DNSc

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Objective To determine the effect of marital status on event-free survival in patients with heart failure who did or did not have depressive symptoms.
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Results Of 166 patients, 56% were married, and 33% had depressive symptoms. Levels of depressive symptoms were similar between married and nonmarried patients (10.9 vs 12.1; $P = .39$). Married patients experienced longer event-free survival than did nonmarried patients ($P = .009$), even with stratification according to depressive symptoms ($P = .01$).
Conclusions Patients with a spouse had longer event-free survival than nonmarried patients did, even in the context of depressive symptoms. (*American Journal of Critical Care.* 2009;18:562-570)

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More than 5 million patients in the United States currently have heart failure.[1] Hospitalization rates have increased 174% since the 1990s.[1] According to recent data from the Framingham Study, the 1-year age-adjusted mortality rates for men and women with heart failure are 28% and 24%, respectively, and the 5-year rates are 59% and 45%, respectively.[2] Accumulating evidence[3-5] suggests that depressive symptoms are an important independent risk factor for hospital readmission and mortality in patients with heart failure. According to estimates, 1 in every 5 patients with heart failure has clinical depression.[5] In one study,[3] approximately 60% of patients with heart failure who had major depressive symptoms were readmitted to the hospital within 1 year of discharge for an exacerbation of heart failure. Patients with heart failure who had depressive symptoms had a 3 times greater risk for readmission and a 2 times greater risk for death within 1 year than did heart failure patients without depressive symptoms.[3]

Social support is another important predictor of survival among patients with coronary heart disease (CHD).[6-8] Positive social support is associated with improved quality of life[9,10] in patients with heart failure, whereas poor social support or lack of such support is associated with increased readmission and mortality.[11-13] Having a spouse often is an indication of the highest available level of social support because spousal caregivers typically live with the patients and provide long-term commitment with continual face-to-face contact. Most studies of social support have focused on subjectively perceived social support or the availability of social support[10,14,15]; relatively few have examined the effects of single marital status, which is often an indicator of poor spousal support or no spousal support.[16] Chin and Goldman[16] followed up 257 patients hospitalized with heart failure and found that single patients had a 2.1 times higher risk for readmission or death within 60 days than married patients did. Although social support decreases risk of readmission and mortality among patients with heart failure, it is unknown whether having a spouse has a positive effect on survival in patients with depressive symptoms.

Social support or marital status might affect outcomes in depressed patients in 2 ways: (1) social support or being married buffers the distress of depression and improves outcomes or (2) social support or marital status has a direct effect on depression and/or outcomes. In the buffering model, social support or marital status protects patients from the potentially harmful influences of depression.[17,18] In the main-effect model, social support or marital status is beneficial in improving outcomes despite the stress of depression; this model has no statistical interaction effects between social support and depression.[19] In 2 recent studies,[7,8] a potential buffering effect of perceived social support on cardiac mortality after acute myocardial infarction (AMI) in patients without depressive symptoms was noted. However, this finding cannot be generalized to patients with heart failure. On the basis of our previous research, we hypothesized that marital status plays a direct role and thus supports the main-effect model.

Depressive symptoms are an independent risk factor for hospital readmission.

Therefore, the purpose of this study was to determine the effect of marital status on event-free survival in patients with heart failure who did or did not have depressive symptoms. The specific aims were as follows:

- To examine whether depressive symptoms and marital status are independent predictors of event-free survival in patients with heart failure
- To determine if depressive symptoms and

About the Authors
Misook L. Chung is an assistant professor, **Jia-Rong Wu** is a postdoctoral fellow, and **Rebecca L. Dekker** is a doctoral student in the College of Nursing, **Terry A. Lennie** is director of the doctoral program and codirector of the RICH Heart Program, College of Nursing and Graduate Center for Nutritional Sciences, and **Debra K. Moser** is a professor and holder of the Gill Endowed Chair and codirector of the RICH Heart Program at the University of Kentucky, Lexington, Kentucky. **Barbara Riegel** is a professor in the School of Nursing at the University of Pennsylvania, Philadelphia.

Corresponding author: Misook L. Chung, RN, PhD, College of Nursing, University of Kentucky, 529 CON, 760 Rose St, Lexington, KY 40536-0232 (e-mail: misook.chung@uky.edu).

marital status have an interactive effect on event-free survival

- To compare the effect of marital status on event-free survival between patients with and without depressive symptoms
- To determine whether marital status is an independent predictor of event-free survival after adjustments are made for depressive symptoms

In one study, singles had 2 times the risk for readmission or death compared to married patients.

Methods

The study was prospective and longitudinal. Patients with heart failure were followed-up for up to 4 years after assessment of depressive symptoms to collect data on death and hospitalization. Patients were included if they had a confirmed diagnosis of chronic heart failure, had no history of AMI within the preceding 3 months, and had no adjustments in dose of heart failure medications in the preceding 3 months. Patients were excluded if they had heart failure due to a valvular or peripartum cause, were referred for heart transplantation, had a terminal illness such as cancer, or had poorly controlled diabetes or end-stage liver or renal disease. Patients were recruited from outpatient clinics, including an academic medical center in central Kentucky.

Three major prospective studies were conducted simultaneously with the same inclusion and exclusion criteria as part of the research profile of the Research and Intervention for Cardiopulmonary Health (RICH) Heart Program at the College of Nursing, University of Kentucky, in Lexington.

Patients with depressive symptoms had worse functional status than patients without depressive symptoms.

Trained research nurses screened medical charts for all 3 studies. After review of the 1472 medical charts for January 2004 to December 2006, a total of 671 patients (45.6%) were ineligible. Of the 801 eligible patients, 274 (34.2%) immediately refused to participate, and 240 considered participating but ultimately did not. Therefore, 259 patients (32.3%) participated in 1 of the 3 studies in the RICH Heart Program. In the study reported here, 166 unique patients were included; patients who participated in more than 1 study during the study period were excluded. This participation rate is similar to that of other studies of patients with heart failure, especially when older patients are recruited.[20]

Measures

Depressive symptoms were assessed by using the Beck Depression Inventory-II (BDI-II). The BDI-II is a well-established instrument with a total of 21 items rated on a scale of 0 to 3.[21-24] The total score can range from 0 to 63. Patients who score 14 or higher are considered to have depressive symptoms.[22] A higher total score indicates more severe depressive symptoms. The BDI-II is a valid and reliable instrument, and it has been used to predict mortality and hospitalizations in CHD patients and patients with heart failure.[4,7,25,26] The reliability of this instrument was acceptable; the Cronbach α was 0.88 in this study.

Marital status was assessed via patient interviews. Data on marital status were initially collected in 5 categories: married, single, widowed, divorced, and cohabitated. This variable was dichotomized into married and nonmarried groups. The unmarried group consisted of single, widowed, and divorced patients. The married group included married and cohabitating patients.

The outcome variable was event-free survival. A combined end point of mortality or all-cause hospitalization, defined as the duration in days from baseline assessment to the first hospitalization or death due to any cause, was used. Date and reasons for hospitalization and death were determined by reviewing hospital records, making monthly follow-up telephone calls, and obtaining death certificates.

Patients' demographic (sex, age, ethnicity, marital status, education, income) and clinical (left ventricular ejection fraction, medications, comorbid conditions, New York Heart Association [NYHA] class) characteristics were collected by reviewing medical charts with a structured questionnaire. Education levels were categorized into 2 groups ($\leq$ high school diploma and $>$ high school). Financial status was assessed by using a single item on how well the household lived on the income available and was rated on 3-point Likert scale (1 = having more than enough to make ends meet, 2 = having enough to make ends meet, and 3 = not having enough to make ends meet).

Procedure

After approval of the study by the appropriate institutional review board, trained nurse researchers from the RICH Heart Program confirmed the eligibility of patients who were referred to the study by doctors or nurse practitioners by screening medical charts that included approval of a waiver for the Health Insurance Portability and Accountability Act. Eligible patients were contacted at their clinic visit

or by telephone. Trained nurse researchers explained the studies to eligible patients and obtained signed informed consent and compliance with the Health Insurance Portability and Accountability Act. Participating eligible patients were helped to complete the study questionnaire; the questionnaire was read to patients who had difficulty reading.

After completion of questionnaires, patients were asked to record their hospitalization history in a log book. They were also informed that they would receive monthly follow-up telephone calls for 1 year. History of rehospitalization was collected via monthly follow-up telephone calls for 1 year, but chart reviews were continued to obtain data on hospitalization for up to 4 years. A trained research nurse identified and validated all causes of readmission and death by using hospital records, interviews with health care providers and patients' family members, death certificates, and review of county death records.

Data Analysis

Patients were grouped into those with (n = 55) and those without (n = 111) depressive symptoms and into groups of married (n = 93) and nonmarried (n = 73). Kaplan-Meier survival analysis with a log rank test was used to compare overall survival time with the combined end point of mortality or hospitalization between patients with and without depressive symptoms, between married and nonmarried patients, and between married and nonmarried patients who were stratified according to the presence or absence of depressive symptoms. Cox proportional hazard regression modeling was used to examine the interaction effect of depressive symptoms and marital status, with controls for age, sex, education, and financial status. The Cox proportional hazard regression was also used to predict outcomes based on having a spouse, with controls for age, sex, education, financial status, NYHA class, ejection fraction, and depressive symptoms. SPSS version 15.0 (SPSS, Inc, Chicago, Illinois) was used for all analyses.

A power analysis was conducted before data collection. With a significance level of .05 and at least 90 patients in each depressive symptoms group, the power of the log rank test to detect a significant difference in the combined end-point distribution between the 2 subgroups was at least 74% if the group without depressive symptoms had a 25% reduction in the combined end point relative to the group with depressive symptoms. With the addition of covariates in the Cox proportional hazards model, the power of the regression to detect significant differences between groups was greater than the power for the corresponding log-rank test. Power estimates were obtained by using nQuery Advisor.[27]

Results

Patients' Characteristics

A total of 166 patients with heart failure participated in this study. The mean age was 61 years (SD, 11.4), and 69% were men. Most patients (86%) were white. Mean ejection fraction was 35% (SD, 14.9), and 62% of patients were classified as NYHA class III or IV.

A total of 33% of patients had depressive symptoms (BDI score >13). Patients who had depressive symptoms were more likely to be younger, less educated, less comfortable given their finances, and to take antidepressants than were those without depressive symptoms (Table 1). Patients with depressive symptoms also had worse functional status than did patients without depressive symptoms (NYHA class III-IV 83% vs 50%; $P < .001$).

There was no difference in prevalence of depressive symptoms between married and nonmarried patients.

Approximately half of the patients (56%) were married. Married patients were more likely to be male and more comfortable with their finances than were nonmarried patients (Table 1). Levels of depressive symptoms were similar between married and nonmarried patients (10.9 vs 12.1; $P = .39$).

The prevalence of depressive symptoms did not differ between married and nonmarried patients (32% vs 34%; $P = .09$). Clinical characteristics (ischemic cause, ejection fraction, and comorbid conditions) of married patients were also similar to those of nonmarried patients (Table 1).

Follow-up Information

No attrition of patients in the study occurred during the follow-up period. A total of 16 deaths (10%) and 41 (25%) hospital readmissions due to a cardiac reason occurred. The percentage of patients rehospitalized was higher in depressed patients than in nondepressed patients (42% vs 16%; $P < .001$), but the death rate did not differ between depressed and nondepressed groups. Married and nonmarried patients had similar death rates and rates of cardiac hospitalization (Table 1).

Marital status is an independent predictor of patients' mortality and morbidity with or without depressive symptoms.

Event-Free Survival

Kaplan-Meier analysis revealed that the time to first cardiac event (death or hospital readmission

Table 1
Characteristics of patients by depressive symptoms and marital status[a]

Characteristic	Depressed (n = 55)	Nondepressed (n = 111)	*P*	Married (n = 93)	Nonmarried (n = 73)	*P*
Age, mean (SD), y	57.8 (10.0)	62.4 (11.7)	.01	61.1 (11.3)	60.6 (11.6)	.79
Male sex	67	69	.46	82	52	<.001
Education ≤ high school	64	44	.03	49	53	.68
Finance, % of patients			<.001			.02
Have more than enough	9	33		33	17	
Have enough	55	52		52	54	
Have not enough	36	14		15	29	
Married	54	57	.46	–	–	–
Depressive symptoms, mean (SD)	21.8 (7.5)	6.4 (3.7)	<.001	10.9 (8.4)	12.2 (9.6)	.39
Ischemic cause	52	61	.31	42	43	>.99
Previous bypass surgery	30	34	.37	40	25	.47
Diabetes	43	46	.65	43	48	.53
Chronic obstructive pulmonary disease	26	11	.01	14	18	.67
Prior myocardial infarction	62	53	.19	57	54	.44
Ejection fraction, mean (SD), %	36.9 (16.1)	34.1 (14.3)	.26	33.7 (13.3)	36.9 (16.6)	.18
New York Heart Association class III or IV	83	50	<.001	58	66	.41
Antidepressant use	37	19	.02	20	32	.10
Implantable cardioverter defibrillator	49	38	.16	48	32	.05
Body mass index,[b] mean (SD)	31.8 (8.1)	31.7 (7.3)	.92	32.3 (7.6)	30.9 (7.5)	.23
Death	11	9	.78	8	12	.43
Cardiac hospitalization	42	16	<.001	20	32	.08
All-cause hospitalization	60	29	<.001	30	51	.01

[a] Values are percentages of patients unless otherwise specified.
[b] Calculated as weight in kilograms divided by height in meters squared.

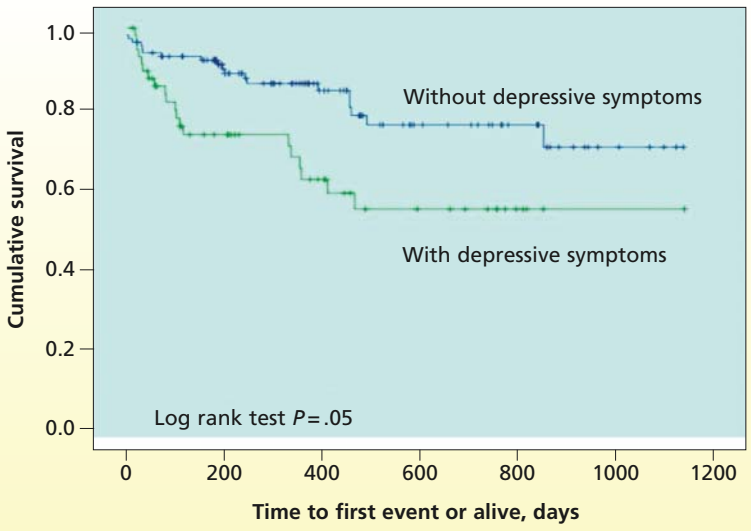

Figure 1 Event-free survival according to depressive symptoms.

due to cardiac reasons) was longer in patients without depressive symptoms (log rank test, $P = .05$) than in patients with depressive symptoms. As indicated in Figure 1, at 2 years' follow-up, approximately 70% of patients without depressive symptoms were event-free, whereas only 50% of patients with depressive symptom were event-free.

Married patients experienced longer event-free survival than did nonmarried patients (log rank test, $P = .009$). As illustrated in Figure 2, the difference in event-free survival rate between married and nonmarried patients increased during the first year of follow-up but increased dramatically between 12 months and 18 months. The event-free survival rate in married patients was 40% better than the event-free survival rate in unmarried patients at 18 months of follow-up.

When we compared survival curves for married and nonmarried groups stratified by presence or absence of depressive symptoms, married patients

experienced longer event-free survival than did nonmarried patients regardless of the presence or absence of depressive symptoms (Figure 3; log rank test, $P = .01$).

Kaplan-Meier analysis also showed that time to first event (death or hospital readmission due to cardiac or noncardiac reasons) was longer in patients without depressive symptoms (log rank test, $P = .004$) than in patients with depressive symptoms and longer in married patients than in nonmarried patients (log rank test, $P = .001$). Event-free survival was longer in married patients than in nonmarried patients when depressive symptoms were stratified (log rank test, $P = .001$).

In a Cox proportional hazard regression model, when we controlled for age, sex, education, financial status, ejection fraction, and NYHA class, both depressive symptoms and marital status remained independent predictors of event-free survival without showing a significant interaction effect (Table 2). Patients with depressive symptoms were 3.68 times more likely to experience death or rehospitalization than were patients without depressive symptoms ($P = .008$). Patients who were not married were 3.86 times more likely to have such an event than were married patients ($P = .001$).

Even when we controlled for depressive symptoms and other covariates, marital status remained an independent predictor of event-free survival (odds ratio, 2.48; 95% confidence interval, 1.38-4.43; Table 3).

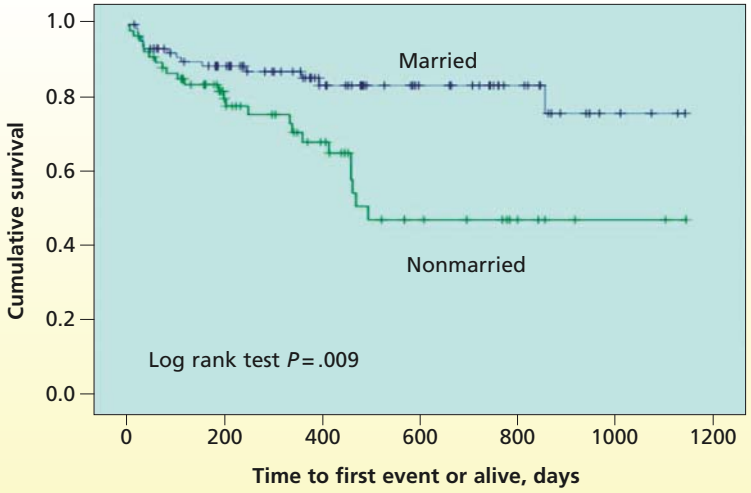

Figure 2 Event-free survival according to marital status.

Discussion

We found that depressive symptoms in patients with heart failure were an independent predictor of death or hospital readmission due to cardiac causes. This finding is consistent with previous reports that depressive symptoms are predictive of mortality and morbidity in patients with heart failure.[3,4] We also found that marital status, which reflects an aspect of social support, was an independent predictor of patients' morbidity and mortality. This finding is comparable to the results of previous research indicating that measures of social support are predictive of prognosis in heart failure.[6-8]

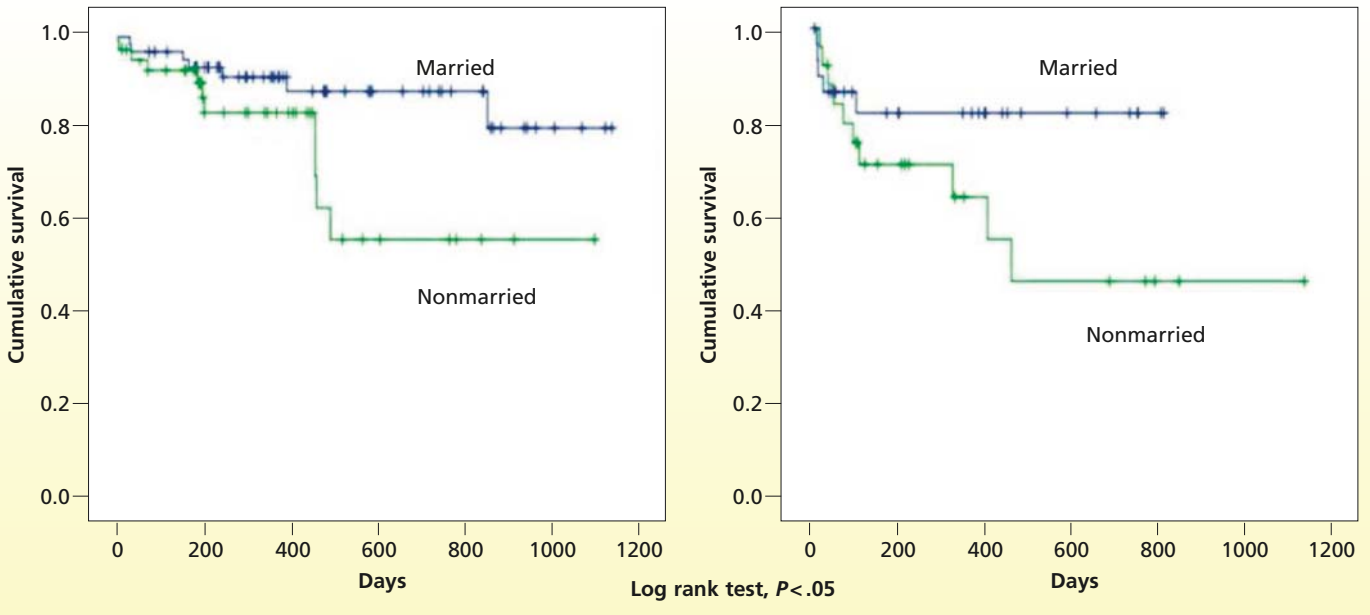

Figure 3 Event-free survival according to marital status with (left) and without (right) depressive symptoms.

Table 2
Cox regression of survival onto depressive symptoms and marital status[a]

Step	Predictors	Odds ratio	95% Confidence interval	P
1	Age	1.01	0.98-1.04	.54
	Female sex	1.47	0.80-2.69	.22
	Education ≤ high school	0.82	0.46-1.44	.48
	Finance			
	Having enough	0.59	0.28-1.23	.16
	Not having enough	0.89	0.38-2.10	.80
	Ejection fraction	0.98	0.97-1.00	.06
	New York Heart Association class			
	III	1.17	0.60-2.26	.65
	IV	0.99	0.43-2.25	.97
2	Depressive symptoms	3.68	1.40-9.69	.008
	Nonmarried	3.86	1.76-8.48	.001
	Depressive symptoms × marital status	0.37	0.12-1.15	.09

[a] This is the final step of the Cox regression (full model $\chi^2 = 16.8$, $P = .006$).

Table 3
Cox regression of survival onto marital status with depressive symptoms controlled for[a]

Step	Predictors	Odds ratio	95% Confidence interval	P
1	Age	1.01	0.98-1.04	.48
	Female sex	1.40	0.77-2.55	.28
	Education ≤ high school	0.90	0.51-1.58	.90
	Finance			
	Having enough	0.60	0.28-1.28	.18
	Not having enough	1.05	0.47-2.46	.91
	Ejection fraction	0.99	0.97-1.00	.10
	New York Heart Association class			
	III	1.13	0.58-2.18	.72
	IV	1.03	0.45-2.36	.95
2	Depressive symptoms	1.96	1.01-3.81	.05
3	Nonmarried	2.48	1.38-4.43	.002

[a] This is the final step of the Cox regression (full model $\chi^2 = 9.6$, $P = .002$).

The finding that depressive symptoms or low social support in CHD are associated with increased risk for poor outcomes is not novel. However, studies[7,8,11] on the effect of depressive symptoms and social support simultaneously in patients with CHD or heart failure are rare. In 2 studies,[7,8] the findings suggested that perceived social support may attenuate cardiac mortality related to depressive symptoms after AMI. In a 1-year follow-up of 887 patients with AMI, Frasure-Smith et al[7] found that depressive symptoms increased the risk of cardiac mortality in patients with low levels of perceived social support but not in patients with high levels of perceived social support. Moreover, perceived social support or other measures of social support alone were not predictive of the risk for cardiac mortality. In 2481 patients with myocardial infarction in the Enhancing Recovery in Coronary Heart Disease (ENRICHD) study who were followed up for up to 4.5 years, Lett et al[8] found that higher levels of perceived social support were associated with improved survival rates for patients without elevated depressive symptoms but not for patients with a high level of depressive symptoms. Neither perceived tangible support nor network support was associated with cardiac mortality in the ENRICHD trial. These 2 studies[7,8] suggest that although perceived social support was not predictive of cardiac mortality independently, perceived social support might play a buffering role in preventing cardiac mortality in patients with AMI.

On the other hand, social isolation was an independent predictor of mortality in patients with heart failure. Friedmann et al[11] reported that both social isolation and depressive symptoms were independent predictors of mortality in patients with heart failure but did not examine the interaction between depressive symptoms and social isolation. In our study, the most important finding was that marital status was an independent predictor of mortality and morbidity outcome irrespective of whether patients did or did not have depressive symptoms. The interaction between depressive symptoms and marital status was not a significant predictor of event-free survival in our study. Furthermore, marital status was as predictive of event-free survival as were depressive symptoms when confounding variables were controlled for. Our results indicate that in patients with heart failure, marital status has a main or direct effect on outcomes rather than a buffering effect.

Inconsistent or discrepant evidence that social support influences outcomes in the context of depressive symptoms in previous CHD studies may be due to use of different measures of social support. Social support has been conceptualized as social networks, social relationships, and resources from different types of support. Measures of social support range from objective (eg, counting numbers of support people) to subjective (eg, self-report on perception or experience of likelihood of receiving help from others) indicators. Social support has also been defined as a structural construct meaning living alone or not or marital status. We attempted to consider social support in its structural aspects by

defining it as having a spouse or partner who generally is the primary support system. Although we do not know the types of support (emotional, instrumental, or functional) or the quality of support provided by spouses in this study, the data suggest that spouses played a pivotal role in contributing to a reduction in the risks for rehospitalization and mortality. Further investigations are needed to examine the effects of various types of support or social support intervention on patients' outcomes.

Although we found that having a spouse or partner was a predictor of better outcomes, our study is limited because we did not investigate the quality of the marital relationship. Marital quality is a potential factor that may affect the buffering ability of social support. Murburg et al[28] found that a poor intimate network support (ie, spousal support) was directly associated with patients' increases in depressive symptoms. Coyne et al[29] also reported that heart failure patients with high marital quality survived longer than did patients with low marital quality. Further examination of these relationships is needed.

Our findings have several implications. First, health care providers should assess each patient's marital status and the primary support source in the patient's family to detect patients at higher risk for poor outcomes. In the United States, currently more than 5 million patients have heart failure, and most of them could benefit from the support of a spouse, family member, or significant other as they cope with living with a chronic syndrome and engage in self-management. In a nationally representative cohort study[30] of adults 65 years or older, 42% of older adults with heart failure received informal home care, and 13% received formal care. The need for informal and formal care in adults with heart failure was 3 times higher than the need for those who had CHD without heart failure. However, patients with heart failure were less likely to have spousal caregivers than were older adults with or without CHD (47.5% vs 56.4% vs 55.2%, respectively). Thus, more than half of patients with heart failure are likely to have an inadequate support system for self-management of heart failure.

Second, interventions need to be developed that address the specific needs of nonmarried patients, particularly patients with depressive symptoms. Interventions to improve depressive symptoms in patients with CHD, including pharmacotherapy and nonpharmacological interventions (eg, cognitive behavioral therapy), can lead to an improvement in the symptoms.[31] The ENRICHD trial is the only study designed to decrease depressive symptoms and improve social support by using cognitive behavioral therapy.[32] The intervention in the ENRICHD trial was effective in improving depressive symptoms and social isolation, but it did not reduce mortality and recurrent infarction in patients with a previous AMI. Recently, intervention programs such as peer mentor support have been developed to improve or enhance social support in patients with heart failure.[33,34] No intervention has been developed to improve both social support and depressive symptoms in patients with heart failure. Identifying and reinforcing current social support networks is helpful to improve adherence behaviors of patients who are not married. Electronic support, such as telephone and computer-based social support interventions, are an alternative support resource, although using these resources successfully may depend on affordability and patients' competence in using technology.

Conclusion

This study was the first one on the effect of marital status in the context of depressive symptoms on cardiac hospitalization and mortality of patients with heart failure. We found that lack of a spouse was a strong predictor of poor outcomes in patients with heart failure. This finding contributes to understanding the pivotal role of spouses in improving outcomes in patients with heart failure, particularly patients who have depressive symptoms.

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SEE ALSO

For more about heart failure, visit the *Critical Care Nurse* Web site, **www.ccnonline.org**, and read the article by Thomas et al, "Depression in Patients With Heart Failure: Prevalence, Pathophysiological Mechanisms, and Treatment" (April 2008).

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