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Research Article

Performance of the GRACE risk score 2.0 for predicting mortality and Medication Use in Acute Coronary Syndrome patients in Ho Chi Minh city

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ABSTRACT

The Global Registry of Acute Coronary Event (GRACE) risk score was recommended to predict mortality in patients with acute coronary syndrome (ACS). Sufficient use of guideline-recommended medications decreases post-discharge mortality rate in ACS patients. Evidence on the relationship between risk stratification and medication use in Vietnamese patients with ACS is limited. The objective of this study was to determine the relationship between risk stratification and medication use at discharge in ACS patients. This was a retrospective cross-sectional study. Data was collected from medical records of all patients with ACS discharged from The Heart Institute in Ho Chi Minh city, Viet Nam between April and October, 2015. Patients were included if having information of 6-month mortality after discharge. The GRACE risk score version 2.0 was used to stratify patients into three risk subgroups. Prescribing indicators were used to assess the use of medications at discharge. Logistic regression was used to determine the relationship between risk stratification and medication use at discharge. There were 217 patients included. Regarding mortality risk within 6 months after discharge, 94 (43.3%) patients were classified into low-risk group, 75 (34.6%) patients into moderate-risk group, and 48 (22.1%) patients into high-risk group. At discharge, antiplatelets were used in almost ACS patients (98.8%). The use of β-blockers was suboptimal (64.8%). Only 61.0% of patients were prescribed all guideline-recommended medications. There was a reverse association between risk stratification and medication use at discharge. The low use of β-blockers in ACS patients needs to be investigated, especially in high-risk patients.

1. INTRODUCTION

Acute coronary syndrome (ACS) is one of the main causes of death worldwide. According to the World Health Organization (WHO) in 2011, it is estimated that 7.3 million people died for ACS[1]. By 2014, ACS is responsible for more than a third of deaths in low- and middle-income countries[2]. In Vietnam, the hospitalization rate of ACS patients increased from 4.2% in 2003 to 9.1% in 2007[3]. The latest international/

national clinical guidelines from cardiovascular organizations such as the American Heart Association (AHA), the European Heart Association (European Society of Cardiology - ESC), The Vietnam National Heart Association (VNHA) have recommended prescribing evidence-based medications to treat patients with ACS[3-7]. Those medications, comprising antiplatelet agents (aspirin, P2Y12 inhibitors, or both), beta blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (ACEIs/ARBs) and statins, have been proved to reduce in-hospital and post-discharge mortality rates in ACS patients[8-10]. However, recent studies have shown that higher risk patients are not always received full and intensive treatments, although they would potentially benefit the most from these therapies[11-15]. This treatment-risk paradox may be caused partly by lacks of proper risk assessment[16]. The pathophysiology of almost all ACS patients is relatively similar, but there are differences in risk status of each individual. Risk stratification in patients with ACS is a necessary approach that helps health care professionals identify ACS patients with high risk and consider the appropriate treatment strategy. Guidelines also state the importance of evaluating risk for ACS patients and recommend that optimal treatment should include early risk stratification .The clinical benefits are not only for predicting each patient's mortality, but also for determining more critical patients who require intensive treatment. The Global Registry of Acute Coronary Events (GRACE) risk score (GRACE 1.0) and updated GRACE 2.0 have been validated to be useful for risk assessment and predicting the risk of short-term and long-term mortality[17]. This scoring model was recommended in several guidelines and applied in clinical practice around the world[4-7, 18]. Data of the GRACE registry are obtained from a worldwide population, including North America, South America, Europe, Australia, and New Zealand[17]. However, stratifying risk is not widely performed in clinical practice for patients with ACS in Vietnamese hospitals and data about the association between risk stratification and medication use are limited. Therefore, this study aims to apply GRACE 2.0 risk score for stratifying Vietnamese ACS patients into risk groups and identify the relationship between risk stratification and medication use at discharge.

2. MATERIALS AND METHODS

2.1. Study design and setting

A retrospective cross-sectional study was conducted at The Heart Institute in Ho Chi Minh city, Viet Nam.

2.2. Data collection

Data was obtained from medical records of all patients with ACS (unstable angina, non-ST elevation myocardial infarction or ST elevation myocardial infarction), discharged from The Heart Institute in Ho Chi Minh city, Viet Nam between April and October, 2015. Patients were included when their information of 6-month mortality after discharge was available. We excluded patients with missing data of at least one variable to calculate GRACE risk score. Information of patients' characteristics and treatment were extracted by two researchers (HMTH and PTBV) from medical records 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 at hospital discharge. Details of all medications prescribed at hospital discharge were collected (brand and generic name of the medication, dose, dosage form, administration route and frequency of administration). Information of patients' contraindications to antiplatelet therapy, beta blockers, ACEI/ARBs or statins was also obtained.

2.3. Ethical consideration

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

2.4. Data analysis

The GRACE risk score version 2.0 includes 8 variables: age; heart rate; systolic blood pressure

(SBP); serum creatinine on hospital admission (history of renal failure or renal function impairment is substituted when there was no information about serum creatinine); Killip classification (diu-retics usage within 24 hours after hospital admission is substituted when there was no information about Killip classification); cardiac arrest; ST-segment deviation on ECG; and elevated cardiac enzyme[17]. Cardiac arrest was defined as rapid ventricular tachycardia with hemodynamic instability, ventricular fibrillation, electrical mechanical dissociation or asystole and requiring cardio-pulmonary resuscitation from onset to admission. ST-segment deviation was defined as ≥ 1-mm elevation or depression of ST-segment level from the baseline on ECG. Increase of cardiac enzyme was defined as positive troponin I[19]. Patients' risk score were calculated using the online GRACE score calculator (http://www.gracescore.org/WebSite/WebVersion.aspx) and classified into three risk groups (high, moderate, low) on GRACE 2.0 scale. According to the predetermined cut-off points in the published risk calculator, patients with a score of ≤ 108 were classified as at low risk, 109-140 moderate risk, and > 140 high risk[20].

Prescribing indicators were used to assess medication use at discharge. Prescribing indicators is defined as the percentage of eligible patients receiving a guideline recommended medication, which was calculated by dividing the number of eligible patients who were prescribed the medication by the total number of eligible patients who should be prescribed the medication, multiplied by 100. Eligible patients for being prescribed the medication were patients who are recommended in guidelines and without contraindications to the medications. In this study, we used published prescribing indicators, which were pooled from previous studies and current guidelines (Table 1)[3-7, 21-25]. The guidelines used were the Vietnam National Heart Association (VNHA), the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA). Multivariable logistic regression with backward stepwise method was used to determine the relationship between patient's risk and medication use at discharge. Other independent variables, which are likely related to the use of medication at discharge, such as risk stratification (moderate vs. low risk and high vs. low risk), sex (male vs. female); diagnosis discharge (NSTEMI vs. UA and STEMI vs. UA), hypertension, dyslipidemia, diabetes, in-hospital invasive procedures, were included in the model to control potentially confounding influences. The variables were selected based on previous studies on factors associated with the use of guideline- recommended medications, except for those that had been already included in the GRACE 2.0 score for risk stratification (such as heart failure or renal failure)[26-27]. Data were analyzed using the Statistical Package for Social Science version 22 (SPSS 22) and Microsoft Excel 2010. Descriptive statistics were used to analyze patients' characteristics and treatment. Differences in patients' characteristics and treatment among risk groups were tested by Chi-square test or Fisher's exact test. Significant level was set at $p < 0.05$.

3. RESULTS

A total of 217 medical records of ACS patients were included in the study, after screening 227 medical records. There were 10 patients excluded because of missing data to calculate GRACE risk score. Regarding mortality risk within 6 months after discharge, 94 (43.3%) patients were classified into low-risk group, 75 (34.6%) patients into moderate-risk group, and 48 (22.1%) patients into high-risk group. A mean age of patients was 68 (ranging from 29 to 94), 59.0% of the patients were over 65 years old. The majority of patients were male (55.3%) and had hypertension (76.5%). Thirty-nine patients (18.0%) reported prior MI and 30 (13.8%) had prior PCI/CABG; 112 (51.6%) patients underwent PCI/ CABG and 105 (41.4%) did not undergo invasive procedures; 174 (81.2%) patients were diagnosed at discharge with US/NTEMI and 43 (19.8%) patients with STEMI.

Table 1. List of prescribing indicators at discharge used in the study[3-7, 21-25]

Indicators	Description
Antiplatelet	ACS patients without contraindications of aspirin or P2Y12 inhibitors who received aspirin or clopidogrel/ ticagrelor at hospital discharge.
Beta blocker	ACS patients without beta blocker contraindications who were prescribed a beta blocker at hospital discharge.
ACEI/ARB	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.
Statin	ACS patients without statin contraindications who were prescribed a statin at hospital discharge.
Received all guideline- recommended medications	ACS patients without contraindications of any guideline- recommended medications who were prescribed an aspirin or a P2Y12 inhibitor, a beta blocker, an ACEI/ARB and a statin at discharge.

ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker; ACS, acute coronary syndrome; LVSD, left ventricular systolic dysfunction.

Table 2. Patient characteristics

Patient characteristics	Overall (n = 217)	Risk groups by GRACE 2.0			P-value
		Low risk (n = 94)	Moderate risk (n = 75)	High risk (n = 48)	
Demographics and general characteristics					
Mean age (±SD)	67.6 (±12.8)	58.7 (±10.5)	71.6 (±9.5)	78.7 (±8.9)	**<0.001**
Male	120 (55.3)	61 (64.9)	42 (56.0)	17 (35.4)	**0.004**
Insurance	176 (81.1)	82 (87.2)	57 (76.0)	37 (77.1)	0.130
Diagnosis discharge					
UA/ NSTEMI	174 (81.2)	81 (86.2)	59 (78.7)	34 (70.8)	**0.001**
STEMI	43 (19.8)	13 (13.8)	16 (21.3)	14 (29.2)	

Table 2. Patient characteristics (Cont.)

Patient characteristics	Overall (n = 217)	Risk groups by GRACE 2.0			P-value
		Low risk (n = 94)	Moderate risk (n = 75)	High risk (n = 48)	
CAD risk factors					
Hypertension	166 (76.5)	71 (75.5)	58 (77.3)	37 (77.1)	0.957
Diabetes	62 (28.6)	28 (29.8)	25 (33.3)	9 (18.8)	0.205
Dyslipidemia	41 (18.9)	20 (21.3)	13 (17.3)	8 (16.7)	0.732
Smoking	56 (25.8)	33 (58.9)	15 (26.8)	8 (14.3)	**0.022**
CRP/fibrinogen increincrease	91 (41.9)	37 (28.7)	26 (48.0)	28 (58.3)	**0.001**
Age ≥65	128 (59.0)	27 (28.7)	56 (74.7)	45 (93.8)	**<0.001**
Medical history and comorbidities					
Prior MI	39 (18.0)	17 (18.1)	17 (22.7)	5 (10.4)	0.225
Prior stroke	4 (1.8)	1 (1.1)	2 (2.7)	1 (2.1)	0.825
Prior undergoing invasive procedure	30 (13.8)	12 (12.8)	13 (17.3)	5 (10.4)	0.567
Peptic ulcer	48 (22.1)	20 (21.3)	12 (16.0)	16 (33.3)	0.075
Asthma/COPD	16 (7.4)	4 (4.3)	8 (10.7)	4 (8.3)	0.273
Heart failure	16 (7.4)	1 (1.1)	3 (4.0)	12 (25.0)	**<0.001**
Renal failure	36 (16.6)	3 (3.2)	12 (16.0)	21 (43.8)	**<0.001**
In-hospital invasive procedure					
Yes (PCI/CABG)	112 (51.6)	55 (58.5)	34 (45.3)	23 (47.9)	0.198
No	105 (48.4)	39 (41.5)	41 (54.7)	25 (52.1)	

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; SEMI, ST elevation myocardial infarction; UA, unstable angina.

At discharge, the use of antiplatelets (aspirin or P_2Y_{12} inhibitors), ACEIs/ARBs and statins were considerably high (more than 90.0%). The prescribing of beta- blockers at discharge was low, accounting for 64.8% of eligible patients.

Antiplatelets were prescribed for all eligible patients in moderate- and high-risk groups and 97.4% of eligible patients in low-risk group (Table 3). Multivariable logistic regression showed that there was no association between risk stratification and the use of antiplatelets (Table 4).

Beta blockers were prescribed for 66.7% and 72.6% eligible patients in low- and moderate-risk groups, respectively. Especially, only 45.5%

of eligible patients at high risk were received beta-blockers at discharge (Table 3). Results from multivariable logistic regression indicated that patients belong to high-risk group were less likely to be prescribed a beta blocker at discharge compared to low risk patients (Table 4).

ACEI/ARBs and statins were prescribed for more than 90.0% of eligible patients in all three risk groups at discharge (Table 3). There was no association relationship between risk stratification and the use of these medications (Table 4).

Only 61.0% of patients were prescribed all guideline-recommended medications. The percentage of eligible patients received all guideline-recommended medications were remarkably low in high-risk group (29.4%, Table 3). Multivariate logistic regression showed that patients with high-risk were less likely to receive all guideline recommended medications at discharge than low-risk patients.

Table 3. Medication use at discharge between risk groups

Prescribing indicators at discharge	Overall % (n/N)	Risk groups by GRACE 2.0			P-value
		Low risk % (n/N)	Moderate risk % (n/N)	High risk % (n/N)	
Antiplatelet	98.8% (166/168)	97.4% (74/76)	100.0% (60/60)	100.0% (32/32)	0.365
Beta blocker	64.8% (118/182)	66.7% (58/87)	72.6% (45/62)	45.5% (15/33)	**0.027**
ACEI/ARB	92.1% (186/202)	90.4% (85/94)	94.5% (69/73)	91.4% (32/35)	0.616
Statin	93.9% (200/213)	91.3% (84/92)	94.6% (70/74)	97.9% (46/47)	0.288
Received all guideline-recommended medications	61.0% (83/136)	61.4% (43/70)	71.4% (35/49)	29.4% (5/17)	**0.009**

n: Number of eligible patients receiving guideline-recommended medication
N: Number of eligible patients
Prescribing indicators: Percentage of eligible patients receiving guideline-recommended medication
ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker.

4. DISCUSSION

This retrospective study gave insight into medication use at discharge in ACS patients with different mortality risk. Similar to previous studies, patients with ACS in our study had a mean age above 60 years, were mainly male and frequently had chronic comorbidities such as hypertension, dyslipidemia and diabetes mellitus[25-28]. The appropriate prescription of guideline-recommended medications seemed relatively good for antiplatelet agents, ACEIs/ARBs and statins, but suboptimal for beta blockers. The use of all guideline recommended medications was also low. Almost all eligible patients were prescribed aspirin or P_2Y_{12} inhibitors at discharge. These findings are in line with many other studies

worldwide[29-32]. It is well established that aspirin has a crucial role in ACS treatment[33-34]. In addition, there is compelling clinical evidence supporting combining a $P_2Y_{12\ inhibitor}$ (clopidogrel or ticagrelor) with aspirin for up to 1 year following an ACS[23-24, 35].

Table 4. Association between risk stratification and medication use at discharge*

	Factor	OR	95% CI	P-value
Antiplatelet	No** association			
Beta blocker	High-risk group †	0.322	0.134-0.772	**0.011**
	Moderate-risk group †	1.277	0.620-2.629	0.507
ACEI/ARB	No association			
Statin	No association			
Received all guideline-recommended medications	High-risk group †	0.193	0.057-0.653	**0.008**
	Moderate-risk group †	1.501	0.663-3.397	0.330

*: Using multivariate logistic regression analysis with backward stepwise method.
**:No association between risk stratification and medication use
†: Low-risk group was used as a reference group
ACEI/ARB, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker; CI, confidence interval; OR, odds ratio.

We observed the higher percentage of eligible patients receiving ACEI/ARBs and statins than those of previous studies[27-28]. This is encouraging as recommendations in guidelines are based on several clinical trials supporting important roles of ACEI/ARBs and statins in the treatment of patients with ACS[36-37].

Among three risk groups, percentages of eligible low-risk patients receiving antiplatelets, ACEI/ARBs and statins are the lowest, which indicated prescribing those medications in low-risk group should be improved. On the other hand, moderate-risk group accounted for the highest proportion of eligible patients being prescribed antiplatelets, beta blockers, ACEI/ARBs and all guideline-recommended medications, compared to the other groups. Noticeably, in the high-risk group, percentages of eligible patients receiving beta blockers and all guideline-recommended medications are significant lower than that in low-risk and moderate-risk groups.

There was a reverse association between risk stratification and the use of beta blockers and all guideline-recommended medications at discharge. The percentage of patients being prescribed beta blockers at discharge was suboptimal and lower than that of other studies (65-83%)[14,21]. Multivariable analysis showed that the patients at high-risk were less likely to receive a beta blocker compared to patients at low-risk ($p = 0.011$, OR = 0.322, 95% CI: 0.134 - 0.772). This can be explained by physicians' concerns

about adverse reactions of beta blockers in patients with comorbidities such as diabetes mellitus or heart failure. It is difficult for health care professionals to evaluate the balance between potential harms and benefits, particularly in high-risk ACS patients. Clinical evidence, however, indicates that beta blockers' benefits outweigh risks in high-risk ACS patients after exclusion of patients that are contraindicated. Therefore, prescribing beta blockers should be improved, especially in high-risk patients with ACS. Patients with contraindications should be re-evaluated during hospital stay for beta blocker usage due to well-known benefits of beta blockers in secondary prevention.[3-7, 38]

The probability for a patient in high-risk group being indicated all guideline-recommended medications (comprising aspirin or $P2Y_{12}$ inhibitor, ACEI/ARB, beta-blocker, and statin) was five time lower than that of a patient in low-risk group ($p = 0.008$, OR = 0.193, 95% CI: 0.057-0.653). This finding is comparable to a study conducted in 6 Middle Eastern countries, when results showed that the proportion of ACS patients in high-risk group being indicated full guideline-recommended medications at discharge was lower than that of patients in low- or moderate-risk groups.[39]

This study can be acknowledged as one of the first studies to determine the relationship between risk stratification and medication use at discharge in ACS patients in Vietnam. Furthermore, the potential confounding impacts of other independent variables on the association between risk stratification and the use of medication at discharge were controlled properly by using multivariable logistic regression. However, evaluation of medication use at admission is beyond the scope of the study. Further studies are needed to investigate the association between risk stratification and medication use at admission in ACS patients in Vietnam.

5. CONCLUSIONS

Pharmacological secondary prevention in patients after an ACS has significantly contributed to decreases in cardiovascular mortality and has undergone important improvements in recent years. Nevertheless, this retrospective cross-sectional study showed that there were differences in medication use between risk groups of ACS patients. The use of guideline-recommended medications, especially β-blockers, in high-risk patients needs to be improved. The reasons why high-risk patients were less likely to receive guideline-recommended medications (particularly β-blockers) than low-risk patients needs to be investigated.

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Conflict of interest

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Ethical approval

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