Characteristics and Outcomes of Treatment for Non-ST-Segment Elevation Acute Coronary Syndrome: Results from a Single Center Registry

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Background: *Acute coronary syndrome (ACS) is a leading health burden worldwide. The Siriraj non-ST-segment elevation acute coronary syndrome (NSTE-ACS) registry was established in 2012. Here, we report in-hospital outcomes and one-year outcomes from patients in the registry.*
Objective: *To investigate and report characteristics and outcomes of treatment for NSTE-ACS at one year from a single center.*
Material and Method: *All patients admitted to Siriraj Hospital with diagnosis of NSTE-ACS were enrolled. Baseline demographic information, presenting signs and symptoms, electrocardiogram, and blood chemistry were recorded. In-hospital complications and outcomes of treatment were also collected and recorded. After being discharged from the hospital, patients were followed-up for one year.*
Results: *Two-hundred patients were evaluated between January 2012 and August 2013. A majority of patients (65.5%) presented with angina. Median TIMI risk score was 4. Thirty-two percent of patients had GRACE risk score greater than 140. In-hospital mortality was 3.5% (95% CI 2.0-7.0). The most common complication was heart failure (36.5%). Three patients had CVA during admission. At one year, the mortality rate was 5% (95% CI 3.0-9.0). Unplanned readmission rate was 9.5%.*
Conclusion: *Most patients in the registry were high-risk ACS patients. In-hospital mortality and one-year mortality rates were 3.5% and 5%, respectively. Results from this study were comparable to results reported by previous studies from the Western world.*

Keywords: *Non-ST-segment elevation acute coronary syndrome, NSTE-ACS, outcomes, Thailand*

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Acute coronary syndrome (ACS) is a leading health burden worldwide[1]. ACS comprises ST-segment elevation myocardial infarction (STEMI), unstable angina (UA), and non-ST-segment elevation myocardial infarction (NSTEMI). UA and NSTEMI have been classified as non-ST-segment elevation ACS (NSTE-ACS). Siriraj Hospital is a 2,000-bed university hospital, Thailand's largest tertiary referral care center. The Siriraj NSTE-ACS registry was established in 2012 as a single center registry. The purpose of the Siriraj NSTE-ACS registry was to collect and record all pertinent demographic and clinical information relating to patients admitted to Siriraj Hospital with NSTE-ACS. This is the first report from Thailand that describes patient characteristics and outcomes of treatment at one year after discharge. The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB).

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Objective

To evaluate in-hospital and 1-year mortality rates, in-hospital complications, and the 1-year unplanned readmission rate for patients with NSTE-ACS.

Material and Method

Patients

All patients admitted to Siriraj Hospital with NSTE-ACS were entered into the Siriraj NSTE-ACS registry. Inclusions were as follows, 1) age greater than

18 years, and 2) presenting with clinical symptoms of and being diagnosed with NSTE-ACS. The exclusion criteria were as follows, 1) patients who were admitted with other diagnosis and developed NSTE-ACS later in their clinical course, 2) patients that developed NSTE-ACS because of having a severe clinical condition, for which ACS was considered to be a secondary condition, and/or 3) patients who refused to participate in the registry.

Definitions

NSTE-ACS was defined as occurrence of ACS without ST-segment elevation on 12-lead electrocardiogram (ECG). Patients with NSTE-ACS were further classified as UA or NSTEMI, based on typical rise and fall patterns of cardiac biomarkers (mostly cardiac troponin).

Statistical analysis

Categorical variables were presented as frequency and percentage. Continuous variables were presented as mean ± standard deviation or median (minimum and maximum). Differences between outcome groups were assessed using Chi-square test for categorical variables. Differences among continuous variables were tested by independent t-test for mean values and by Mann-Whitney U test for median values. All statistical tests were 2-tailed with p-value <0.05 considered statistically significant. Sample size determination was based on use of the following variables, estimated NSTE-ACS patient mortality rate of 8%, allowable error of 4%, 95% confidence interval, and α of 0.05. Based on the formula $N = (Z_{\alpha/2})^2P(1\text{-}P)/d^2$, the estimated sample size was calculated to be 177. Twenty-three patients were added to the cohort to compensate for patients lost to follow-up. Accordingly, the final number of patients in this study was 200. All statistical analysis was performed using SPSS Statistics version 17 (SPSS, Inc., Chicago, IL, USA).

Results

Between January 6, 2012 and August 20, 2013, 200 consecutive patients were enrolled in this study. Most patients were male (55%) with mean age of 70.8±11.3 years. Only 10% of patients were referred from outside hospitals. Regarding payment for medical services, 50%, 38%, 6.5%, and 5.5% of patients were on government paid, universal coverage, social security, and self-pay/private insurance policy, respectively. Hypertension was found in 80% of patients, which was the most frequent cardiovascular risk factor. History of diabetes mellitus and hyperlipidemia were found in 54% and 71.5% of patients, respectively. Seventeen percent of patients were current smokers. Thirty-eight percent of patients had established coronary artery disease, defined as history of stable angina, previous myocardial infarction (MI), previous percutaneous coronary intervention (PCI), and/or previous coronary artery bypass graft (CABG). For cardiovascular medications, 59.5%, 33%, 44%, 41%, and 60.5% of patients were currently taking aspirin, clopidogrel, beta-blockers, angiotensin-converting enzyme/angiotensin receptor blockers (ACEI/ARB), and statin, respectively. Patient baseline characteristics were presented in Table 1.

Presenting symptoms, signs, and electrocardiogram

Most patients (65.5%) had angina at presentation. Congestive heart failure (CHF) was presented in 36.5% of patients. Among patients with heart failure, 38.3% and 56.2% had Killip class II and III, respectively. Four patients (2%) presented with cardiogenic shock and 1 patient (0.5%) presented with cardiac arrest. ECG suggestive of

Table 1. Patient baseline characteristics

Characteristics	Patients (n = 200)
Male, n (%)	111 (55.0)
Age (years), mean ± SD	70.8±11.3
Reimbursement policy, n (%)	
Government paid	100 (50.0)
Universal coverage	76 (38.0)
Social security	13 (6.5)
Private insurance/self-pay patient	11 (5.5)
History of diabetes, n (%)	109 (54.5)
History of hypertension, n (%)	160 (80.0)
History of hyperlipidemia, n (%)	143 (71.5)
Smoking, n (%)	34 (17.0)
Previous MI, n (%)	52 (26.0)
Previous PCI, n (%)	44 (22.0)
Previous CABG, n (%)	19 (9.5)
History of chronic stable angina, n (%)	102 (56.0)
Current cardiovascular medication, n (%)	
Aspirin	119 (59.5)
Clopidogrel	66 (33.0)
Beta-blockers	88 (44.0)
ACEI/ARB	82 (41.0)
Statin	121 (60.5)

MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; ACEI/ARB = angiotensin-converting enzyme/angiotensin receptor blockers

cardiac ischemia was seen in 102 (51%) patients. Dynamic ST depression and deep symmetrical T wave inversion, the most common ECG findings, were observed in 45.5% and 17.5% of patients, respectively. Compared to patients with UA, patients with NSTEMI had significantly higher rate of heart failure at presentation (44.7% vs. 16.9%, $p = 0.03$). Detailed information regarding patient presentation relative to UA and NSTE-ACS were presented in Table 2.

Risk stratification

Among 200 patients, 141 (70.5%) were classified as NSTEMI. All patients were stratified by both of two risk estimation schemes: TIMI risk score and GRACE risk score. One hundred sixty eight patients (84%) had TIMI risk score of 3 or higher and were classified as high-risk patients. However, only 64 patients (32%) had GRACE risk score of 140 or higher. Thirty patients (15%) had left ventricular systolic dysfunction; defined as left ventricular systolic ejection fraction (LVEF) of less than or equal to 35%. Eighty-one patients (40.5%) had serum creatinine level of 1.3 mg/dl or higher. Compared to patients with UA, patients with NSTEMI had higher GRACE risk score (106.7±85.5 vs. 136.8±50.4, $p = 0.04$). Data regarding patient risk stratification were presented in Table 3.

Management strategies

It was intended for 118 patients (59%) to be treated with early invasive strategy, but only 65 patients (32.5%) underwent in-hospital angiogram. The remaining 53 patients underwent outpatient angiogram after discharge from the hospital. Of 82 patients for whom non-invasive treatment strategy was intended, 28 underwent in-hospital angiogram. Left main coronary artery disease, triple-vessel disease, and double-vessel disease were presented in 23 (15.7%), 52 (35.6%), and 57 (39.1%) of patients, respectively. Angiogram results of the remaining patients (14, 9.5%) revealed either single-vessel disease or non-significant coronary artery disease. Regarding revascularization procedure, a majority of patients (113, 77.4%) underwent PCI. Twenty-seven patients (18.5%) underwent CABG, with six patients (4.1%) refusing revascularization.

In-hospital outcomes

Of seven patients that developed cardiogenic shock, five patients did not survive. However, only one of these deaths was defined as cardiac death. During hospital admission, 50 (25.0%) patients, 17 (8.5%) patients, 12 (6.0%) patients, and three (1.5%) patients developed heart failure, worsening of renal function, major hemorrhage, and stroke, respectively. All strokes were ischemic stroke. Seven patients (3.5%) died during admission. Compared to patients with NSTEMI,

Table 2. Patient presentation relative to unstable angina and non-ST-segment elevation acute coronary syndrome

Presentation	UA (n = 59)	NSTEMI (n = 141)	*p*-value
Angina, n (%)	41 (69.5)	90 (63.8)	0.44
Heart failure, n (%)	10 (16.9)	63 (44.7)	<0.01*
Killip class II	5 (8.4)	23 (16.3)	-
Killip class III	5 (8.4)	36 (25.5)	-
Cardiogenic shock, n (%)	0 (0)	4 (2.6)	0.32
Cardiac arrest, n (%)	0 (0)	1 (0.1)	1.00
Abnormal ECG suggesting cardiac ischemia, n (%)	28 (47.5)	74 (52.5)	0.23

UA = unstable angina; NSTEMI = non-ST-segment elevation myocardial infarction; ECG = electrocardiogram
* *p*-value of less than 0.05 are considered to be statistically significant

Table 3. Patient risk stratification relative to unstable angina and non-ST-segment elevation acute coronary syndrome

Risk score/parameters	UA (n = 59)	NSTEMI (n = 141)	*p*-value
TIMI risk score, median (min, max)	4 (2, 6)	4 (1, 6)	0.26
GRACE risk score, mean ± SD	106.7±85.5	136.8±50.4	0.04*
LVEF ≤35%, n (%)	7 (11.8)	23 (16.3)	0.25
Serum creatinine ≥1.3 mg/dl, n (%)	22 (37.2)	59 (41.8)	0.55

LVEF = left ventricular systolic ejection fraction
* *p*-value of less than 0.05 are considered to be statistically significant

patients with UA experienced less heart failure, but had similar rate of worsening of renal function, major hemorrhage, and stroke.

One-year outcomes

Follow-up was complete in 192 patients (96%). During and up to one year after discharge from the hospital, 10 patients (5%) had died. Cause of death was described as non-cardiac in seven patients (3.5%), with the death of only two (1%) patients being attributed to cardiac cause. Cause of death in the remaining patient was ruled as unidentifiable. Eight patients were lost to follow-up. Patients with NSTEMI had a higher rate of death compared to UA, but the difference was not statistically significant. Unplanned readmission rate was 13.5% and 7.8% in the group of patients with UA and NSTEMI, respectively. Overall unplanned readmission rate was 9.5% at one year after hospital discharge. Readmission rates after discharge between groups were similar. Overall, 58 (29%) patients were admitted within one year after hospital discharge for planned revascularization. Patient in-hospital outcomes and one-year outcomes were presented in Table 4.

Discussion

Patients in the Siriraj NSTE-ACS registry were high-risk patients, as determined by clinical signs, symptoms, and risk stratification schemes. Fifty-four (27%) patients presented with heart failure, among these, 35 (17.5%) were in Killip class III. TIMI risk score classified most patients to be high-risk, as 84% of patients had a TIMI score of 3 or more. This may, in part, be explained by the fact that Siriraj Hospital is national tertiary care referral center. Most patients classified as low-risk were not admitted and received out-patient treatment. Difference was observed in patient classification when comparing TIMI risk score and GRACE risk score. This difference between classifications was consistent with reported findings from previous studies. One previous study found TIMI risk score to be superior in c-statistic and ROC curve analysis[2]. GRACE risk score tended to classify most patients into low-risk group in this study. Other studies, however, revealed GRACE risk score superiority in prediction of left main disease or triple-vessel disease[3] and death or MI[4]. There was a trend in our study that GRACE risk scores seemed to be more accurate for in-hospital outcomes prediction. This study, however, was not designed to test and compare these risk stratification schemes and further study was needed. No study has yet been conducted that compares the efficacy of these two scoring systems in Thai patients with NSTE-ACS.

Management strategy is also important. Although most patients in the Siriraj registry were at high-risk, there was intent to treat only 59% of patients with invasive strategy. Whether treating patients more aggressively with invasive strategy would have improved outcomes for the patients in this study is not known. However, 90.4% of patients who underwent angiogram had severe coronary disease, defined as left main disease, triple-vessel disease, or double-vessel disease. This suggests that invasive strategy would likely be more appropriate for most patients.

One-year mortality rate was 5%, which was lower than the expected rate of 8% that we predicted at the beginning of this study. Despite the presence of high-risk patients in the registry, patient in-hospital and one-year mortality rates were comparable to results

Table 4. Patient in-hospital outcomes and one-year outcomes relative to unstable angina and non-ST-segment elevation acute coronary syndrome

Outcomes	UA (n = 59)	NSTEMI (n = 141)	*p*-value
In-hospital outcomes, n (%)			
Death	0 (0)	7 (4.9)	0.10
Ischemic stroke	0 (0)	3 (2.1)	1.00
Heart failure	9 (5.6)	41 (29.1)	0.049*
Cardiogenic shock	1 (1.7)	6 (4.2)	0.21
Worsening of renal function	2 (3.3)	15 (10.6)	0.16
Major hemorrhage	1 (1.7)	11 (7.8)	0.12
One-year outcomes, n (%)			
Readmission ≤30 days	9 (15.2)	18 (12.8)	0.26
Readmission >30 days to 1 year	14 (23.7)	36 (25.5)	0.31
Planned readmission, n	15	43	-
Unplanned readmission, n	8	11	-
Death (total since enrollment)	1 (1.7)	9 (6.4)	0.29

reported from similar international studies. Data from Western researchers revealed a significant difference in prognosis between STEMI and NSTE-ACS, with better short-term prognosis in the NSTE-ACS group[5-9]. One landmark clinical trial revealed a 30-day mortality rate of as low as 3.6% in NSTE-ACS patients[6]. However, the long-term outcomes of patients in this study were different from previously published findings. From previous study, long-term outcomes in NSTE-ACS were worse than in STEMI[10]. One study reported a 20% ACS recurrence rate in NSTE-ACS patients who underwent PCI at 3.4 years[11]. ACS recurrence rate of patients in this registry was low. Although readmission rate at one-year was high at 25%, a majority (20.5%) of readmissions was due to scheduled PCI or CABG, not to recurrent ACS.

Recently, Wongpraparut et al reported results from a cohort of patients who underwent PCI for NSTE-ACS, which revealed in-hospital mortality and morbidity rates that were comparable to those found in our study[12]. However, our results were different from two previous studies in Thailand. Data from Thai ACS registry were significantly different than data from the West, with regard to patient characteristics and prognosis[13]. Kiatchoosakun et al reported a surprisingly high in-hospital mortality rate in NSTE-ACS[14]. Tungsubutra et al described an in-hospital mortality rate of as high as 15.7% in NSTEMI patients[15]. One of the reasons for the difference was patient characteristics. The patients evaluated in this study were truly ACS patients. We excluded all patients with secondary MI and patients who were admitted with other clinical problems to ensure that the results reflected the effects of ACS management. The results demonstrate that management of NST-ACS in our center is comparable to the results reported in international/Western registries.

Conclusion

Most patients admitted to Siriraj Hospital with NSTE-ACS were high-risk patients. A majority (59%) of patients were treated with invasive strategy. Patient in-hospital mortality was 3.5%. Five of seven patients who died presented with cardiogenic shock. Patient one-year mortality was 5%. Unplanned readmission rate was 9.5%.

What is already known on this topic?

NSTE-ACS is a leading health burden worldwide. Results of treatment reported from Thailand were different from results reported from the Western world. There were conflicting results regarding application of risk stratification.

What this study adds?

Results of treatment for NSTE-ACS from a single center in Thailand were comparable to previous reports from the Western world. Patient in-hospital mortality and one-year mortality were 3.5% and 5%, respectively. GRACE risk score seemed to be more accurate than TIMI risk score in predicting prognosis of Thai NSTE-ACS patients.

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Potential conflicts of interest

None.

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ผลการรักษาผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิดไม่มี ST segment ยก จากโรงพยาบาลศิริราช

สัชชนะ พุ่มพฤกษ์, วรางคณา บุญญพิสิฎฐ์, จรีทิพย์ วงศ์สา, นงค์นุช แนะแก้ว, ดารณี เดชะ

ภูมิหลัง: *โรคหลอดเลือดหัวใจตีบเฉียบพลันเป็นปัญหาสุขภาพที่สำคัญ คณะแพทยศาสตร์ศิริราชพยาบาลได้มีการจัดทะเบียนประวัติของผู้ป่วยกลุ่มนี้ การศึกษานี้รายงานผลการรักษาผู้ป่วยที่ระยะเวลา 1 ปี*

วัตถุประสงค์: *เพื่อทราบอัตราตายในโรงพยาบาล และที่ 1 ปี อัตราการเกิดภาวะแทรกซ้อนขณะนอนในโรงพยาบาล และอัตราการเกิดซ้ำของผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิดไม่มี ST segment ยก*

วัสดุและวิธีการ: *ผู้ป่วยที่เข้าร่วมการศึกษา คือ ผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิดไม่มี ST segment ยก ที่เข้ารับการรักษาในโรงพยาบาลศิริราช ประวัติข้อมูลพื้นฐาน อาการ การตรวจทางห้องปฏิบัติการจะถูกเก็บรวบรวมในฐานข้อมูล และมีการติดตามผู้ป่วยที่ระยะเวลา 1 ปี นับจากวันที่มารักษา*

ผลการศึกษา: *ผู้ป่วยเข้าร่วมการศึกษา 200 ราย ส่วนใหญ่เป็นผู้ป่วยความเสี่ยงสูงประเมินจาก TIMI risk score และ GRACE risk score อัตราตายในโรงพยาบาล คือ ร้อยละ 3.5 ภาวะแทรกซ้อนที่พบบ่อยที่สุด คือ ภาวะหัวใจล้มเหลว อัตราตายที่ 1 ปี คือ ร้อยละ 5 ผู้ป่วยร้อยละ 9.5 ต้องเข้ารับการรักษาในโรงพยาบาลซ้ำโดยไม่คาดการณ์ล่วงหน้าที่ระยะเวลา 1 ปี*

สรุป: *ผู้ป่วยส่วนใหญ่ในการศึกษาเป็นผู้ป่วยความเสี่ยงสูง อัตราตายในโรงพยาบาลและที่ 1 ปี คือ ร้อยละ 3.5 และ 5 ตามลำดับ ผลการรักษาใกล้เคียงกับรายงานจากต่างประเทศ*