Relationship of medication adherence and quality of life among heart failure patients

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ABSTRACT

Background: Little is known regarding the relationship between medication adherence and quality of life in heart failure patients. We therefore aimed to examine the nature of relationship between medication adherence and quality of life.
Methods: A prospective, cross-sectional study of chronic heart failure patients with reduced ejection fraction was performed at a tertiary-care, university hospital in Thailand. Quality of life and medication adherence were assessed using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) and Morisky Medication Adherence Scale-8 (MMAS-8), respectively. Relationship of MLHFQ and MMAS-8 were examined using Spearman's correlation coefficient and multiple regression analysis for covariates adjustment.
Results: Among 180 patients, 38.3%, 50.0% and 11.7% were found to have high, medium and poor adherence, respectively. For quality of life, the overall median score on the MLHFQ was relatively low. A positive relationship was identified between medication adherence and quality of life. After covariate adjustment, medication adherence was found to have the strongest relationship with quality of life, compared to other covariates.
Conclusions: Medication adherence has a small and positive relationship with quality of life among heart failure patients

Introduction

Heart failure (HF) is a major health problem in both developed and developing countries. In the United States, HF affects approximately 5.7 million people[1], with 870,000 new cases per year[2]. The incidence of HF was 10 per 1000 population per year after age 65 years and increased to 40 per 1000 population per year over the age of 85 years[2,3]. In Thailand, among cardiovascular diseases, HF was the leading cause of hospital admissions in 2015[4]. The morbidity rate of patients with HF was 291.98 per 100,000 Thai population in 2015, and its incidence and prevalence has been rising[4]. With the increasing use of neurohormonal antagonists, the survival rate of HF with reduced ejection fraction (HFrEF) patients has improved markedly over the past decade[5]. Although prolonged survival rates are clinically important, quality of life of patients living with HF also deserves attention[6]. Hobbs et al.[7] showed that HF patients had statistically significant impairment of all aspects of quality of life, not simply physical function. Compared with other serious common chronic disorders, patients with HF have a significantly greater physical

health burden[7]. Furthermore, medical management of patients with HF has become increasingly complex. Based on the 2016 American College of Cardiology Foundation / American Heart Association Guideline recommendation[8], HF patients require at least four medications to reduce mortality and relieve symptoms. With increasing age, severity, and comorbid conditions, medication regimens can become even more complex and pose significant challenge for patients to adhere to such regimen[8−10]. Despite the proven efficacy of recommended pharmacological therapy for patients with HF, adherence to treatments remains suboptimal, contributing to lower treatment effectiveness. It is estimated that at least one out of four patients with HF do not adhere to his or her medications[11−13]. Several have reported that a high number of medications, complexity of medication regimens, insufficient care of healthcare providers, no healthcare insurance, and no transportation are influential factors that show the association with poor medication non-adherence in HF patients[14−16]. The interplay among health system, socioeconomic status, disease severity, treatment, and patient factors are involved in this complex issue[15,16]. Studies[17−19] have demonstrated the impact of medication adherence on clinical outcomes. For example, poor medical adherence in hypertension, HIV, asthma, tuberculosis, and diabetes mellitus affect patients' quality of life[17−24]. However, there is a paucity of

evidence in terms of the relationship of medication adherence and quality of life in HF patients[25]. We therefore aimed to examine the relationship between medication adherence and quality of life, and assess whether medication.

Methods

Study design and setting

This prospective, cross-sectional study was conducted at the Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand. This university hospital is the largest hospital in northern Thailand and provides tertiary medical care in all medical disciplines for the region. The hospital's cardiovascular clinic is managed by the healthcare professional team, which include cardiovascular specialists, training residents, nurses, and pharmacists, etc. This clinical aims to provide ambulatory care for cardiovascular patients (around 300 patients per week).

Ethical considerations

The study was approved by the Ethical Committee of Maharaj Nakorn Chiang Mai Hospital (Code: NONE-2558-02965). All eligible patients were given information related to the trial by the investigators, both as written and verbal means, to ensure informed decision about participation in the trial. All participants gave their written informed consent prior to their participation in the trial.

Data collection

Data were collected using questionnaires by self-report or, for patients with were illiterate, by interview. Data collection was done by a clinical pharmacist prior to a visit with cardiologists at the outpatient cardiology clinic. On average, patients completed the questionnaire in approximately 20−30 min. All questionnaires were checked for completeness, additional explanation was provided when unclear responses were encountered. Since the majority of patients were elderly and needed the assistance, we decided to use patient interview to collect the data. Hence, our data were complete.

Study sample

Patients with chronic HF who visited the outpatient cardiology clinic during June 2015−March 2017 were screened and recruited. The inclusion criteria were: age of ≥ 18 years old, ejection fraction of ≤ 40%, and receiving HF medications for ≥ 1 year at the study hospital. The study excluded patients with terminal phase cancer, a previous stroke, severe dementia, or ≥ 2 hospitalizations during the previous 6 months for HF exacerbations. After screening, a total of 180 patients met the inclusion criteria and provided consent to participate in the study. The main reason for exclusion was having EF of > 40%. Fig. 1 shows detail of study recruitment along with detailed reasons for exclusion.

Variables and measures

The Minnesota Living with Heart Failure Questionnaire (MLHFQ) was used to measure quality of life. It is a specific, quality-of-life questionnaire that is widely used with HF patients in many countries[26,27]. This instrument is short, easily understood by HF patients, can be self-administered, and easy to score. Originally available in English, it has been validated in many countries[27−32] and translated into several languages, including Thai[33]. The MLHFQ-Thai version has been validated in Thailand, Cronbach's alpha coefficients and interclass correlation coefficients of the MLHFQ were 0.86−0.93 and 0.61−0.77, respectively[33]. MLHFQ consists of 21 questions that evaluate the impact of HF on
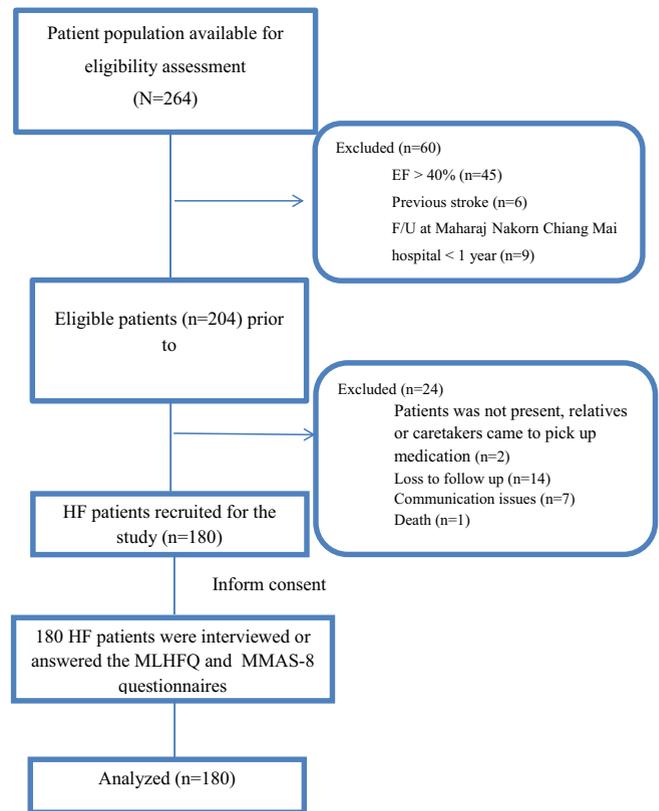

Fig. 1. Flow chart of study population.

physical, psychological, and social aspects of patients' lives. Each question is rated on a 6-point Likert-type scale from 0 (no effect) to 5 (very much), with a total score that can range from 0 to 105; higher scores indicate a poorer quality of life. In addition to the overall score, MLHFQ measures the physical dimensions (eight items; range 0−40) and emotional dimensions (five items; range 0−25) of quality of life. The instructions for use of the MLHFQ specifies that a clinical site checks to make sure the patient has responded to each question and that only one answer is clearly marked for each question[33].

Medication adherence was evaluated using the Morisky Medication Adherence Scale (MMAS-8), a self-reported questionnaire with eight questions that focus on a patient's medication experience over the prior two weeks[34]. MMAS-8 is low-cost, noninvasive, with minimal burden on a patient, easy to administer, and offers flexible timing and mode of administration[34−36]. Originally available in English[36], it has been validated in many countries[37−42] and translated into several languages, including Thai[43]. The internal consistency (Cronbach's alpha reliability) of MMAS was 0.83[34]. The sensitivity and specificity were 93 % and 53%, respectively[34]. Seven of the eight questions are yes/no, with a dichotomous response. The last question requires a 5-point Likert response. All items were reverse coded, no = 0 and yes = 1, except item 8. For item 8, if a patient chooses response "0", the score is "1" and if they choose response "4", the score is "0". Responses "1,2,3" are respectively rated as "0.25, 0.50, 0.75". The total score of the MMAS-8 can range from 0 to 8 − the higher the score, the higher the medication adherence (less than 6 = low, 6 to 7 = medium, and 8 high).

Patients were interviewed to collect socio-demographic data: age, sex, marital status, education level, health insurance and income. Clinical data − duration of heart failure, New York Heart Association (NYHA) functional class, left ventricular ejection fraction (LVEF), comorbidities, current medications and any history of previous acute decompensated HF− was obtained from a patient's medical history.

Statistical analyses

The data were analyzed using either descriptive or inferential statistics, where appropriate. The quality-of-life score was compared among groups stratified by adherence level using non-parametric tests (Kruskal−Wallis test) for non-normal distribution. The Spearman's correlation was used to assess the relationship between quality of life and medication adherence. Univariate and multivariate regression analyses were performed to determine the association between baseline covariates and the quality of life. Multivariate regression analyses for quality of life were constructed using a $p < 0.05$ on the univariate analysis for entry. Otherwise, statistically significant was defined using a 2-tailed p value ≤ 0.05. The data were analyzed using the Statistical Package for Social Science (SPSS) version 17.

Results

From June 2015 through March of 2017, 264 HF patients were screened. After screening, a total of 180 patients met the inclusion criteria and provided consent to participate in the study.

Key demographic, social and clinical characteristics of the study population are shown in Table 1. The mean age was 63.1 ± 11.7 years with about one third were ≥ 70 years of age, and 38.9% of the patients were women. Most patients (75%) had primary and secondary education and had relatively low income (8048 baht or 230 USD/month) comparing to the national average income of 13,500 baht or 385 USD/month. Although patients generally had low incomes, coverage of health insurance in the study population was nearly 100%, partly due to the universal healthcare coverage scheme of the country. Two thirds of patients were either living with a spouse or relatives which reflected the nature of Asian social structure.

The mean duration of HF was 4.6 ± 3.5 years. Nearly all patients (97.8%) were in NYHA functional class I-II, with average LVEF of 28.2%. The patients had substantial rates of coexisting illnesses. More than half (54.4%) of the study population had ≥ 4 comorbidities. The five most common comorbidities were coronary artery disease (47.3%), hypertension (43.3%), dyslipidemia (39.3%), valvular heart disease (33.3%) and diabetes (30%). Of all samples recruited, 15.6% had a history of hospital admission with acute decompensated HF after they were initially diagnosed with this disease. (Table 1).

Data on medication use are provided in Table 1. Overall, key HF medications including beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), diuretics, and mineralocorticoid receptor antagonists (MRAs) were used at very high rates in consistent to contemporary guidelines. Achievement of target doses (beta-blockers, ACEIs/ARBs and MRAs) were found in 43.6% of patients. On average, each patient received 6.6 ± 2.1 types of medication per day which amounted to an average number of 8.1 ± 4.2 tablets per day.

We found that age, sex, number of comorbidities, number of medications, marital status, educational level, income, HF severity, dose of diuretics, employment status, types of health insurance, history of HF admission along with support from caregivers were not associated with medication adherence in our study population.

For medication adherence, the median ± interquartile range (IQR) and mean ± SD of total MMAS-8 were 7.0 ± 1.2 and 7.1 ± 1.0, respectively. Only 38.3% of patients were classified as having high medication adherence (Table 2). For quality of life, the overall score on the MLHFQ was relatively low compare with total score (105). The median ± IQR and mean ± SD of the total MLHFQ score were 11 ± 10 and 13 ± 8.6, respectively. Physical MLHFQ had a median ± IQR and mean ± SD score of 5 ± 8 and 6.4 ± 5.2, respectively, while emotional MLHFQ had a median ± IQR of 2 ± 4 and mean ± SD of 2.6 ± 2.6.

Based on a univariate analysis, a small positive relationship was identified between medication adherence and quality of life

Table 1
Baseline clinical and demographic characteristics of the sample

	Total (n = 180)
Male gender	110 (61.1%)
Age (years)	63.1 ± 11.7
Marital status	
Married	127 (70.6%)
Single, divorced, widowed	53 (29.4%)
Education	
≤ 12 years	136 (75.6%)
> 12 years	44 (24.4%)
Health insurance	
Universal Coverage Scheme	79 (43.9%)
Civil Servant Medical Benefit Scheme	78 (43.3%)
Social Security Scheme	22 (12.2%)
Others	1 (0.6%)
Income (USD per month)	257.33 ± 264.68
Duration of heart failure	4.6 ± 3.5
NYHA functional class I or II	176 (97.8%)
LVEF (mean ± SD)	28.2 ± 8.5
Co-morbidities	
Coronary artery disease	71 (47.3%)
Hypertension	65 (43.3%)
Dyslipidemia	59 (39.3%)
Valvular heart disease	50 (33.3%)
Diabetic mellitus	45 (30.0%)
Chronic kidney disease	34 (22.7%)
COPD	9 (6.0%)
Others*	103 (68.7%)
Four or more comorbidities	98 (54.4%)
Types of medication per day	6.6 ± 2.1
Average number of medications (tablets per day)	8.1 ± 4.2
Current medications	
Beta-blockers	171 (95%)
ACEIs or ARBs	147 (81.7%)
Diuretics	125 (69.4%)
MRAs	109 (60.6%)
Warfarin	41 (22.8%)
Isosorbide dinitrate + hydralazine	23 (12.8%)
Digoxin	15 (8.3%)
Ivabradine	6 (3.3%)
Achievement of target doses (Beta-blockers, ACEIs or ARBs and MRAs)	43.6%
History of previous ADHF	28 (15.6%)

Abbreviations: NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; MRAs, mineralocorticoid receptor antagonists; ADHF, acute decompensated heart failure.
* atrial fibrillation, gout, old cerebrovascular accident, cancer, rheumatoid arthritis, osteoarthritis, obesity, hyperthyroid, hypothyroid, pulmonary hypertension, cirrhosis, asthma, thalassemia, major depressive disorder, deep vein thrombosis, pulmonary embolism, osteoporosis, benign prostatic hyperplasia, gastroesophageal reflex disease, systemic lupus erythematous.

(Spearman's correlation coefficient r = 0.177; p = 0.018). Patients with poor medication adherence had significantly higher scores on the MLHFQ emotional domain subscale, suggesting poorer quality of life, compared with patients with medium or high medication adherence (Kruskal−Wallis test p = 0.03), as shown in Table 3. From the univariate analysis, income, NYHA classification, number of comorbidities, number of medications, a history of previous acute decompensated HF and duration of HF were found to be statistically significant $p < 0.05$. Therefore, those variables were chosen to enter to the multiple regression analysis in the second step. After covariate adjustment using multiple regression analysis, medication adherence was found to be associated with quality of life (R = 0.426; adjusted R^2 = 0.149; F = 5.460; $p < 0.001$), and shown to have the strongest relationship compared to other covariates (Table 4). No multicollinearity was found among the independent variables (the minimum tolerance was 0.803 and the maximum variance inflation factor (VIF) for multicollinearity was 1.246).

Table 2
Quality of life and medication adherence in chronic heart failure patients

	Mean	Median	Std. deviation	Percentiles of scores			Medication adherence		
				25	50	75	High	Medium	Poor
Total MLHFQ (0−105)	13.0	11.0	8.6	17	11	7	N/A	N/A	N/A
Physical MLHFQ score (0−40)	6.4	5.0	5.2	10	5	2	N/A	N/A	N/A
Emotional MLHFQ score (0−25)	2.6	2.0	2.6	4	2	0	N/A	N/A	N/A
MMAS-8 (0−8)	7.1	7.0	1.0	6.8	7	8	69 (38.3%)	90 (50.0%)	21 (11.7%)

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Abbreviations: MLHFQ, Minnesota Living with Heart Failure Questionnaire; MMAS, Morisky Medication Adherence Scale; N/A, not available.

Table 3
Quality of life stratified by adherence level

MLHFQ score (mean rank score)	Adherence level			p-value
	Poor (n = 21)	Medium (n = 90)	High (n = 69)	
Total score	109.7	92.0	82.7	0.11
Physical score	106.2	92.4	83.3	0.18
Emotional score	106.7	96.0	78.4	0.03[a]

Abbreviations: MLHFQ, Minnesota Living with Heart Failure Questionnaire.
[a] Statistical significance of differences estimated with the Kruskal−Wallis test.

Discussion

To the best of our knowledge, this is the first study that addressed the relationship between medication adherence and quality of life in patients living with chronic HF. We found a relatively good quality of life in HF patients with medium to high medication adherence. We also found a small positive relationship between quality of life and medication adherence. Althought, average LVEF was low, almost all patients had low levels of NYHA functional classificaiton. Because our setting is the biggest affiliated-teaching university located in the north of Thailand. We have a multi-disciplinary medical team to take care of HF patients who visit our clinic. Although HF patients with low EF would receive good care and appropriate HF medications, we believe that this would delay the progression of HF symptoms. As a result, patients would prolong in stable condition.

Several reasons may explain the good quality of life found in the HF patients in this study. First, the majority of our subjects (97.8%) were classified as NYHA class I or II, which may lead to a better quality of life. Second, 62% of the patients in this study were elderly in retirement age (> 60 years old in Thailand). Therefore, the MLHFQ score is quite low. Finally, our patients had stable chronic HF, with no more than two exacerbations from HF during the previous six months, leading to a good quality of life. Our findings were relevant to other studies[28,33,44,45] in terms of low overall MLHFQ scores. This might be due to similar target populations: NYHA class I or II, elderly (mean age about 65 years), and an outpatient setting. In contrast, poorer quality of life reported by

several studies were most likely due to difference in patient populations such as patients with NYHA class III or IV, hospitalized patients, or those with unstable HF (1 month after discharge)[29,46−50].

In our study, 159 participants (88.3%) reported medium to high medication adherence. The results were consistent with other studies[18,19,51] that used the same method to evaluate medication adherence. In addition, cost is not a major barrier to medication adherence in Thai HF patients, as the Thai government ensures healthcare access to all Thais through a variety of health insurance schemes: Universal Coverage Scheme (UCS), Civil Servant Medical Benefit Scheme (CSMBS), and Social Security Scheme (SSS). In our study, 99.4% of the HF patients were covered by one of the above three schemes, providing access to medications that rarely require any out of pocket expense.

The results from the present study showed a positive relationship between quality of life and medication adherence among patients with HF. Participants with poor medication adherence had a low quality of life; those with good medication adherence were likely to have a good quality of life. The emotional domain of the quality-of-life score showed a statistically significant relationship with the adherence level (p = 0.03). Based on our findings, patients who adhere to their treatment regimen should experience improvements in quality of life. This is consistent with studies of medication adherence in other diseases, such as hypertension[20,52], HIV[21], and asthma[22].

Quality of life has also been shown to be related to other factors, including gender, age, NYHA classification, depression symptom, income, number of drugs, social support, duration of HF, aldosterone antagonist, and digoxin[37,53-57]. We found that, income, NYHA classification, number of comorbidities, number of medications, a history of previous acute decompensated HF and duration of HF had statistically significant relationships with quality of life (Table 4). All of these factors were treated as covariates in our multiple regression model. After adjusting for these, medication adherence was still significantly related to quality of life (adjusted R^2 = 0.149; p < 0.001). We also performed additional analysis by including statistically significant covariates (age, gender, marital status, education, aldosterone antagonist, and digoxin) based on a literature review. The results showed a statistically significant relationship between quality of life and medication adherence (adjusted R^2 = 0.152; p < 0.001).

Table 4
Regression of quality of life on medication adherence

Variable	Unstandardized coefficients	SE	Standardized coefficients	t	p value
Medication adherence	−1.751	0.608	−0.203	−2.882	0.004
Income	0.000	0.000	−0.187	−2.681	0.008
NYHA classification	10.274	4.008	0.177	2.563	0.011
Number of comorbidities	0.392	0.415	0.073	0.946	0.345
Average number of medications (tablets per day)	0.345	0.155	0.167	2.225	0.027
History of previous ADHF	−2.614	1.732	−0.111	−1.509	0.133
Duration of heart failure diagnosis	0.108	0.173	0.044	0.625	0.533

After covariate adjustment using multiple regression analysis, medication adherence was found to be associated with quality of life after controlling for the remaining predictors. (Adjusted R^2 = 0.149).
Abbreviations: NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; ADHF, acute decompensated heart failure; SE, standard error.

This study had several potential limitations. First, this study enrolled a convenient sample of HF outpatients and, therefore, may have limited generalizability. Second, the cross-sectional design precludes drawing conclusions about causality in the relationship between medication adherence and quality of life. Third, by the nature of HF patients in an outpatient setting, who rarely bring their medications to the hospital, we were unable to use other measurements for medication adherence, such as pill count. The appropriate method for measuring medication adherence was self-reported. We believe that our findings were useful based on Haynes et al.[58], who found a similarity between pill count and self-report measurements. Finally, symptoms of depression are another factor that affects quality of life[25]. However, we decided not to collect this data in our study, as our patients did not provide accurate information, which could have led to misleading results.

Conclusion

In conclusion, a small and positive relationship between medication adherence and quality of life was found among chronic heart failure patients. While further study may be needed, it may be prudent to promote medication adherence which may positively impact quality of life in heart failure patients.

Disclosures

None

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Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.hrtlng.2018.09.009.

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