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Abstract

The purpose of the study was to explore the association between depression and medication adherence in heart failure (HF) patients. Studies have shown that people with depression are likely to be nonadherent to their prescribed medication treatment. But other studies suggest that nonadherence may be overestimated by people with depression. A total of 244 adults with Stage C HF completed the study. Self-reported medication adherence was obtained using the Basel Assessment of Adherence Scale (BAAS); objective data on medication adherence were collected using the electronic Medication Event Monitoring System (MEMS). Depression was measured via self-report with the Patient Health Questionnaire (PHQ-9). There was a significant difference between depressed and nondepressed participants in self-reported medication nonadherence ($p = .008$), but not in objectively measured medication nonadherence ($p = .72$). The depressed sample was 2.3 times more likely to self-report poor medication adherence than those who were nondepressed ($p = .006$).

The Role of Depression in Medication Adherence Among Heart Failure Patients

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Abstract

The purpose of the study was to explore the association between depression and medication adherence in heart failure (HF) patients. Studies have shown that people with depression are likely to be nonadherent to their prescribed medication treatment. But other studies suggest that nonadherence may be overestimated by people with depression. A total of 244 adults with Stage C HF completed the study. Self-reported medication adherence was obtained using the Basel Assessment of Adherence Scale (BAAS); objective data on medication adherence were collected using the electronic Medication Event Monitoring System (MEMS). Depression was measured via self-report with the Patient Health Questionnaire (PHQ-9). There was a significant difference between depressed and nondepressed participants in self-reported medication nonadherence ($p = .008$), but not in objectively measured medication nonadherence ($p = .72$). The depressed sample was 2.3 times more likely to self-report poor medication adherence than those who were nondepressed ($p = .006$).

Keywords

Introduction

Proper adherence to a treatment plan, especially taking medication regularly and as prescribed is a common clinical challenge for both patients and clinicians. The projected medication adherence rate in chronic illness ranges from 20% to 80% (DiMatteo, 2004).

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This estimation corresponds with the reported 50% overall adherence rate for any given treatment plan (Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Haynes, McDonald, Garg, & Montague, 2002) and the 40% to 60% nonadherence in adults with heart failure (HF; Wu, Moser, Lennie, & Burkhart, 2008). Poor medication adherence has been found to be associated with higher medical costs (Kane & Shaya, 2008) and increased mortality in chronic illness (Ho, Magid, Masoudi, McClure, & Rumsfeld, 2006; McGinnis, Olson, Delate, & Stolcpart, 2009).

Medication adherence is generally defined as the extent to which patients take medications as prescribed by their health-care providers (Osterberg & Blaschke, 2005). The World Health Organization (WHO) described medication adherence as a multidimensional phenomenon influenced by five domains, one of which is the condition-related factors (e.g., severity of the symptoms and comorbidity). In the condition-related domain, depression has been shown to be a key factor in medication adherence (De Geest & Sabate, 2003). It was noted that symptoms of major depressive disorders such as fatigue, lack of motivation, inability to concentrate, social withdraw, and feelings of worthlessness hinder individuals' abilities to follow the treatment plan.

A meta-analysis revealed that most of the literature in this area examined the dynamic between depression and medication adherence in the context of chronic illnesses; across the 31 studies (18,245 participants) that were reviewed, the majority of the studies were about cardiovascular diseases and diabetes. The authors of the meta-analysis found that depressed people were 1.76 to 3.03 times more likely to be nonadherent compared to those who were not depressed (DiMatteo, Lepper, & Croghan, 2000; Gonzalez et al., 2008; Grenard et al., 2011). In addition, a recent study of hospitalized cardiac patients showed that improvement in the depression score was positively associated with self-reported medication adherence (Bauer et al., 2012). High rates of poor medication adherence in depressed people call attention to the need for intervention in these patients but the authors also pointed out inconsistencies in the literature. They found wide variation in the manner in which depression was defined and in how medication adherence was measured: whether it was by self-report, electronic medication monitoring system, or pharmacy record (Grenard et al., 2011). Importantly, some studies have shown that people who were acutely or persistently depressed tended to over-report their treatment nonadherence, compared to those who were in remission from depression, and those who were not depressed (Kronish et al., 2006; Morgado, Smith, Lecrubier, & Widlocher, 1991). It was this observation that stimulated our interest in conducting the current study.

HF is recognized as one of the most common cardiovascular disorders globally. More than 6 million Americans and 23 million people worldwide suffer from HF (McMurray, Petrie, Murdoch, & Davie, 1998; Roger et al., 2011; Roger et al., 2012), which is a progressive syndrome with a heavy symptom burden (Lam et al., 2011). HF is a chronic illness that requires lifelong adherence to a complex medication regimen. Psychological symptoms such as depression and anxiety are common in HF (Rutledge, Reis, Linke, Greenberg, & Mills, 2006; Yohannes, Willgoss, Baldwin, & Connolly, 2010). The prevalence rate of depression has been reported to be as high as 25% (outpatient) and 70% (inpatient) for people with HF (Lossnitzer et al., 2012; Rutledge et al., 2006). Medication nonadherence is a primary reason

for poor medical outcomes among individuals with HF (Dunlay, Eveleth, Shah, McNallan, & Roger, 2011; Esposito, Bagchi, Verdier, Bencio, & Kim, 2009) and these high rates of depression and anxiety may have an effect on medication adherence and patient health.

A review of literature using the WHO five-dimensions framework to examine medication adherence in HF population reported that strong social support, good patient–provider relationship, a simple medication regimen, affordable cost, increased symptom severity, perceived treatment benefit, and minimum medication side effects are factors that promote medication adherence. Conversely, cognitive and psychological causes such as depression, lack of motivation for self-care, and forgetfulness were found to impair medication adherence (Wu, Moser, Lennie et al., 2008). Similar to the challenges faced by other investigators with different populations regarding the relationship between depression and medication adherence, careful consideration is advisable when generalizing the findings. Although adherence is complex and may require multiple measures to adequately describe it, most of the studies used only a single measure of medication adherence such as electronic monitoring (Carney, Freedland, Eisen, Rich, & Jaffe, 1995; Morgan et al., 2006), pharmacy refill (Wang et al., 2002), or self-report (van der Wal et al., 2006; Ziegelstein et al., 2000).

To date there are few studies using both subjective and objective measures to examine the role of depression on medication adherence in the HF population. A study by Hansen and colleagues (2009) assessed the effectiveness of a pharmacist-based intervention for medication adherence in depressed versus nondepressed HF patients and explored the influence of depressive symptoms on medication adherence. In this study, objective medication adherence was measured by electronic medication monitoring system and self-reported medication adherence was measured by the Morisky Compliance Assessment Scale and a 1-item scale by Inui, Carter, and Pecoraro, 1981. The study showed that depression was a predictor for self-reported medication adherence but not the objective measure. The depressed group was 6% lower on the self-reported medication adherence compared to the nondepressed group. The results revealed a surprising discrepancy between the objectively measured and subjectively reported medication adherence; the nondepressed group overestimated their medication adherence (81% self-report vs. 69% objective) while the depressed group self-reported an adherence rate that was comparable to that measured objectively (75% self-report vs. 71% objective). The authors suggested that such a relationship may be attributed by the tendency of the depressed patient to self-report poor adherence (DiMatteo et al., 2000; Hansen et al., 2009; Jerant, DiMatteo, Arnsten, Moore-Hill, & Franks, 2008). The findings of this study are important because they influence how the results of prior studies in this area can be interpreted. The discrepancy between the two measures of adherence suggests that the relationship between depression and medication adherence may be more complex than we realized.

Aims

The purpose of the study was to explore the association between depression and medication adherence in HF patients. The primary hypothesis was that depression was associated with lower self-reported medication adherence than objectively measured medication adherence.

Method

Sample and Setting

This was a secondary analysis of data from a prospective descriptive study. A total of 280 patients were enrolled from three outpatient sites in the northeastern United States. Recruitment criteria specified that participants have current or prior HF symptoms (i.e., Stage CHF) and be physically, psychologically, and cognitively capable to participate in a longitudinal study (Riegel et al., 2011; Riegel et al., 2012). HF was confirmed by echocardiography and clinical evidence. All participants were community dwelling and self-sufficient in medication administration. Patients were excluded if they worked at night or rotating shifts because the primary study focused on the relationship between sleep and self-care. Other exclusionary criteria were terminal illness, history of recent alcohol or drug abuse, and severe cognitive impairment (screened by Telephone Interview of Cognitive Status). We also excluded patients with severe depression (screened by Patient Health Questionnaire [PHQ-9] Patient Depression Questionnaire). Those with major depressive disorder were excluded because previous research has shown that depression is associated with treatment adherence and sleep (Phillips et al., 2005). This was operationalized as excluding anyone reporting five or more of the nine symptoms more than half of the days in the past 2 weeks, and if one of the symptoms was depressed mood or anhedonia. Subsyndromal depression has been shown also to have an impact on overall functioning (Grabovich, Lu, Tang, Tu, & Lyness, 2010), and thus was the focus of this study. Participants were followed for 6 months with data collected at three time points: baseline, 3 months, and 6 months. Data collected at 6 months were used in this analysis so that we had objective data on medication adherence for a full 6 months.

Measures

After excluding patients with major depressive disorder, throughout the course the study depression was measured at each testing interval using the PHQ-9. The PHQ-9 is a well-established scale that anchors the DSM-IV diagnostic criteria for major depressive disorders. The items ask how often in the past 2 weeks the individual has been bothered by the identified depressive symptoms. The rating options are not at all, several days, more than half the days, and nearly every day. Scores on the PHQ-9 range from 0 to 27 (1–4 minimal depression; 5–9 mild depression; 10–14 moderate depression; 15–19 moderately severe depression; 20–27 severe depression; Kroenke, Spitzer, & Williams, 2001). In this study, we compared those participants with minimal or no depression (PHQ-9 score less than 5) versus those with at least some depression groups (PHQ-9 score 5 and above). These groups do not represent presence/absence of major depressive disorder, but for clarity of presentation we designate those with elevated depressive mood as the "depressed" group.

Medication adherence was measured with both subjective and objective methods. Self-reported medication adherence was obtained using the Basel Assessment of Adherence Scale (BAAS). The BAAS is a structured questionnaire with 4 dichotomous items measuring dosing, timing and frequency adherence; and a visual analog scale to capture self-assessment of overall adherence. Each positive response indicates an aspect of medication nonadherence. A positive answer on any of the questions classifies a patient as nonadherent

with the medication regimen. This stringent operationalization of nonadherence increases the sensitivity of measurement. The psychometric properties of the BAAS have been validated in HIV-infected (Deschamps et al., 2008) and renal transplantation population and the BAAS has been used successfully in HF research (Riegel et al., 2011).

Objective data on medication adherence were collected using the electronic Medication Event Monitoring System (MEMS; AARDEX, Union City, CA). The MEMS system uses a device or cap that fits on a conventional medicine bottle. Using electronic microcircuitry in the medication cap, each opening and closing of the container is recorded. This recording allows easy calculation of the percentage of prescribed doses taken and the percentage of the correct number of doses taken. Nonadherence was defined as taking less than 80% of the prescribed medication doses. MEMS has been used in studies with HF population (Wu, Moser, Chung, & Lennie, 2008; Wu et al., 2009).

Data Analysis

Descriptive statistics including mean, standard deviation (*SD*), frequency, and percentage were used to describe patient's demographic characters and severity of depression. To address the study aim, PHQ-9 depression scores at 6 months, self-report and objectively measured medication adherence at 6 months were used. General Linear Modeling (GLM) was used to explore the role of depression in self-reported and objectively measured medication adherence, controlling for age, gender, race, and data collection site. Medication adherence was dichotomized and χ^2 analysis was used to examine differences between the nondepressed and depressed groups on medication adherence. Then, the odds of nonadherence were calculated using χ^2 and Mantel-Haenszel Common Odds Ratio (OR) Estimate tests. All analyses were conducted using Statistical Package for Social Sciences (SPSS) version 20 (IBM Corporation, Armonk, New York, the United States). The level of statistical significance was set at $p < 0.05$.

Results

A total of 244 of the 280 enrolled participants completed the study at the 6 months. The attrition rate of the primary study was 13.6%. Reasons for attrition were withdrawal, unable to follow-up, too ill to participate, and death. At 6 months the participants were 63 ± 12 years old on average, 63% male, and 64% White. More than half had some college education (57.9%; Table 1). At baseline, depression scores ranged between 0 to 18 and 43% had at least mild depression. At 6 months, the depression scores ranged from 0 to 20; 34% had at least mild depression. The details are illustrated in Table 2. The range of depression in participants did not change from baseline to 6 months.

At 6 months, there was a significant difference between those with depressed mood and participants without depressed mood on the self-report measure of medication adherence. The depressed participants (i.e., PHQ-9 5) were more likely (7% increase) to report nonadherence on the BASS ($p = .012$); whereas the association between depression and objectively measured medication was not significant ($p = .56$). Specifically, self-reported nonadherence was significantly higher in the depressed sample compared to the nondepressed subjects (75% vs. 57%, $p = .008$). Objective medication nonadherence was not

significantly different in the depressed and nondepressed subjects (28% vs. 33%, $p = .72$; Figure 1). Participants with depression were 2.3 times more likely to self-report medication non-adherence than those who were not depressed; OR 2.26 (95% CI: 1.26–4.07, $p = 0.006$).

Discussion

We found that depressed HF patients significantly underestimated their medication adherence. In spite of comparable medication adherence documented objectively on electronic monitoring, the depressed group was twice as likely to report poor medication adherence. These results suggest that depression, even at the subsyndromal level, can be a potent influence on patients' perceptions of their behavior.

This is one of the few studies using both subjective and objective measures to assess medication adherence in the HF population. The results of this study are consistent with the findings of Hansen et al. (2009) that depression was associated with lower self-reported medication adherence in HF patients (6% in Hansen's study and 7% in this study); whereas in both studies, depression did not influence the objective measure of medication adherence. Further, the patterns of nonadherence were similar in the two studies (29% for depressed, 31% for nondepressed in Hansen's study; 28% for depressed and 31% for nondepressed in this study). The major difference between the studies was that the self-reported medication nonadherence was generally higher in this study (25% for depressed, 19% for nondepressed in Hansen's study; 75% for depressed and 57% for nondepressed in this study). This difference could be due to the instruments used to measure self-reported nonadherence. In Hansen and colleagues' study, the Morisky Compliance Assessment Scale was used to measure self-reported medication adherence. The Morisky scale and the single Likert-type item questionnaire both broadly assess whether respondents ever forgot, missed, or cut back on their medicine, whether they took the medicine yesterday, and their perceived health stability. In this study, the self-reported medication adherence was assessed by BAAS which specifically solicited individual's self-assessment of adherence taking, dosing, timing, and forgetting of medicines during the past month.

In this study, the discrepancy between subjective and objective measures of medication adherence may be explained by the unique phenomenon captured with each measurement method. Specifically, the subjective and objective measures both target essential components of medication adherence such as dosing, timing, frequency, and forgetting; however, the self-reported adherence also captures the individual's perceived ability to perform self-care, whereas the objective measure records the behavioral construct only. Medication adherence is one element of self-care that involves both cognitive and behavioral processing. Even mild to moderately depressive mood is associated with pessimistic thoughts, feeling of hopelessness, and worthlessness, which may explain over-reporting of nonadherence in this sample. The existence of mild and moderate levels of subsyndromal depression affects how much confidence we can put into self-reports of medication adherence. These results suggest that in individuals who are depressed, reports of poor medication adherence may need objective validation before major treatment changes are implemented.

One limitation of the current study is the exclusion of severely depressed patients. Our rationale for exclusion was related to the potential for confounding in measurement, but the exclusion of people with severe mental illnesses is an issue for longitudinal studies with various chronic illnesses. These patients are often excluded due to the existing disease burden and individual's ability to participate and to follow the research protocol. But, in spite of this exclusion, we were still able to demonstrate that even mild depression affects perceptions of adherence. Another limitation is the lack of qualitative data to inform the condition of medication adherence; specifically, "why" one chose to adhere or "how" one managed to follow the medication regimen.

Future research is needed to (a) develop a feasible clinical assessment matrix that combines subjective, objective, and qualitative feedback for medication adherence monitoring, and (b) test if routine screening of depression and provider training on behavioral coaching would change patient's self-care patterns.

Acknowledgments

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Clinical Implication

These study findings highlight the importance of comprehensive assessment of a well-being even in a clinical context when the psychological condition is not the predominant focus.

When working with individuals with HF and any chronic illness, providers should consider both subjective and objective data when evaluating the effectiveness of a treatment plan and adherence. It is also important for providers to take time understanding patient's self-perception of their health state and related self-care behaviors. Finally, this study provides one more compelling reason why it is essential to assess for depression in HF patients.
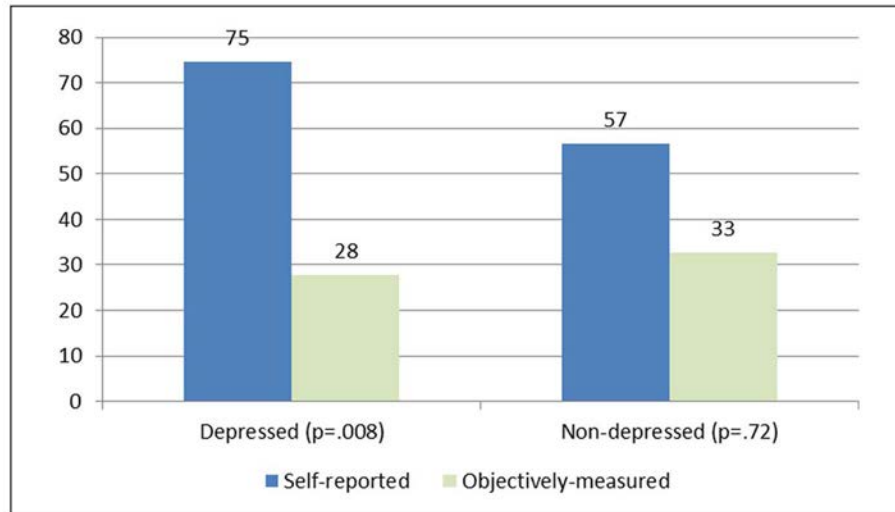
Figure 1.
Self-reported versus objectively measured medication nonadherence (%).

Table 1

Summary of Demographic and Clinical Characteristics (*N* = 244).

Overall sample		
Age	63 + 12	
Gender	Male *n* = 150 (63%)	Female *n* = 90 (37%)
Ethnicity	Black *n* = 79 (32%) White *n* = 157 (64%)	Other *n* = 8 (3%)
Education	< HS *n* = 23 (9%) HS graduate *n* = 79 (32%)	College *n* = 142 (58%)

	Nondepressed	Depressed
Age	64.7 + 11.5	59.7 + 11.6
Gender	Male *n* = 95 (67%)	Male *n* = 59 (57%)
	Female *n* = 46 (33%)	Female *n* = 44 (43%)
Ethnicity	Black *n* = 38 (27%)	Black *n* = 41 (40%)
	White *n* = 98 (70%)	White *n* = 60 (58%)
	Other *n* = 5 (3%)	Other *n* = 2 (2%)
Education	< HS *n* = 14 (10%)	< HS *n* = 9 (9%)
	HS graduate *n* = 43 (30%)	HS graduate *n* = 36 (35%)
	College *n* = 84 (60%)	College *n* = 58 (56%)

Note. HS = high school.

Table 2

Depression Baseline and 6 months by PHQ-9.

	Baseline N = 280	6 months N = 244
Mean	4.35 ± 3.64	3.68 ± 3.86
Range	0–18	0–20
< 5 (minimal depression)	56.8%	65.7%
5–9 (mild depression)	32.8%	26.4%
10–14 (moderate depression)	9.3%	6.2%
15–19 (moderately severe depression)	1.1%	1.3%
20–27 severe depression	0.0%	0.4%