Original article

Prevalence and determinants of medication adherence among patients with acute coronary syndrome in Vietnam

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ABSTRACT

Data on medication adherence in patients with acute coronary symptom (ACS) in Vietnam is scarce. To determine the prevalence and determinants of medication adherence of these patients within six months after hospital discharge, we conducted a prospective observational study in Can Tho City, Vietnam. We defined medication adherence as patients' returning for their scheduled outpatient appointments and having a score of >5 on the medication adherence questionnaire at follow-ups. Patient characteristics, illness perception, and beliefs about medicines were measured during hospitalization. We used logistic regression to analyze data. We included 95 patients with median (interquartile range) age 64 (58 to 79) years, 56.8% of whom were males. Rates of medication adherence at one, three, and six months were 83.2%, 80.0%, and 76.8%, respectively (Cochran Q test p=0.354). Patients who had a higher score in perception of ACS consequences (OR=1.23; 95%CI=1.01-1.50), believed more in the necessity of medications (OR=1.21; 95%CI=1.04-1.40), or who had been adherent at one-month (OR=7.50; 95%CI=1.69-33.35) or three-months (OR=11.56; 95%CI=2.98-44.77), were more likely to be adherent. Patients who perceived themselves to have more personal control of ACS (OR=0.72; 95%CI=0.54-0.96) or believed that physicians overused medicines (OR=0.76; 95%CI=0.63-0.93) were less likely to be adherent. In conclusion, the prevalence of medication adherence of patients with ACS in Vietnam was relatively high and stable during six months after discharge, but there is still room for improvement.

1. INTRODUCTION

Of patients with acute coronary syndrome (ACS), one form of ischemic heart disease (IHD), 54% to 86% adhered inadequately to their cardio-protective medications[1]. In low- and middle-income countries, adherence levels seem to be even lower[2,3]. Good adherence reduces mortality and morbidity and decreases costs to the healthcare system[4-7].

Various factors influence adherence, including patients' demographic and health condition characteristics and factors related to therapy and healthcare systems[1]. Previous studies also showed associations between adherence and illness perception and beliefs regarding medicine, but these associations varied in extent and dimensions[8-11]. Determination of these patient factors may be helpful in predicting their adherence to the use of cardioprotective medications during a long-term follow-up after hospital discharge,

and also for developing appropriate interventions aimed at improving adherence[1]. In Vietnam, where ACS is one of the leading causes of death, data on medication adherence in patients with ACS is scarce[12]. We therefore aimed to determine the prevalence and determinants of medication adherence of these patients within six months after hospital discharge.

2. MATERIALS AND METHODS

2.1. Study population

We conducted a prospective observational study in two public hospitals in Can Tho City between January 2015 and April 2016. In Vietnam, after discharge from hospital an ACS patient is followed up as an outpatient at a public or private healthcare center. Appointments are scheduled every two to four weeks to assess health status and the progress of the disease, issue a new prescription, and schedule the next appointment. The patient can receive medication dispensed at the hospital pharmacy free of charge (if having social health insurance), or at any private pharmacy upon payment. Prescriptions can be redeemed up until the date of the next appointment.

We recruited all ACS patients discharged from the study hospitals from January 2015 to October 2015. Included patients were followed for six months after discharge. The follow-up period ended in April 2016. We included patients who lived in Can Tho City with a discharge diagnosis of unstable angina (I20.0), acute myocardial infarction (I21) or subsequent myocardial infarction (I22)[13], and who gave written informed consent. We excluded patients (1) who could not communicate in Vietnamese; (2) who had cognitive impairment (with a mini mental state examination score less than 18)[14,15]; or (3) who died within six months after discharge. The institutional review boards of two study hospitals approved the study.

2.2. Data sources and data collection

Three researchers (DNQ, NHLB, and TTNT) collected data from medical records and patient interviews. Patients' medical records were retrieved from the medical record archives of the hospitals and data were collected using a predefined data collection form. Data collected from medical records included patient characteristics at baseline: demographic characteristics, risk factors for coronary artery disease, medical history

and comorbidities, discharge diagnoses, whether or not patients underwent a percutaneous coronary intervention (PCI) during hospitalization, and discharge prescriptions.

There were four in-person interviews for each included patient during the study period. The first interview was carried out during hospitalization using the data collection form, the Brief Illness Perception Questionnaire (BIPQ)[16], and the Beliefs about Medicines Questionnaire (BMQ)[17]. The second, third, and fourth interviews were carried out in patients' homes using the Eight-item Morisky Medication Adherence Scale (MMAS-8)[18] at one, three, and six months after discharge, respectively. During these follow-ups, we also asked patients whether or not they complied with medical visits, i.e. attended the last scheduled medical appointments.

2.2.1. Instruments and tools

In the Vietnamese health care context, many measures of medication adherence such as the use of refill data are not feasible due to the absence of electronic dispensing data. We therefore relied on a self-reporting instrument. We used the MMAS-8 because the scale has been widely used in many different languages and illness populations[19]. The MMAS-8 is an eight-item questionnaire to identify barriers and behaviors associated with adherence to medication. Response choices are yes/no for items 1 to 7, and a 5-point Likert response scale for item 8[18].

The BIPQ is a nine-item questionnaire to evaluate dimensions of illness perception. Five items evaluate cognitive illness aspects: consequences (BIPQ 1), timeline (BIPQ 2), personal control (BIPQ 3), treatment control (BIPQ 4), and identity (BIPQ 5). Two items evaluate emotional aspects: concern (BIPQ 6) and emotions (BIPQ 8). One item evaluates illness comprehensibility (BIPQ 7). Responses to the eight items are scored on a scale ranging from 0 to 10. Causality is evaluated using an open-ended response item (BIPQ 9)[16]. We used only the first eight items of this questionnaire in the study.

The BMQ is an 18-item questionnaire to evaluate the cognitive aspect of medications. It comprises two sections. The BMQ Specific evaluates patients' beliefs about the particular medications prescribed for them, and comprises two subscales: Specific Necessity and Specific Concerns. The BMQ General evaluates more general beliefs about medications as a whole, comprising two subscales: General Harm and General Overuse. Each item of the BMQ subscales

is scored on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree)[17].

These questionnaires were previously translated and cross-culturally adapted into Vietnamese[20].

2.2.2. Main outcome measure

Primary outcome was the proportion of adherent patients at six months after discharge. Secondary outcomes were the proportion of adherent patients at one and three months after discharge, and reasons for and factors associated with non-adherence at six months after discharge.

2.2.3. Medication adherence

Based on previous studies on medication adherence using MMAS-8[18,21-23] and the Vietnamese context, we defined patients' medication adherence at each time point of follow-up as having attended their latest scheduled outpatient appointment (complying with medical visits) and having an MMAS-8 score of six or higher upon follow-up measurement.

2.3. Data analysis

We presented data as absolute numbers, percentages, means with standard deviations (SDs), or medians with interquartile ranges (IQRs) as appropriate. The frequencies of categorical variables of two patient groups completing or dropping out of the follow-up were compared using the Chi-square test or Fisher's exact test. Continuous variables were compared using the Student's t-test or Mann-Whitney test. The difference in adherence among three follow-ups was compared using the Cochran Q test. Univariable logistic regression was used to estimate the unadjusted odds ratio (OR) with 95% confidence interval (CI) of factors associated with adherence at the six months. Multivariable logistic regression was used to estimate the adjusted OR with 95% CI of significantly associated factors in univariable analysis. Factors included in univariable analysis were the baseline characteristics collected from medical records, the perception of illness, beliefs about medicines, and adherence at one and three months after discharge. In addition, we explored the impact of attrition bias due to dropouts in sensitivity analyses using multiple imputations to impute missing adherence at six months after discharge, and repeating the analysis based on an imputed sample of all patients included at baseline. All tests were two-sided. P-values of 0.05 or less were considered statistically significant. Analyses were performed using the Statistical Package for the Social Sciences, version 24 (SPSS 24).

3. RESULTS

Overall, 120 patients were included at baseline; 20 patients choose to withdraw from the study (dropout rate 16.7%), and five died (4.2%) during six months after discharge. Therefore, in total, 95 patients were included in our analysis (Figure 1).

The median age of patients (IQR) was 64 years (59 to 79), 56.8% were males, and 86.3% had social health insurance. The majority of patients had hypertension (85.3%) and a discharge diagnosis of NSTEACS (76.8%); did not undergo PCI (73.7%); and received antiplatelet agents (94.7%), ACEIs/ARBs (93.7%), and statins (93.7%). There were no differences in baseline characteristics
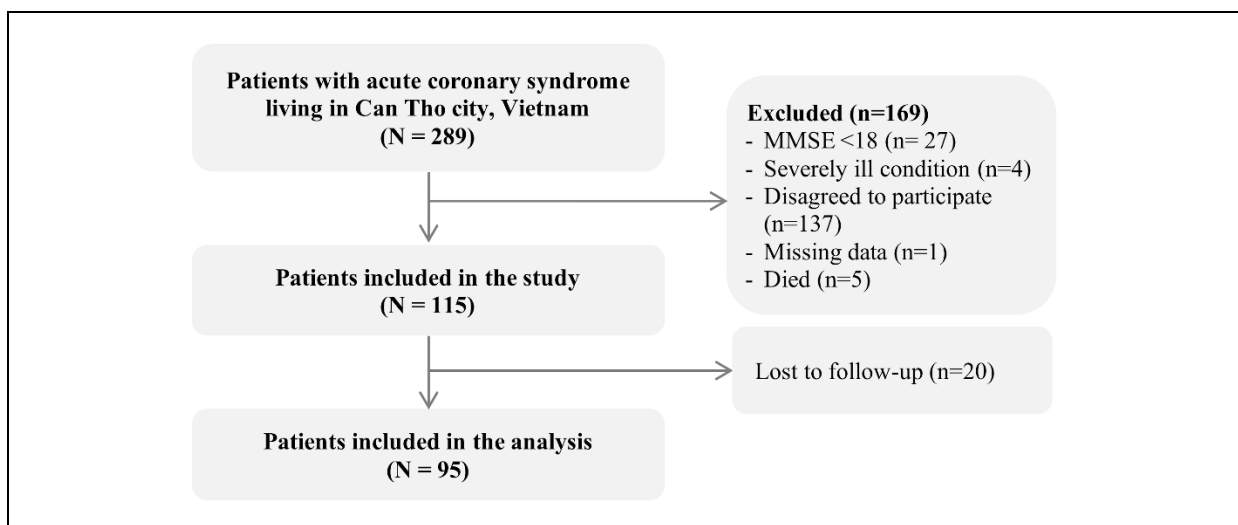
Figure 1. Flowchart of the study population.

Table 1. Patient characteristics.

Patient characteristic	Included patients (N = 115) n (%)		Patients completing the follow-up (N=95) n (%)		Patients dropping out the follow-up (N=20) n (%)		*p*-value[a]
Demographics and general characteristics							
Age, median (IQR)	64 (57-79)		64 (58-79)		67 (49-79)		0.577[b]
Ages ≥65	56	(48.7)	44	(46.3)	12	(60.0)	0.266
Male	63	(54.8)	54	(56.8)	9	(45.0)	0.333
Social health insurance	95	(82.6)	82	(86.3)	13	(65.0)	0.618[c]
Education grade ≥6	45	(39.1)	36	(37.9)	9	(45.0)	0.554
Married	77	(67.0)	63	(66.3)	14	(70.0)	0.750
Financial dependence	60	(52.2)	50	(52.6)	13	(52.0)	0.830
Caregiving dependence	17	(14.8)	15	(15.8)	2	(10.0)	0.733[c]
Caregiver interview	27	(23.5)	23	(24.2)	4	(20.0)	0.780[c]
CAD risk factors and comorbidities							
CAD family history	13	(11.3)	9	(9.5)	4	(20.0)	0.237[c]
Hypertension	96	(83.5)	81	(85.3)	15	(75.0)	0.319[c]
Diabetes	33	(28.7)	29	(30.5)	4	(20.0)	0.344
Dyslipidemia	33	(28.7)	26	(27.4)	7	(35.0)	0.493
Smoking	66	(57.4)	52	(54.7)	14	(70.0)	0.210
Heart failure	16	(13.9)	14	(14.7)	2	(10.0)	0.578[c]
Renal failure	6	(5.2)	5	(5.3)	1	(5.0)	1.000[c]
Peptic ulcer	45	(39.1)	38	(40.0)	7	(35.0)	0.717
Asthma/COPD	4	(3.5)	4	(4.2)	0	(0)	1.000[c]
No. of comorbidities ≥ 2	35	(30.4)	32	(33.7)	3	(15.0)	0.099
Discharge diagnoses							
NSTEACS	92	(76.7)	73	(76.8)	16	(80.0)	1.000[c]
STEACS	28	(23.3)	22	(23.2)	4	(20.0)	
Revascularization and discharge medications							
PCI	28	(24.3)	25	(26.3)	3	(15.0)	0.394[c]
Antiplatelet agent	107	(93.0)	90	(94.7)	17	(85.0)	0.142[c]
Beta blocker	67	(58.3)	55	(57.9)	12	(60.0)	0.862
ACEI/ARB	108	(93.9)	89	(93.7)	19	(95.0)	1.000[c]
Statin	111	(96.5)	92	(96.8)	19	(95.0)	0.540[c]

ACEI/ARB, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; NSTEACS, non-ST elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEACS, ST evaluation acute coronary syndrome.
[a]Using Chi-square test if other tests were not mentioned. [b]Using Mann-Whitney test. [c]Using Fisher's exact test.

Table 2. Patients' perception of illness and belief about medicines.

Patients' perception and belief	Included patients (N = 88) Median (IQR)		Patients completing the follow-up (N=72) Median (IQR)		Patients dropping out the follow-up (N=16) Median (IQR)		*p-value**
BIPQ item							
BIPQ1-Consequences	5	(3-8)	5	(3-7)	5	(3-9)	0.615
BIPQ2-Timeline	10	(3-10)	10	(3-10)	10	(8-10)	0.541
BIPQ3-Personal control	8	(5-10)	8	(5-10)	9	(5-10)	0.719
BIPQ4-Treatment control	8	(6-10)	8	(6-10)	9	(7-10)	0.338
BIPQ5-Identity	6	(2-10)	6	(2-10)	8	(4-10)	0.328
BIPQ6-Concern	10	(8-10)	10	(7-10)	10	(9-10)	0.207
BIPQ7-Understanding	4	(0-8)	5	(0-8)	4	(0-8)	0.747
BIPQ8-Emotional response	2	(0-6)	2	(0-6)	0	(0-8)	0.512
BMQ subscale							
BMQ Specific Necessity	25	(24-25)	25	(23-25)	25	(25-25)	0.159
BMQ Specific Concern	13	(9-17)	12	(9-17)	15	(10-20)	0.322
BMQ General Overuse	14	(11-16)	14	(10-16)	14	(12-15)	0.705
BMQ General Harm	8	(6-11)	8	(6-12)	8	(6-19)	0.449

BPIPQ, Brief Illness Perception Questionnaire; BMQ, Beliefs about Medicine Questionnaire; IQR, interquartile range.
**Using Mann-Whitney test.*

between patients who completed and who dropped out of the study. Median scores ranged from 2 to 10 for BIPQ items (the highest scores in BIPQ 2-Timeline and BIPQ 6-Concern and the lowest score in BIPQ 8-Emotional response) and from 8 to 25 for BMQ subscales (the highest score in BMQ Specific Necessity and the lowest score in BMQ General Harm) (Table 1 and Table 2).

The proportions of adherent patients at one, three, and six months after discharge were 83.2%, 80.0%, and 76.8%, respectively (p=0.354) (Table 3). In sensitivity analysis, imputing values of patients who dropped out, 72.7% were adherent at six months.

Reasons for being non-adherent at six months after discharge were: missing to take medicines in the past two weeks (21.5%), not complying with medical visits (16.9%), sometimes forgetting to take medicine (16.5%), and finding it hassling to stick to treatment (12.7%) (Table 4).

In univariable analysis, factors significantly associated with patient adherence at six months after discharge were BIPQ 1, BIPQ 3, BMQ Specific Necessity, BMQ General Overuse, and patient adherence at one and three months after discharge. In multivariable analysis, BIPQ 1-Consequences (OR 1.35, 95% CI 1.01-1.80, p=0.040), BIPQ 3-Personal control (OR 0.69, 95% CI 0.49-0.98, p=0.035), and adherence at three months after discharge (OR 9.49, 95% CI 1.27-70.66, p=0.028) were associated with adherence at six months (Table 5).

Table 3. Medication adherence among patients with acute coronary syndrome in six months after discharge.

	At one month after discharge (N=95) n (%)		At three months after discharge (N=95) n (%)		At six months after discharge (N=95) n (%)	
Adherence to treatment*	79	(83.2)	76	(80.0)	73	(76.8)
Non-adherence to treatment	16	(16.8)	20	(20.0)	22	(23.2)
Not complying with medical visits	7	(7.4)	8	(8.4)	16	(16.8)
Medication adherence questionnaire scores < 6	9	(9.5)	12	(12.6)	6	(6.3)

Cochran Q test showed no difference in adherence to treatment at one, three, and six months after discharge (p=0.354).

Table 4. Non-adherence behaviors at six months after discharge.

Behavior	Frequency	Percentage (N = 79)
Not complying with medical visits	16	16.9*
Forgetting to take medicine sometimes	13	16.5
Missing taking medicine over past 2 weeks	17	21.5
Stopping medicine when feeling worse	5	6.3
Forgetting to take along medicines when travelling	1	1.3
Not taking all medications yesterday	4	5.1
Stopping medicine if condition is under control	4	5.1
Hassling to stick to treatment	10	12.7
Having difficulty remembering to take all medications	1	1.3

N = 95 (All patients completing the six-month follow-up were interviewed)

4. DISCUSSION

4.1. Principal findings

Over three-quarters of patients with ACS in Vietnam were adherent to treatment in the first six months after discharge and this proportion remained stable during the follow-up period. At six months after discharge, missing/forgetting taking medicine, not complying with medical visits, and hassling to stick to treatment were the most frequently reported reasons for non-adherence; patients who perceived that ACS has serious consequences, who believed stronger in the necessity of prescribed medications, or who were adherent at one or three months after discharge were more likely to be adherent; patients who perceived they had personal control of ACS or believed that physicians overused medicines were less likely to be adherent.

4.2. Strengths and weaknesses of the study

Major strengths of this study are the observational design, prospectively following patients for six months after discharge; the evaluation of patient adherence to treatment for ACS at different time points; and identification of reasons for and factors associated with non-adherence, using validated questionnaires that had

Table 5. Factors associated with medication adherence at six months after discharge.

Factors	Non-adherence (N = 14)		Adherence (N = 58)		Univariable analysis			Multivariable analysis		
					OR	95% CI	*p*-value	OR	95% CI	*p*-value
BIPQ 1	5	(0; 7)	6	(4; 8)	1.23	1.01-1.50	**0.041**	1.35	1.01-1.80	**0.040**
BIPQ 3	10	(10; 10)	8	(3; 10)	0.72	0.54-0.96	**0.026**	0.69	0.49-0.98	**0.035**
BMQ Specific Necessity	25	(17; 25)	25	(24; 25)	1.21	1.04-1.40	**0.013**	0.94	0.78-1.14	**0.532**
BMQ General Overuse	15	(13; 18)	12	(10; 14)	0.76	0.63-0.93	**0.009**	1.06	0.88-1.29	**0.527**
Patient adherence at one month after discharge	9	64.3	54	93.1	7.50	1.69-33.35	**0.008**	5.27	0.53-52.34	**0.156**
Patient adherence at three months after discharge	6	42.9	52	89.7	11.56	2.98-44.77	**<0.001**	9.49	1.27-70.66	**0.028**

BIPQ, Brief Illness Perception Questionnaire; BMQ, Beliefs about Medicines Questionnaire; CI, confidence interval; OR, odds ratio.

been translated and cross-culturally adapted into Vietnamese. Little is known as to what extent physicians in Vietnam assess medication adherence in patients and discuss this with them. The findings of our study can encourage physicians to identify reasons for and associated factors of non-adherence and promote adherence to prescribed medications during long-term follow-up after discharge. These findings can form the basis for further studies on medication adherence (patterns, associated factors, reasons, interventions, etc.) of patients with coronary diseases in Vietnam.

Several issues in our study should be considered. First, we could not estimate the sample size because of lack of previously appropriate studies. Second, data derived for this study was limited to two hospitals in Can Tho and restricted to the local residents. However, these are the two largest public hospitals in Can Tho that provide medical services to most patients with ACS in the city. Third, our study relied on the MMAS-8, which could be biased by inaccurate patient recall or patients giving socially desirable responses. However, the scale has been proven to be reliable and to correlate well with other methods measuring patients' medication adherence and health outcomes[18,21,22]. More studies should consider more tools for measuring medication adherence. Patients were interviewed by trained pharmacy students, but neither physicians nor pharmacists were able to make patients feel more self-confident about reporting their behaviors of non-adherence to treatment. Moreover, it might be the most economically feasible method for measuring medication adherence in a resource-limited country like Vietnam. Fourth, due to the long-term benefits of using cardioprotective

medications in patients with ACS, further studies should be conducted to evaluate patient adherence to treatment over longer periods, especially up to 12 months after hospital discharge. Fifth, although every effort was made to obtain information for all patients at the time of follow-up, information was available for only 83% of the patients. However, the baseline characteristics of dropouts and patients completing the follow-up were similar, and the proportion of adherent patients in the sensitivity analysis was still approximately three-quarters. Finally, many factors can be associated with patient adherence, such as prior myocardial infarction, patient knowledge of the disease, number of prescription medications, etc. that need to be considered in further studies.

4.3. Possible explanations and comparison with other studies

Approximately one-quarter of patients were non-adherent to secondary prevention medications. Poor adherence in patients with IHDs has been well documented[1]. Results from the Global Registry of Acute Coronary Events (GRACE) project demonstrated that, after 6 months, 8-20% of patients were no longer taking medication prescribed upon discharge[24]. Others have reported similar figures[25,26]. In line with a systematic review by Naderi (2012)[27], adherence was relatively stable over 6 months. Missing/ forgetting to take medicine and hassling to stick to treatment were reasons frequently reported by patients for non-adherence to their medications; these reasons were consistent with previous studies[26,28,29].

A systematic review by Chen et al. (2015)[1] reported many factors associated with adherence, but the associations varied between

studies. Our findings showed that patient adherence to treatment was associated with perceived lower consequences and higher personal control of ACS. Previous studies also showed associations between adherence and illness perception, but variable in extent and dimensions[11]. Our study indicated that adherence was positively associated with patients' beliefs regarding the necessity of their medications. This association was seen previously in IHDs and chronic diseases[9,10], and suggests that stronger beliefs about general overuse of medications would lead to lower medication adherence.

The findings of our study warrant further research to develop strategies aimed at patients having concerns about their illness and treatment. Such interventional strategies may include counselling the patients about their illness and medications upon discharge and during follow-up[30]. This role could be taken up by a clinical pharmacist[31,32]. The role of pharmacists in Vietnam has been expanding from dispensing medications to providing services about medication management to support a rational use of medicine[33]. With an increasing number of patients needing long-term use of secondary prevention medications for treatment of chronic diseases, the pharmacist should become an essential partner to help other healthcare professionals and patients to make optimal use of available resources and to achieve expected therapeutic outcomes.

5. CONCLUSIONS

Medication adherence among patients with acute coronary syndrome in Vietnam was relatively high and stable, at about three-quarters, during six months after discharge, but there is still room for improvement.

6. ACKNOWLEDGMENTS

Conflict of interest
The authors declare no potential conflicts of interest with respect to this research and publication.

Ethics approval
The study was approved by the institutional review boards of the Can Tho Central General Hospital and Can Tho General Hospital in Can Tho City, Vietnam. Informed consent was obtained from all participants.

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