Original Article

Mahidol Univ J Pharm Sci 2016; 43 (3), 143-152

Adherence to clinical practice guidelines on prescribing for patients with acute coronary syndrome in Vietnamese hospital practice and its association with clinical outcomes

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Abstract

Sufficient use of guideline-recommended medications reduced in-hospital and post-discharge mortality rates in acute coronary syndrome (ACS) patients. Little is known about prescribing patterns for ACS patients in Vietnam. The objectives of this study were to identify the extent of adherence to clinical guidelines on prescribing for ACS patients in Vietnamese hospitals and its association with patients' mortality and re-admission rates within one month after discharge. The study was conducted at two large public hospitals in Ho Chi Minh city, Vietnam to include patients with ACS discharged between April and June 2015. Patients' characteristics and details of medications prescribed were reviewed relying on prescribing indicators. The patients then were followed up for one month after discharge to collect information about clinical events. There were 106 ACS patients included (mean age of 64 years and 66.0% male). The percentages of patients receiving aspirin, P_2Y_{12} inhibitors, dual antiplatelet therapy, or statins were high (around 90%). The prescribing of beta blockers was low (39.6% at arrival and 52.4% at discharge). The use of angiotensin converting enzyme inhibitors/ angiotensin II receptor blockers was 62.1% at arrival and increased at discharge (91.8%). There were 16 patients loss to follow-up and 13 patients experienced clinical events. There has been no significant difference in one-month-after-discharge mortality and re-admission rates between patients receiving all guideline-recommended medications and those with fewer recommended medications. Overall, adherence to ACS guidelines in Vietnamese hospital practice was good. Large studies are needed to identify the association between full adherence to guideline-recommended medications and patients' clinical events.

Keyword: Guideline adherence; Prescribing indicators; Acute coronary syndrome; Vietnam

1. INTRODUCTION

Ischemic heart disease (IHD) is one of the leading causes of death worldwide. There were more than 7 million people died due to IHD in 2008 (12.7% of total global mortality), and more than 80% of those were from low- and middle-income countries[1]. Ischemic heart disease is a group of heart diseases including acute coronary syndrome (ACS), which is considered as the main cause of IHD deaths[2]. In practice, ACS could be seen with three clinical manifestations: ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA)[3]. Several international/ national guidelines have been published to guide physicians on prescribing evidence-based medications for patient with ACS. According to these guidelines, the use of antiplatelet agents (aspirin and/or P2Y12 inhibitors), beta blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACEIs/ARBs) and hydroxymethylglutaryl-coenzyme A reductase inhibitors (HMG-CoA reductase inhibitors or statins) to treat patients with ACS has been recommended[4-8]. Continuous and consistent use of guideline-recommended medications reduced in-hospital and post-discharge mortality rates in ACS patients[9-11]. However, recent studies

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found that the adherence to clinical guidelines was not optimal in the treatment of ACS[12-15].

Ischemic heart disease is also a major leading cause of death in Vietnam[16]. The Vietnam National Heart Association (VNHA) adopted international guidelines and published the first guideline on management of ACS in 2006 and updated it in 2008[8]. So far, knowledge about prescribing patterns for patients with ACS in Vietnamese hospitals as well as the association between guideline adherence and patients' health outcomes is limited. Therefore, the aim of this study was to identify the extent of adherence to clinical practice guidelines on prescribing for patients with ACS in Vietnamese hospital and its association with patients' mortality and re-admission rates within one month after discharge.

2. MATERIALS AND METHODS

2.1 Study design and setting

A prospective, cross-sectional study was conducted in two cardiology wards (about 50 beds each) at two large provincial general public hospitals in Ho Chi Minh city.

2.2 Ethical consideration

The study was approved by the medical ethics committee, management board of the study hospitals.

2.3 Data collection

We included patients diagnosed with ACS (ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction and unstable angina), who were discharged between April and June 2015. We excluded patients who did not fully complete treatment i.e. patients who were transferred to another hospital for further treatment or patients who were discharged with or without permission of their physicians when the therapy was incomplete. Patients' characteristics and details of treatment were collected from medical records of patients by a researcher using a pre-defined data collection form. Data included age, sex, health insurance, coronary artery disease risk factors, medical history of myocardial infarction, invasive procedures (including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG)), comorbidities (peptic ulcer, asthma/ chronic obstructive pulmonary disease, renal failure, hepatic failure and heart failure), in-hospital revascularization (invasive procedure (PCI or CABG) or non-invasive procedure (with or without fibrinolysis)), and medications prescribed within the first 24 hours after hospital admission and at hospital discharge. The patients then were followed up for one month after discharge to collect information about their health status and clinical events (deaths and re-admissions) by calling directly to the patients (and/or their relatives) once a week, from discharge till the end of follow-up (30 days). If the patient had more than one event in this period, we only included the most severe event. Patients were considered as loss to follow-up if they could not be reached after 3 phone calls during the study time.

The prescribed medications were reviewed for a list of prescribing indicators to assess guideline adherence. The indicators were pooled from current guidelines of the Vietnam National Heart Association (VNHA), the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) and published literature (Table 1)[4-8,12,25-28]. By definition of the indicators, adherence to guidelines was evaluated based on the appropriateness of medications/ medication groups, medication combinations, starting time and route of administration for individual patients according to their medical status (e.g., having no contraindications to specific medications). For example, giving aspirin to an ACS patient having asthma is considered inappropriate.

Table 1. List of prescribing indicators used in the study [4-8,12,25-28]

Indicators	Description	Class and level of recommendations					
		VNHA		ACC/AHA		ESC	
		NSTE ACS	STE ACS	NSTE ACS	STE ACS	NSTE ACS	STE ACS
At arrival							
Aspirin or a P_2Y_{12} inhibitor at arrival	ACS patients without contraindications of aspirin or P_2Y_{12} inhibitors who received aspirin or clopidogrel/ticagrelor within the first 24 hours after hospital admission.	I	I	I-A	I-A	I-A	I-A
Dual antiplatelet therapy at arrival	ACS patients without contraindications of aspirin and P_2Y_{12} inhibitors who received a combination of aspirin and clopidogrel/ticagrelor within the first 24 hours after hospital admission.	I	I	I-B	I-B	I-A	I-A
Beta blocker at arrival	ACS patients without beta blocker contraindications who received a beta blocker within the first 24 hours after hospital admission.	I	I	I-B	I-B	I-A	I-A
ACEI/ARB at arrival	ACS patients with evidence of heart failure, LVSD, diabetes or hypertension; and without ACEI/ARB contraindications who received an ACEI/ARB within the first 24 hours after hospital admission.	I	I	I-C	I-C	NA	NA

Table 1. List of prescribing indicators used in the study (Continued) [4-8,12,25-28]

Indicators	Description	Class and level of recommendations					
		VNHA		ACC/AHA		ESC	
		NSTE ACS	STE ACS	NSTE ACS	STE ACS	NSTE ACS	STE ACS
Statin at arrival	ACS patients without statin contraindications who received a statin within the first 24 hours after hospital admission.	NA	I	NA	NA	I-A	I-B
At discharge							
Aspirin or a P_2Y_{12} inhibitor at discharge	ACS patients without contraindications of aspirin or P_2Y_{12} inhibitors who received aspirin or clopidogrel/ticagrelor at hospital discharge.	I	I	I-A	I-A	I-A	I-A
Dual antiplatelet therapy at discharge	ACS patients without contraindications of aspirin and P_2Y_{12} inhibitors who were prescribed a combination of aspirin and clopidogrel/ ticagrelor at hospital discharge.	I	I	I-B	I-B	I-A	I-A
Beta blocker at discharge	ACS patients without beta blocker contraindications who were prescribed a beta blocker at hospital discharge.	I	I	I-B	I-B	I-A	I-A
ACEI/ARB at discharge	ACS patients with evidence of heart failure, LVSD, diabetes or hypertension; and without ACEI/ARB contraindications who were prescribed an ACEI/ARB at hospital discharge.	I	I	I-A	IIa-A	I-A	IIa-A

Table 1. List of prescribing indicators used in the study (Continued) [4-8,12,25-28]

Indicators	Description	Class and level of recommendations					
		VNHA		ACC/AHA		ESC	
		NSTE ACS	STE ACS	NSTE ACS	STE ACS	NSTE ACS	STE ACS
Statin at discharge	ACS patients without statin contraindications who were prescribed a statin at hospital discharge.	I	I	I-A	I-B	I-B	I-A
Received all guideline-recommended medications	ACS patients without contraindications of any guideline-recommended medications who were prescribed aspirin, a P_2Y_{12} inhibitor, a beta blocker, an ACEI/ARB and a statin at hospital discharge.	NA	NA	NA	NA	NA	NA

I, class I of recommendation; I-A, class I of recommendation and level A of evidence; I-B, class I of recommendation and level B of evidence; IIa-A, class IIa of recommendation and level A of evidence; NA, not available. ACC/AHA, American College of Cardiology/American Heart Association; ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker; ACS, acute coronary syndrome; ESC, European Society of Cardiology; LVSD, left ventricular systolic dysfunction; NSTEACS, non-ST elevation acute coronary syndrome; STEACS, ST elevation acute coronary syndrome; VNHA, Vietnam National Heart Association.

2.4 Data analysis

Descriptive analysis was performed using statistical package for the social sciences (SPSS) version 20.0 to calculate percentages of eligible patients who were prescribed guideline-recommended medications during the first 24 hours of hospitalization and at hospital discharge. Eligible patients for being prescribed aspirin, a P_2Y_{12} inhibitor, dual antiplatelet therapy, a beta blocker or a statin were patients without contraindications to the medications. Differences in clinical events between patients receiving all guideline-recommended medications (aspirin, a P2Y12 inhibitor, a beta blocker, a statin, and an ACEI/ARB) and those with fewer recommended medications were tested by Fisher's exact test. Significant level was set at $p < 0.05$.

3. RESULTS

A total of 106 ACS patients were included. Of which, 37 (34.9%) patients were diagnosed with NSTEMI, 36 (34.0%) with STEMI and 33 (31.1%) with UA. A mean age of patients was 64 (ranging from 33 to 91), with 46.2% of the patients were over 65 years old. The majority of patients were male (66.0%) and had hypertension (68.9%). Thirty-six (34.0%) patients reported having prior myocardial infarction, 50 (47.2%) underwent PCI, and no patients underwent CABG or received fibrinolysis (Table 2).

Table 2. Patient characteristics

Patient characteristics	Type of ACS			Overall (n = 106)
	UA (n = 33)	NSTEMI (n = 37)	STEMI (n = 36)	
Demographics and general characteristics				
Mean age (±SD)	67 ± 13	66 ± 14	59 ± 11	64 ± 13
Male	17	21	32	70 (66.0 %)
Health insurance	34	28	29	91 (85.8%)
Hospitalized with chest pain	28	29	32	89 (84.0%)
Hospitalized early	14	8	11	33 (31.1%)
CAD risk factors				
CAD family history	0	0	1	1 (0.1%)
Hypertension	32	24	17	73 (68.9%)
Diabetes	17	9	9	35 (33.0%)
Dyslipidemia	8	10	2	20 (18.9%)
Smoking	8	5	14	27 (25.5 %)
CRP/fibrinogen increased	10	11	10	31 (29.2 %)
Age ≥65	22	19	8	49 (46.2%)
Medical history and comorbidities				
Prior MI	14	9	13	36 (34.0%)
Peptic ulcer	19	12	8	39 (36.7%)
Asthma/COPD	1	0	1	2 (1.9%)
Renal failure	3	4	2	9 (8.5%)
Heart failure	0	1	0	1 (0.9%)
In-hospital revascularization				
PCI	14	13	23	50 (47.2%)
CABG	0	0	0	0 (0.0%)
Using fibrinolysis	0	0	0	0 (0.0%)

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

The percentages of patients receiving guideline-recommended medications (aspirin, P_2Y_{12} inhibitors or aspirin, dual antiplatelet therapy, statins) at arrival and at discharge were considerably high (around 90%). The prescribing of beta blockers at arrival and at discharge was low, accounting for 39.6% and 52.4% of eligible patients, respectively. The use of angiotensin converting enzyme inhibitors or angiotensin II receptor blockers (ACEIs/ARBs) at arrival was limited (62.1%); however, this increased at discharge (91.8%). Only 43.6% (17/39) of eligible patients were prescribed all guideline-recommended medications at discharge (Table 3).

Table 3. Drugs prescribing in ACS management

Indicators	Number of eligible patients receiving guideline-recommended medication	Number of eligible patients	Percentage of eligible patients receiving guideline-recommended medication
At arrival			
Aspirin or P2Y12 inhibitor	82	80	97.6
Dual antiplatelet therapy	82	74	90.2
Beta blocker	91	36	39.6
ACEI/ARB	103	64	62.1
Statin	96	89	92.7
At discharge			
Aspirin or P2Y12 inhibitor	82	81	98.8
Dual antiplatelet therapy	82	71	86.6
Beta blocker	84	44	52.4
ACEI/ARB	98	90	91.8
Statin	104	98	94.2
Received all guideline-recommended medications	39	17	43.6

ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker.

All 106 patients were followed up for clinical events within 30 days after discharge. There were 16 patients loss to follow-up. Among 90 remaining patients, 13 experienced clinical events (3 deaths and 10 re-admissions).

As presented in Table 3, 39 out of 106 patients were delivered all guideline-recommended medications. After reviewing patients' prescriptions, two groups of patients were identified for sub analysis: patients receiving all guideline-recommended medications (aspirin, a P_2Y_{12} inhibitor, a beta blocker, a statin, and an ACEI/ARB) and those receiving some of recommended medications. There were no significant differences in one-month-after-discharge mortality and re-admission rates between these two groups (41.7% vs 58.3%, p=0.125).

4. DISCUSSION

This prospective study gave insight into medication management for ACS patients at arrival and at discharge from two large Vietnamese hospitals. In line with previous studies, patients with ACS in our study had a mean age above 60 years, were predominantly male and frequently had chronic comorbidities such as hypertension, dyslipidemia and diabetes mellitus[15,17-19]. In general, physicians highly adhered to clinical practice guidelines. Adherence to the guidelines seemed relatively good for antiplatelet agents, ACEIs/ARBs and statins, but suboptimal for beta blockers. Almost all eligible patients were prescribed aspirin alone or dual antiplatelet agents at arrival and at discharge. These findings are consistent with many other studies from around the world[18-23]. It is well known that aspirin has an essential role in ACS treatment[24,25]. In addition, there is also much evidence supporting giving a P_2Y_{12} inhibitor (clopidogrel or ticagrelor) together with aspirin for up to 1 year following an ACS,[26-28] but physicians may have concerns about the balances between benefit and risk as well as an additional cost of the second anti-platelet agent.

The percentage of patients prescribed beta blockers at arrival was suboptimal and lower than that of other studies (65-83%)[12-14]. An explanation of underused beta blockers, especially within the first 24 hours after hospital

admission, may be physicians'concerns about adverse effects of beta blockers on patients with diabetes mellitus or heart failure. The initiation of oral beta blockers at arrival is recommended for all ACS patients without contraindications. Furthermore, it has been suggested that patients with contraindications should be re-assessed during hospital stay for beta blocker indication because of well-established its benefits for secondary prevention[4-8,15,20]. The use of ACEIs/ ARBs and statins in our study is higher compared to previous studies[21-23]. This is encouraging since there has been much evidence provided in the guidelines supporting the role of ACEIs/ ARBs (ISIS-4, GISSI-3 trials, etc.) and statins (PROVE-IT TMI 22, MIRACL, A to Z trials, etc.) in the management of patients with ACS[4-7].

It has been proven that sufficient use of guideline-recommended medications could reduce re-admission and mortality rates of ACS patients during hospital stay and post discharge[9-11]. However, this association has not been found in our study. Reasons for this may be due to a small sample size (39 eligible patients) and/or short time of follow-up. Studies including higher number of patients and in longer time should be conducted to find this relationship.

In conclusion, adherence to ACS prescribing guidelines in Vietnamese hospital practice was good. However, the use of beta blockers was still suboptimal. The association between full adherence to guideline-recommended medications and patients' clinical events within one month after discharge has not been found.

5. ACKNOWLEDGEMENTS

The authors would like to thank the two study hospitals for the great collaborations as well as for giving permission to conduct the present study.

REFERENCES

1. Finegold JA, Asaria P, Francis DP. Mortality from ischaemic heart disease by country, region, and age: statistics from World Health Organisation and United Nations. Int J Cardiol. 2013; 168:934-45.
2. Moran AE, Forouzanfar MH, Roth GA, Mensah GA, Ezzati M, Murray CJ, et al. Temporal trends in ischemic heart disease mortality in 21 world regions, 1980 to 2010: the Global Burden of Disease 2010 study. Circulation. 2014;129:1483-92.
3. Allen LA, O'Donnell CJ, Camargo CA, Giugliano RP, Lloyd-Jones DM. Comparison of long-term mortality across the spectrum of acute coronary syndromes. Am Heart J. 2006;151(5):1065-71.
4. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2011;32:2999-3054.
5. Jneid H, Anderson JL, Wright RS, Adams CD, Bridges CR, Casey DE Jr, et al. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/non-ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): A report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2012;60:645-81.
6. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al. 2013 ACCF/ AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2013;61: e78-e140.
7. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012;33:2569-619.
8. Vietnam National Heart Association. Recommendations in 2008 on the Cardiovascular and Metabolic Diseases. Ha Noi: Vietnamese Medical Publisher; 2008.

9. Fox KA, Steg PG, Eagle KA, Goodman SG, Anderson FA Jr, Granger CB, et al. Decline in rates of death and heart failure in acute coronary syndromes, 1999-2006. JAMA. 2007;297(17):1892-1900.
10. Jernberg T, Johanson P, Held C, Svennblad B, Lindbäck J, Wallentin L. Association between adoption of evidence-based treatment and survival for patients with ST-elevation myocardial infarction. JAMA. 2011;305 (16):1677-84.
11. Mandelzweig L, Battler A, Boyko V, Bueno H, Danchin N, Filippatos G, et al. The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. Eur Heart J. 2006;27(19): 2285-93.
12. Flotta D, Rizza P, Coscarelli P, Pileggi C, Nobile CG, Pavia M. Appraising hospital performance by using the JCHAO/ CMS quality measures in Southern Italy. PLoS ONE. 2012;7(11):e48923.
13. Longenecker JC, Alfaddagh A, Zubaid M, Rashed W, Ridha M, Alenezi F, et al. Adherence to ACC/AHA performance measures for myocardial infarction in six Middle-Eastern countries: association with in-hospital mortality and clinical characteristics. Int J Cardiol; 2013:167 (4):1406-11.
14. Roe MT, Peterson ED, Newby LK, Chen AY, Pollack CV Jr, Brindis RG, et al. The influence of risk status on guideline adherence for patients with non-ST-segment elevation acute coronary syndromes. Am Heart J. 2006;151(6):1205-13.
15. Lopez-Sendon J, Swedberg K, McMurray J, Tamargo J, Maggioni AP, Dargie H, et al. Expert consensus document on beta-adrenergic receptor blockers. Eur Heart J. 2004;25(15):1341-62.
16. Ngo AD, Rao C, Hoa NP, Adair T, Chuc NT. Mortality patterns in Vietnam, 2006: findings from a national verbal autopsy survey. BMC Res Notes. 2010;3:78.
17. Chew DP, Amerena J, Coverdale S, Rankin J, Astley C, Brieger D. Current management of acute coronary syndromes in Australia: observations from the acute coronary syndromes prospective audit. Intern Med J. 2007;37(11):741-8.
18. Liosis S, Bauer T, Schiele R, Gohlke H, Gottwik M, Katus H, et al. Predictors of 1-year mortality in patients with contemporary guideline-adherent therapy after acute myocardial infarction: results from the OMEGA study. Clin Res Cardiol. 2013; 102(9):671-7.
19. Vermeer NS, Bajorek BV. Utilization of evidence-based therapy for the secondary prevention of acute coronary syndromes in Australian practice. J Clin Pharm Ther. 2008;33(6):591-601.
20. Vietnam National Heart Association. Consensus of experts on beta-blockers in cardiovascular diseases and internal medicine. Ho Chi Minh city: Vietnamese Medical Publisher; 2010.
21. Spencer FA, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Decade-long changes in the use of combination evidence based medical therapy at discharge for patients surviving from acute myocardial infarction. Am Heart J. 2005;150(4):838-44.
22. Syed IA, Riaz A, Ryan A, Reilly MO. Secondary prevention for coronary artery disease: are we following the guidelines? Ir J Med Sci. 2010;179(4):535-7.
23. Kassab YW, Hassan Y, Aziz NA, Akram H, Ismail O. Use of evidence-based therapy for the secondary prevention of acute coronary syndromes in Malaysian practice. J Eval Clin Pract. 2013;19(4):658-63.
24. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ 2002;324(7329): 71-86.
25. Berger JS, Brown DL, Becker RC. Low-dose aspirin in patients with stable cardiovascular disease: a meta-analysis. Am J Med. 2008; 121(1):43-9.
26. Chen ZM, Jiang LX, Chen YP, Xie JX, Pan HC, Peto R, et al. Addition of clopidogrel to aspirin in 45,852 patients with acute

myocardial infarction: randomised placebo-controlled trial. Lancet. 2005;366(9497): 1607-21.
27. Sabatine MS, Cannon CP, Gibson CM, López-Sendón JL, Montalescot G, Theroux P, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. N Engl J Med. 2005;352(12):1179-89.
28. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med. 2001;345(7):494-502.