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Medication Adherence, Social Support, and Event-Free Survival in Patients with Heart Failure

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Abstract

Background—Medication adherence and perceived social support are independent predictors of mortality in patients with heart failure (HF). However, the predictive power of the combination of medication adherence and perceived social support for hospitalization and death has not been investigated in patients with HF.

Objective—To explore the combined influence of medication adherence and perceived social support for prediction of cardiac event-free survival in patients with HF.

Method and Results—A total of 218 HF patients monitored medication adherence for 1-3 months and completed the Multidimensional Perceived Social Support Scale (MPSSS) at baseline. Medication adherence was measured using a valid and objective measure, Medication Event Monitoring System (MEMS). Patients were followed for up to 3 1/2 years to collect data about cardiac event-free survival (i.e., cardiac emergency department visits, hospitalizations, and death). To test the association of the combination of medication adherence and perceived social support with outcomes, first, the interaction term of medication adherence and perceived social support was entered in a Cox regression to predict outcomes. Second, patients were grouped using an evidence-based cut-point of 88% for medication adherence from the MEMS data and a median score 71 of the MPSSS. Kaplan-Meier and Cox proportional hazards models were used to

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compare cardiac event-free survival among groups. Medication adherence and perceived social support were independent predictors of cardiac event-free survival (p = .006 and .021, respectively). Patients with medication nonadherence and lower PSS had a 3.5 times higher risk of cardiac events than those who were adherent and had higher PSS.

Conclusion—Medication adherence mediated the relationship between perceived social support and cardiac event-free survival in this sample. Moreover, medication adherence and social support independently, and in combination, predicted cardiac event-free survival in patients with HF. Interventions to improve clinical outcomes should address both medication adherence and social support.

INTRODUCTION

Heart failure (HF) is a chronic condition that requires patients to consistently adhere to their prescribed medications to prevent exacerbations that lead to emergency department (ED) visits, hospital admissions, or death (Chin & Goldman, 1997b; Chui et al., 2003; Happ, Naylor, & Roe-Prior, 1997; Joshi, Mohanan, Sengupta, & Salkar, 1999; Li, Morrow-Howell, & Proctor, 2004; Miura et al., 2001). Social support has been widely studied in many conditions and is an important factor that contributes to physical and mental health (DiMatteo, 2004). There are two main types of social support: structural (e.g., marital status, living arrangement) and functional (e.g., practical/instrumental, emotional, family cohesion) social support (DiMatteo, 2004). Patients with HF need effective social support to help them adhere to their prescribed medications, keep their health care provider appointments, refill prescriptions, and in some instances, administer the medications (DiMatteo, 2004; Riegel, et al., 2009; Sayers, Riegel, Pawlowski, Coyne, & Samaha, 2008; Wu, et al., 2008). Without adequate social support, patients with HF are likely to fail to adhere to their medication prescriptions (DiMatteo, 2004; Riegel, et al., 2009; Sayers, et al., 2008; Wu, Moser, Lennie, et al., 2008).

Hospitalization and mortality rates are higher in HF patients with lower social support compared to patients with higher social support (Burg, et al., 2005; Chin & Goldman, 1997a; Happ, et al., 1997; Krumholz et al., 1998; Lofvenmark, Mattiasson, Billing, & Edner, 2009; Luttik, Jaarsma, Moser, Sanderman, & van Veldhuisen, 2005; Schwarz & Elman, 2003; Tsuchihashi-Makaya, Kato, Chishaki, Takeshita, & Tsutsui, 2009; Vinson, Rich, Sperry, Shah, & McNamara, 1990; Wright, et al., 2003). Luttik et al. (2005) reviewed studies published from 1993 to 2003 of the relationship between social support and hospitalization and death and found that lower social support was related to more hospital readmissions and deaths. In a prospective study, Tsuchihashi-Makaya et al. (2009) followed 139 patients with HF for 12 months and found that patients with lower social support had a significantly higher rate of HF-related readmissions than those with higher social support. In prior studies, medication adherence independently predicted emergency department visits, hospitalizations, and death in patients with HF (Ambardekar, et al., 2009; Annema, Luttik, & Jaarsma, 2009; Chui, et al., 2003; Cole, Norman, Weatherby, & Walker, 2006; Esposito, Bagchi, Verdier, Bencio, & Kim, 2009; Granger et al., 2005; Li, et al., 2004; Miura, et al., 2001; Murray et al., 2009; Murray et al., 2007; Sun, Ye, Lee, Dupclay, & Plauschinat, 2008; Wu, Moser, Chung, & Lennie, 2008). However, the power of the combination of medication adherence and perceived social support for prediction of cardiac event-free survival has not been previously investigated in patients with HF. Accordingly; the purpose of this study was to explore the predictive power of the combination of medication adherence and perceived social support for cardiac event-free survival in patients with HF.

METHODS

Study Design

This was secondary data analysis using data from two prospective, longitudinal studies in which medication adherence was measured using the MEMS. Patients with HF were followed to collect data about cardiac events (ED visits, hospitalizations, and deaths) (Wu, Corley, Lennie, & Moser, 2012; Wu, et al., 2008). Both studies used identical inclusion and exclusion criteria; all patients were recruited from an academic medical center in one Southern state. In the current study, we explored the association of the combination of medication adherence and perceived social support with cardiac even-free survival in patients with HF.

Procedure

Both studies received approval from the appropriate Institutional Review Boards. A trained research nurse confirmed patient eligibility, explained study requirements to eligible patients, and all patients provided written, informed consent.

Patient sociodemographic and clinical characteristics were collected by interview and medical record review at baseline. After completion of the baseline assessment, detailed written and verbal instructions about the use of the MEMS bottle were then given to patients. Patients were instructed to take the specified medicine from the MEMS bottle and to close the cap after each use. A MEMS diary was given to patients to record unscheduled MEMS cap openings (defined as all cap openings unrelated to taking medications, such as refill without taking medications).

Patients returned the MEMS bottle after one or three months of daily use of the MEMS device. The MEMS data were downloaded to a personal computer and transferred into a database for analysis. Unscheduled cap openings were excluded from analysis based on the MEMS diary recorded by patients. Outcome data about ED visits, hospitalizations and death were collected for up to 3.5 years.

Samples and Setting

Patients enrolled in this study were recruited from outpatient cardiology clinics and inpatient cardiology units. We recruited patients who had a confirmed diagnosis of chronic HF and were prescribed stable doses of HF medications. Patients who had a myocardial infarction or stroke within 3 months, obvious cognitive impairment, were discharged to a skilled nursing facility, or were diagnosed with a co-existing terminal illness were excluded.

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Measurement of Variables

Independent variable

Medication adherence: Medication adherence was measured daily for 1-3 months (3 months for the first study and 1 month for the second study) using a microelectronic medication monitoring device (MEMS, AARDEX®-USA, Union City, CA). The MEMS recorded the date and time of each cap opening. MEMS data were collected for one prescribed HF medication with priority given to medications taken twice a day. The medication chosen for monitoring using the MEMS was selected in the following order: beta-adrenergic antagonist agent, angiotensin-converting-enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), aldosterone antagonist, digoxin, or a diuretic. Medication adherence from the MEMS was defined as the percentage of days the correct number of doses was taken during the monitoring period (Chung et al., 2008). Patients who took the correct number of doses on at least 88% of days were categorized as adherent; all others were categorized as nonadherent. This cutpoint was chosen based on a recent study demonstrating that adherence at or above 88% predicted better event-free survival (Wu, et al., 2009).

Perceived social support: Perceived social support (PSS), subjective self-reported perceived social support from family, friends, or others, was measured using the Multidimensional Perceived Social Support Scale (MPSSS) (Canty-Mitchell & Zimet, 2000; Picardi et al., 2005). The MPSSS consists of 12 items rated using a 7-point Likert scale from 1 (very strongly disagree) to 7 (very strongly agree). The instrument is scored by adding the item ratings. The total score can range from 12 to 84, with higher scores reflecting higher levels of perceived social support from family, friends, or significant others. The MPSSS is a reliable and valid instrument (Canty-Mitchell & Zimet, 2000; Picardi, et al., 2005). Internal consistency reliability of the MPSSS for this study was demonstrated by a Cronbach's alpha of .85.

Outcome variable—The outcome variable was the composite end-point of time to the first occurrence of one of the following events: cardiac ED visits, cardiac hospitalizations, and cardiac mortality (i.e., cardiac event-free survival). Patients were followed for up to 3 1/2 years to collect data about cardiac events by patient/family interview, and confirmed by medical records and/or death certificates. The date and reasons for ED visits, hospitalization and death were captured by a research assistant.

Variables of interest

Demographics: Age, gender, ethnicity, and whether the patient lived alone or not were collected as demographic factors by patient interview and medical record review.

Clinical variables: Left ventricular ejection fraction (LVEF), New York Heart Association (NYHA) functional class, functional status, body mass index (BMI), history of hypertension and diabetes, presence of depressive symptoms, angiotensin-converting enzyme inhibitor (ACEI) use, and beta-antagonist use were collected as clinical variables to characterize/compare patients by groups. NYHA class was assessed by careful patient interview and was based on how patients were able to perform their daily activities related to HF symptoms

(Mills & Haught, 1996). Functional status was measured using the Duke Activity Status Index (DASI). The DASI consists of 12 items. The total score can range from 0 to 58.2, with higher scores indicating better functional status. The DASI is a reliable and valid questionnaire (Parissis, et al., 2009). In this study, Cronbach's alpha was .83.

Depressive symptoms are an important and well-known factor associated with increased morbidity and mortality (Carney, Freedland, Miller, & Jaffe, 2002; Macchia, et al., 2008; Okonkwo, Sui, & Ahmed, 2007). In this study, depressive symptoms were included as a potential confounder in the Cox regression modeling and were measured using the Patient Health Questionnaire-9 (PHQ-9) (Ackermann, et al., 2005; Kroenke, Spitzer, & Williams, 2001). The PHQ-9 consists of nine items on a scale rated from 0 (not at all) to 3 (nearly every day). Total scores of the PHQ-9 can range from 0 to 27; higher scores indicate worse depressive symptoms. The PHQ is a reliable (Kroenke, et al., 2001) and valid (Ackermann, et al., 2005; Kroenke, et al., 2001) scale that has been used to measure depression level in patients with HF (Ackermann, et al., 2005). In this study, Cronbach's alpha was .83.

Patient LVEF, history of hypertension and diabetes, ACEI use and beta-antagonist use were abstracted from the medical record or collected by patient interview. BMI was calculated as weight (kg)/height (m^2).

Data Management and Analysis

All data analyses were performed using SPSS (Chicago, IL), version 18.0; a *p* value of .05 indicated significance. Patient characteristics were summarized using means and standard deviations or frequency distributions. Differences in demographic and clinical variables between the two studies were assessed with independent t-tests or chi-square tests of association based on the level of measurement.

We conducted the analyses with medication adherence and perceived social support as continuous variables. First, we tested whether medication adherence was a mediator between perceived social support and cardiac events following the steps outlined by Baron et al. (Baron & Kenny, 1986; Bennett, 2000; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002; MacKinnon, MacKinnon, & Dwyer, 1993). Second, we entered the interaction term of medication adherence and perceived social support into a Cox proportional hazards regression model to predict cardiac event-free survival from the combination of medication adherence and perceived social support in patients with HF.

Following these analyses, an evidence-based cutpoint of 88% medication adherence for the monitored time using the MEMS (Wu, et al., 2009) was used to categorize patients into adherent and nonadherent groups. Patients were also categorized as higher or lower social support groups based on the median score of the MPSSS (71); the median score was used because there is no established cutpoint for this scale. Based on these categories, patients were divided into 4 groups: (1) medication adherent with higher PSS; (2) medication adherent with lower PSS; (3) medication nonadherent with higher PSS; and (4) medication nonadherent with lower PSS. Log-rank tests were used to compare the time to cardiac event-free survival between patients in medication adherent and nonadherent groups, in lower and higher PSS patients, and among the four groups defined by combinations of adherence and

PSS. Kaplan-Meier plots and log-rank tests were used to depict and test for group differences in cardiac event-free survival. Cox proportional hazards regression modeling was used to assess the time to cardiac event-free survival among these four groups with and without adjusting for the following potential confounding variables: age, gender, ethnicity, living status, NYHA functional class, and depressive symptoms. To account for potential differences between the two studies, we also controlled for study group in the final regression model.

RESULTS

Patient Characteristics

A total of 218 patients with HF and complete MEMS data were included in the analysis. The mean age and standard deviation of the patients was 60 ± 12 years; about two thirds of patients were male and more than half had advanced HF (NYHA class III or IV) with an average LVEF of 36 ± 14%. The majority of the patients were Caucasians (85%) who lived with another person (74%). In Table 1, the baseline characteristics of patients recruited in study 1 ($n = 136$) and study 2 ($n = 82$) were compared. The percentage of patients who were in NYHA Class III/IV HF was 60% for the study 1 and 50% for the study 2 ($p = .04$) and there were fewer minority patients in study 1 (10% vs. 22%, $p = .03$). No other demographic and clinical characteristic differed between the two study groups.

When we compared the characteristics of the 4 patient groups stratified by medication adherence and perceived social support, there were significant differences in living status and depressive symptoms among groups (Table 2). Patients who reported higher perceived social support tended to live with others compared with those who had lower perceived social support ($p = .001$). Patients who were medication adherent and had higher perceived social support also reported fewer depressive symptoms compared with those in the other three groups. No other demographic and clinical characteristic differed among the four study groups.

Medication Adherence

Comparisons of medication adherent vs. non-adherent and high vs. low PSS groups are presented in Table 3. The mean of medication adherence (percentage of days the correct number of doses taken) was 83 ± 21%. Of the total sample, 129 (59%) were classified as adherent to prescribed HF medication, while 90 patients (41%) were nonadherent (cutpoint 88%). Patients with medication nonadherence reported more depressive symptoms ($p = .01$) than those who were adherent.

Perceived Social Support (PSS)

The mean score of the MPSSS was 66.9 ± 19.5 and the median was 71, indicating moderately high PSS. Patients with lower social support were more likely to live alone ($p < .001$), to be a non-Caucasian minority ($p = .04$), and to have more depressive symptoms ($p = 0.2$). Medication adherence rate was similar between higher and lower PSS groups. No age or gender differences between higher and lower PSS groups were found.

Medication Adherence and Cardiac Event-free Survival

During the follow-up period, 5 (2%) patients died due to cardiac reasons and 48 (21%) were hospitalized due to HF or other cardiovascular-related diagnoses. There were no differences in cardiac mortality between medication nonadherent and adherent patients (1% vs. 2%, p =. 6). Cardiac hospitalizations were significantly greater in medication nonadherent patients compared to adherent patients (30% vs. 15%, p = .01). Kaplan-Meier analysis demonstrated that the composite endpoint of cardiac event-free survival was significantly shorter in nonadherent patients than in adherent patients (744 days vs. 930 days, p = .006). In a simple Cox proportional hazards model (without adjusting for covariates), patients who were medication nonadherent had 2.09 times the risk of experiencing a cardiac event than patients who were adherent (Table 4). While the effect size of the group comparison for the Cox proportional hazards model is not directly estimable, the observed hazard ratio associated with the corresponding log-rank test was 1.88 (Elashof, 1995-2005; Schoenfeld, 1983). For the Cox proportional hazards model, the observed hazard ratio for the same group effect increased to 2.09, consistent with the expected increased power of this regression to detect a significant group difference relative to the log-rank test (Elashof, 1995-2005; Schoenfeld, 1983).

Perceived Social Support and Cardiac Event-free Survival

There were no differences in cardiac mortality between patients with lower PSS and higher PSS (3% vs. 2%, p = .5). Cardiac hospitalizations were significantly greater in patients with lower PSS compared to patients with higher PSS (25% vs. 17%, p = .03). In Kaplan-Meier analysis, the composite endpoint of cardiac event-free survival was significantly shorter in patients with lower PSS patients than in those with higher PSS (731 days vs. 947 days, p = . 02). In a simple Cox regression model, patients who had lower PSS had 1.89 times the risk of experiencing a cardiac event than those patients who had higher PSS (Table 4). The observed hazard ratio for the log-rank group comparison was 1.75; this increased to a hazard ratio of 1.89 for the group comparison within the Cox regression model.

Perceived Social Support, Medication Adherence, and Cardiac Event-free Survival—Mediation Model

In a series of regression models and Cox-survival analyses with medication adherence and perceived social support analyzed as continuous variables, medication adherence mediated the relationship between perceived social support and cardiac event-free survival based on the following sequence of regression analyses. First, in Path A (Figure 1), perceived social support independently predicted medication adherence (p = .008). Second, in Path B, medication adherence predicted cardiac event-free survival (p = .023). Third, in Path C, perceived social support was an independent predictor of cardiac event-free survival (p = . 03). In the final Path D, perceived social support was no longer a significant predictor of cardiac event-free survival when medication adherence was entered into the model (p = .09), indicating medication adherence mediated the relationship between perceived social support and better event-free survival.

Perceived Social Support, Medication Adherence, and Cardiac Event-free Survival—prediction of cardiac event-free survival from the combination of medication adherence and perceived social support

First, we entered the interaction term of medication adherence and perceived social support analyzed as continuous variables into a Cox proportional hazards regression model. The interaction term of medication adherence and perceived social support significantly predicted cardiac event-free survival before and after adjusting for study group, age, gender, ethnicity, living status, NYHA class, and presence of depressive symptoms (p = .002 and .040, respectively).

Second, we classified patients into one of the four groups stratified by medication adherence and perceived social support. Of the total sample, 70 (32%) patients were classified as medication adherent with higher perceived social support, 58 (27%) were medication adherent with lower perceived social support, 40 (18%) were medication nonadherent with higher perceived social support, and 50 (23%) were medication nonadherent with lower perceived social support. These 4 groups were relatively equal in size. Using Kaplan-Meier survival curves and log-rank tests, patients who were nonadherent and had lower levels of PSS experienced the shortest cardiac event-free survival among all groups (p = .003). Based on Cox regression modeling (Figure 2 & Table 5), patients with medication nonadherence and lower level of PSS had a 3.46 times higher risk of adverse events than those with medication adherence and higher levels of PSS (p = .001). When adding study group, age, gender, ethnicity, living status, NYHA functional class, and presence of depressive symptoms to the model, patients who were nonadherent and had lower levels of PSS had a 2.5 times higher risk of cardiac events than patients who were adherent and had higher level of PSS (Table 5). The interaction term of medication adherence and perceived social support predicted cardiac event-free survival and the lowest survival rate and highest hazard ratio were found in patients who were nonadherent and had lower levels of PSS (Figure 2 & Table 5), which demonstrated that medication adherence and higher PSS in combination, predicted better cardiac-event survival.

In addition, minority status and greater depressive symptoms also predicted lower cardiac event-free survival (p < .05). The observed hazard ratios ranged from 1.72 to 3.46 in the unadjusted model and between 1.25 and 2.47 in the Cox regression model with covariates included. For both models, the hazard ratio for the comparison of the low adherence/lower PSS group to others was significant, while other group comparisons were not.

DISCUSSION

This is the first study to explore the prediction of cardiac event-free survival from the combination of medication adherence and perceived social support in patients with HF. We found that medication adherence and perceived social support both independently predicted cardiac event-free survival in patients with HF when medication adherence and perceived social support were analyzed as either dichotomized or continuous variables. Consistent with prior studies, HF patients who were adherent to prescribed medications had a lower risk of cardiac events than those who were nonadherent (Wu, et al., 2008; Wu, et al., 2009). Likewise, HF patients who reported lower perceived social support had a higher risk of cardiac events than those who reported higher perceived social support (Burg, et al., 2005; Happ, et al., 1997; Krumholz, et al., 1998; Luttik, et al., 2005; Tsuchihashi-Makaya, et al., 2009; Vinson, et al., 1990). Our study extends these findings by demonstrating that medication adherence mediates the relationship between perceived social support and outcomes in patients with HF. This finding underscores the importance of bolstering perceived social support in patients with HF, leading to better medication adherence, which positively affects outcomes.

The most striking finding from this study was that medication adherence and perceived social support, not only had independent effects, but in combination, medication adherence and PSS also predicted cardiac event-free survival in patients with HF. In this study, the interaction term of medication adherence and perceived social support predicted cardiac event-free survival. When medication adherence and PSS were dichotomized and used in the Cox regression model, the risk of experiencing a cardiac event for patients with medication nonadherence and lower PSS was 3.5 times compared to those who were medication adherent with higher PSS; while the risk of experiencing a cardiac event for patients with only one risk factor was about 2 times that of those with neither risk factor.

Perceived social support has previously been identified as a predictor of hospitalization and death in many studies (Burg, et al., 2005; Chin & Goldman, 1997a; Happ, et al., 1997; Krumholz, et al., 1998; Lofvenmark, et al., 2009; Luttik, et al., 2005; Schwarz & Elman, 2003; Tsuchihashi-Makaya, et al., 2009; Vinson, et al., 1990; Wright, et al., 2003). Schwarz et al. (2003) found that caregiver informal social support significantly decreased the risk of patient hospitalization and Chin and Goldman (1997a) found that HF patients who were single were twice as likely to be readmitted to the hospital or to die , even after adjusting for demographic and clinical factors (e.g., gender, history of diabetics, comorbidity burden, admission systolic blood pressure, admission serum sodium level, serum creatinine, and ST-T-wave changes on the initial electrocardiogram) (Chin & Goldman, 1997a). Krumholz et al. (1998) found that the absence of emotional support was associated with 3 times the risk over 1-year of any fatal or nonfatal cardiovascular events and Wright et al. (2003) linked the presence of social problems to a longer length of hospital stay in HF patients. Patients who reported loneliness also had more days hospitalized ($p = .044$) and more readmissions to the hospital ($p = .027$) (Lofvenmark, et al., 2009). Thus, there is evidence that perceived social support influences outcomes. However, the mechanisms that produce better outcomes are unclear.

Prior investigators suggested that better outcomes of those with higher levels of social support might be associated with better medication adherence (DiMatteo, 2004; Edwards, 2006; Johnson, Jacobson, Gazmararian, & Blake, 2010; Molloy, Perkins-Porras, Bhattacharyya, Strike, & Steptoe, 2008; Sayers, et al., 2008; Simoni, Frick, & Huang, 2006; Voils, Steffens, Flint, & Bosworth, 2005). In our study, when medication adherence and perceived social support were analyzed as continuous variables, higher perceived social support predicted better medication adherence. Of the six prior studies in which self-report measures of adherence were used, all reported a relationship between medication adherence and social support (Edwards, 2006; Johnson, et al., 2010; Molloy, et al., 2008; Sayers, et al., 2008; Simoni, et al., 2006; Voils, et al., 2005). Sayers et al. found that emotional support was associated with better self-reported medication adherence (p = .05) (Sayers, et al., 2008). In DiMatteo's meta-analysis (2004), medication nonadherence was 2 times higher among patients who did not receive practical support, 1.35 times higher among those who did not receive emotional support, and 1.74 times higher among patients reporting lower levels of family cohesion. In five other studies, greater social support was associated with better medication adherence (Edwards, 2006; Johnson, et al., 2010; Molloy, et al., 2008; Simoni, et al., 2006; Voils, et al., 2005). Therefore, social support is important for patients to achieve better medication adherence and lead to better outcomes.

In this study, a majority of patients with higher perceived social support were adherent to medication prescription, and most patients with lower perceived social support were medication nonadherent. However, it is unclear why some patients with HF who reported higher social support were nonadherent, and why some patients with lower perceived social support were adherent. Investigators have suggested that medication adherence is largely facilitated by practical support (DiMatteo, 2004; Molloy, et al., 2008; Wu, Moser, Lennie, et al., 2008). In DiMatteo's meta-analysis (2004), practical support bore the highest correlation with medication adherence. From our previous qualitative study (Wu, Moser, Lennie, et al., 2008), patients reported that their spouse or other caregiver contributed a great deal to increased medication adherence through practical support by sorting their complicated prescribed medicines and directly supervising medication administration. Because most HF patients have physical limitations, practical support is needed to ensure that patients attend their health care appointments to keep prescriptions current, refill the prescription, and adhere to their medication regimen (DiMatteo, 2004; Riegel, et al., 2009; Sayers, et al., 2008; Wu, Moser, Lennie, et al., 2008). In our study, 58 out of the 218 patients (27%) who had lower PSS were medication adherent. And 40 patients (18%) who had higher PSS were medication nonadherent. One possible explanation is that our measure of perceived social support did not fully capture practical, emotional, or other important components of social support that may promote adherence. Therefore, it is possible that patients who reported lower perceived social support had other forms of support that allowed them to be adherent. Moreover, medication adherence is a complex phenomenon. There are many factors related to poor medication adherence, including lower financial status which would preclude the purchase of medications and influence adherence behavior (Wu, Moser, Chung, & Lennie, 2008). Thus, it is possible that patients who reported higher perceived social support had other factors that reduced their ability to be adherent to medication prescriptions.

We only identified one study in which both social support and medication adherence predicted hospitalization in patients with HF (Vinson, et al., 1990). Vinson et al. (1990) found that poorer social support and medication nonadherence were independent predictors of preventable readmissions. However, the relationships among medication adherence, social support and outcomes were not examined and the ability of these variables to predict cardiac event-free survival from medication adherence and social support in combination was not examined either. Our study advances our understanding of this relationship by demonstrating that: 1) medication adherence was a mediator of the relationship between perceived social support and cardiac event-free survival; 2) better medication adherence and higher perceived social support in combination, predicted better cardiac event-free survival in patients with HF before and after controlling for age, gender, ethnicity, living arrangement, and depressive symptoms.

When we compared sociodemographic, clinical, and psychological variables between medication adherent and nonadherent and between higher PSS and lower PSS groups, living arrangements (lived with another person or not), ethnicity, and the degree of depressive symptoms were different between groups. Patients in the lower PSS group were less likely to live with others, were more likely to be in a minority ethnicity, and had more depressive symptoms than those in the higher PSS group. However, when we adjusted for ethnicity, living status, and depressive symptoms in the Cox regression model, patients with medication nonadherence and lower perceived social support still had the highest risk of experiencing a cardiac event.

LIMITATIONS

First, there are many components of social support, such as practical and emotional social support, and family cohesiveness and conflict (DiMatteo, 2004) that we did not measure. These components of social support may influence medication adherence and outcomes differently. Further research is needed to examine these components of social support, and their influence on medication adherence and outcomes in patients with HF.

Second, medication adherence was measured for different durations in the two studies. The difference in duration may have a potential influence on the recorded adherence level. Therefore, we compared demographic and clinical variables, medication adherence and perceived social support between the two samples to determine whether the two were comparable. We also controlled for study group in the final regression model to account for potential differences between the two studies.

Third, medication adherence measured by the MEMS may be inflated when patients know their medication-taking behaviors were monitored (i.e., Hawthorne effect). However, the MEMS is an objective measure of adherence and has been used widely to assess medication adherence in the research settings (Cramer, 1995). In this study, there was a strong relationship between adherence and outcomes, suggesting adherence was accurately reflected by the MEMS.

CONCLUSION

Better medication adherence and higher perceived social support independently, and in combination, predicted better cardiac event-free survival in patients with HF. These findings highlight the importance of medication adherence and patient social support network on patient outcomes. Interventions to improve clinical outcomes should address both medication adherence and social support.

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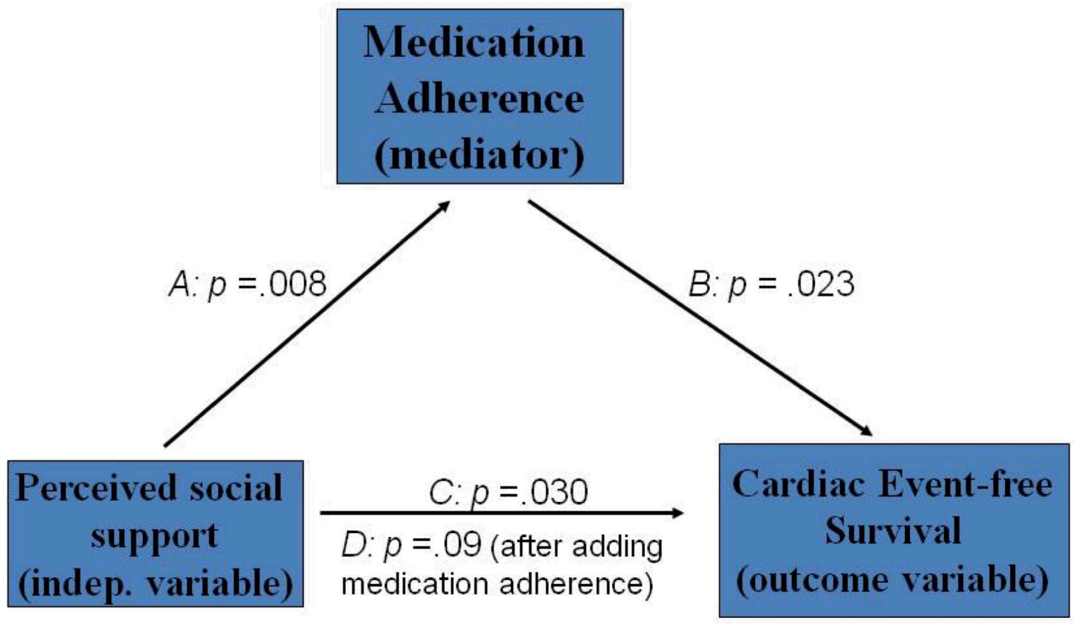


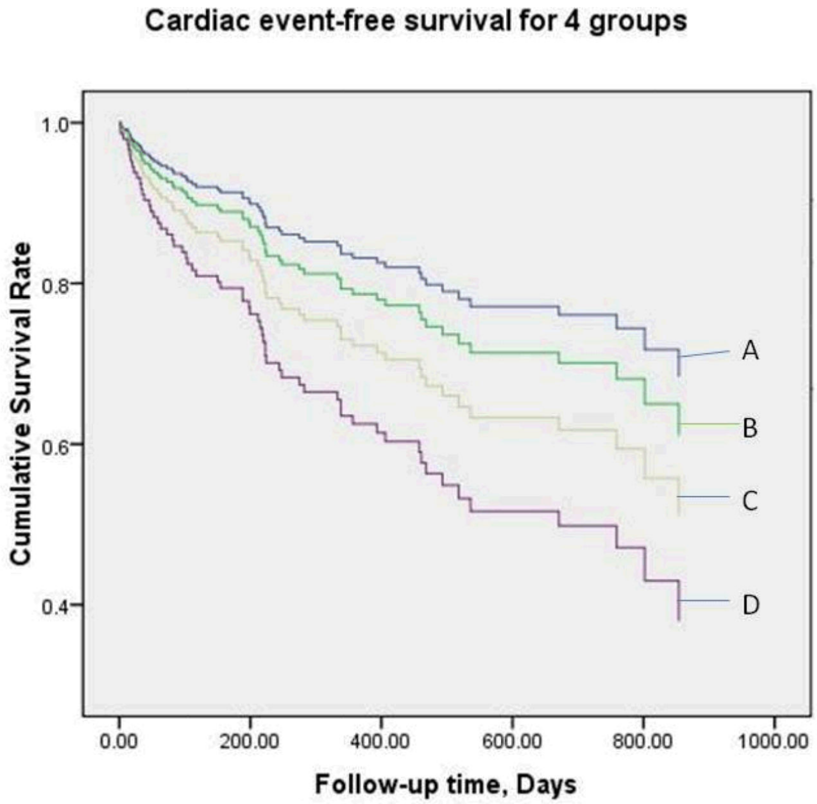
Path A: Test of whether perceived social support is a predictor of medication adherence.

Path B: Test of whether medication adherence is a predictor of cardiac event-free survival.

Path C: Test of whether perceived social support is a predictor of cardiac event-free survival.

Path D: Test of whether perceived social support and medication adherence together are predictors of event-free survival.

Figure 1.
Perceived social support, medication adherence, and cardiac event-free survival



A: Medication adherent with higher perceived social support (n = 70)

B: Medication adherent with lower perceived social support (n = 58)

C: Medication nonadherent with higher perceived social support (n = 40)

D: Medication nonadherent with lower perceived social support (n = 50)

Figure 2.
Cardiac event-free survival for patients who were stratified by medication adherence and perceived social support.

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Table 1

Sample characteristics and comparison of patient characteristics* from study 1 (adherence was measured for 3 months) and study 2 (adherence was measured for 1 month)

Characteristics	Overall (N = 218)	Study 1 (n = 136)	Study 2 (n = 82)	*p*
Age, years	60 ±12	61 ± 11	60 ± 12	.54
Female, %	77 (35)	41 (30)	35 (43)	.08
Live with others, %	160 (73)	95 (70)	65 (79)	.16
Ethnicity: minority, %	32 (15)	14 (10)	18 (22)	.03
LVEF, %	36 ±14.3	35 ± 14.1	38 ± 14.1	.10
NYHA III/IV, %	123 (56)	82 (60)	41 (50)	.04
Hypertension, %	168 (79)	104 (79)	64 (78)	.86
Diabetes, %	96 (44)	64 (48)	32 (39)	.26
Body Mass Index, kg/m^2	32.2 ±7.6	31.8 ± 6.6	32.8 ± 8.8	.40
Taking ACEI, %	153 (71)	97 (71)	56 (69)	.76
Taking Beta-blocker, %	200 (91)	121 (89)	79 (95)	.14
Medication adherent	129 (59)	76 (56)	53 (64)	.26
High perceived social support	110 (51)	70 (52)	40 (49)	.14

Data are presented as means ± SD, or N (%), interval level data compared by independent t-test, categorical by Chi-square; ACEI =Angiotensin-converting-enzyme inhibitor; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association

Table 2

Comparison of characteristics among four groups stratified by medication adherence and perceived social support

	Medication adherent		**Medication nonadherent**		***p* value**	**Post hoc by LSD test**
	Higher PSS (n = 70)	**Lower PSS (n = 58)**	**Higher PSS (n = 40)**	**Lower PSS (n = 50)**		
Group	A	B	C	D		
Age, years	62 ± 12	60 ± 11	61 ± 15	58 ± 9	.41	-
Female, %	20 (29)	22 (38)	17 (43)	17 (35)	.48	-
Live with others, %	61 (87)	34 (59)	33 (83)	32 (65)	.001	A, C > B, D
Ethnicity: minority, %	5 (7)	11 (19)	6 (15)	10 (20)	.15	-
LVEF, %	36.6 ± 14.6	34.5 ± 14.8	39.2 ± 14.8	33.6 ± 12.3	.26	-
NYHA III/IV, %	30 (43)	36 (62)	27 (68)	30 (60)	.12	-
Hypertension, %	48 (69)	46 (82)	34 (87)	39 (83)	.08	-
Diabetes, %	24 (35)	28 (49)	23 (58)	20 (41)	.11	-
Body Mass Index, kg/m^2	30.9 ± 7.4	33.0 ± 7.8	33.4 ± 8.0	32.0 ± 6.8	.29	-
Taking ACEI, %	57 (83)	39 (67)	26 (65)	31 (65)	.07	-
Taking Beta-blocker, %	66 (94)	52 (90)	33 (83)	47 (96)	.10	-
Depressive symptom score	4.6 ± 4.7	6.6 ± 5.5	6.9 ± 5.9	7.8 ± 5.8	.01	A < B, C, D
Functional status	16.4 ± 12.6	12.1 ± 12.3	12.4 ± 9.5	14.1 ± 15.3	.22	-

Data are presented as means ± SD, or N (%), interval level data compared by Analysis of Variance (ANOVA with the Least Significant Difference [LSD] post hoc tests), categorical by Chi-square; NYHA = New York Heart Association; LVEF = left ventricular ejection fraction; ACEI =Angiotensin-converting-enzyme inhibitor.

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Table 3

Comparison of clinical and demographic characteristics by medication adherence and perceived social support group classification

Characteristics	Medication Adherent (n = 128)	Medication Nonadherent (n = 90)	*p*	Higher PSS (n = 110)	Lower PSS (n = 108)	*p*
Age, years	61 ±11	59 ±12	.32	61 ±13	59 ±11	.10
Female, %	42 (32.8)	35 (38.9)	.39	37 (33.6)	40 (37)	.67
Live with others, %	95 (74.2)	66 (72.3)	.88	94 (85.5)	67 (62)	< .001
Ethnicity: minority, %	16 (12.5)	17 (18.9)	.25	11 (10)	22 (20.4)	.04
LVEF, %	35.7 ±14.7	36.4 ±13.7	.74	37.5 ±14.6	34.3 ±13.8	.10
NYHA III/IV, %	66 (51.6)	57 (63.3)	.16	57 (51.8)	66 (61.1)	.23
Hypertension, %	94 (74.6)	74 (85.1)	.09	82 (75.2)	86 (82.7)	.24
Diabetes, %	52 (41.3)	44 (48.9)	.27	47 (43.1)	49 (45.8)	.78
Body Mass Index, kg/m^2	31.8 ±7.6	32.8 ±7.5	.37	31.8 ±7.7	32.6 ±7.4	.44
Taking ACEI, %	96 (75.6)	58 (64.4)	.10	83 (76.1)	71 (65.7)	.10
Taking Beta-blocker, %	118 (92.2)	81 (90.0)	.63	99 (90.0)	100 (92.6)	.63
Medication Adherence, %	95.9 ±3.7	64.3 ±21.9	< .001	84.6 ±20.3	81.2 ±21.8	.23
Perceived Social Support score	68.6 ±18.8	64.5 ±20.2	.13	81.5 ±10.8	52.1 ±14.5	< .001
Depressive symptom score	5.5 ±5.2	7.4 ±5.8	.01	5.3 ±5.2	7.2 ±5.7	.02
Functional status score	14.5 ±12.6	13.4 ±13	.56	15.0 ±11.7	13.1 ±13.7	.29

Data are presented as means ± SD, or N (%), interval level data compared by independent t-test, categorical by Chi-square; ACEI =Angiotensin-converting-enzyme inhibitor; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association

Table 4

Cox regression models*: Medication adherence alone and perceived social support alone on cardiac event-free survival (N = 218)

Variables	Hazard Ratio	95% CI	*p*
Medication adherence**			
Medication adherent	1.0	-	-
Medication non-adherent	2.09	1.257 - 3.478	.01
Perceived social support§			
Higher perceived social support	1.0	-	-
Lower perceived social support	1.89	1.136 - 3.152	.01

CI: confidence interval

*These models are simple Cox proportional hazards regression models without inclusion of covariates.

**Chi-square = 6.202; $p = .013$

§Chi-square = 8.430; $p = .004$

Table 5

Cox regression modeling: medication adherence, perceived social support and cardiac event-free survival (N = 218)

Variables	Hazard Ratio	95% CI	*p*
Simple Cox Regression: without adjustment*			
Medication adherent and higher PSS	1.0	-	-
Medication adherent and lower PSS	1.718	0.803 - 3.676	.16
Medication nonadherent and higher PSS	1.937	0.855 - 4.392	.11
Medication nonadherent and lower PSS	3.458	1.710 - 6.996	.001
Cox Regression: adjusting for covariates**			
Step 1			
Study_group	.836	0.484-1.444	.52
Age	.996	0.974 – 1.018	.73
Gender	.953	0.548 – 1.658	.86
Ethnicity: minority	2.197	1.150 – 4.195	.02
Did not live with others	1.345	0.770 – 2.350	.30
Step 2			
NYHA functional class	1.275	0.820-1.982	.28
Depressive symptoms	1.052	1.003 - 1.104	.04
Step 3			
Medication adherent and higher PSS	1.0	-	-
Medication adherent and lower PSS	1.246	0.549 - 2.831	.60
Medication nonadherent and higher PSS	1.685	0.731 – 3.881	.22
Medication nonadherent and lower PSS	2.465	1.155 - 5.263	.02

CI: confidence interval, PSS = perceived social support, NYHA = New York Heart Association

*Chi-square = 13.8, p = .003

**Chi-square = 24.5, p = .006