

In-Hospital Invasive Strategy and Outcomes in Non-ST Elevation Acute Coronary Syndrome Management from Thai Acute Coronary Syndrome Registry

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Background: The management guideline of acute coronary syndrome has been changed in recent years, especially in the group of non-ST elevation acute coronary syndrome (NSTEMI-ACS). Presently, there is no existing guideline in Thailand. Additionally, several different management factors of health care from Western countries being used.

Objective: Evaluate the real management strategy, including the utilization of invasive management and pharmacotherapy of NSTEMI-ACS Thai patients in the absence of official clinical management guideline.

Material and Method: Thai Acute Coronary Syndrome (Thai ACS) Registry is a large, observational prospective, population-based registry designed to collect the data of "real-life" patient management. The full details of methods have been published in the present supplement.

Results: Five thousand five hundred and thirty-seven consecutive patients were registered between August 1, 2002 and July 31, 2005. Among these patients, 3,548 (64.1%) were diagnosed with non-ST elevation myocardial infarction (NSTEMI) and 1,989 (35.9%) with unstable angina. Coronary angiography was performed during hospitalization in 2,476 patients (44.7%). From 2,476 patients who underwent coronary angiogram, 405 (16.4%) had revascularization within 2 days and 1,019 (42.9%) after 2 days. Overall, in-hospital mortality was 9.5% and cardiac mortality was 6.3%. Patients with NSTEMI had more than 4 times the mortality of patients with unstable angina (13.1 vs. 3.0%, $p < 0.001$). Patients who received only medical treatment without coronary angiogram had the highest mortality rate. The in-hospital outcomes were not different between patients who received early or delayed revascularization.

Conclusion: Mortality rate of NSTEMI-ACS in the authors' registry was very high. NSTEMI had the worse prognosis. Invasive strategy is associated with better in-hospital outcome but is underutilized.

Keywords: Non ST elevation acute coronary syndrome (NSTEMI-ACS), Non ST segment elevation myocardial infarction (NSTEMI), Unstable angina (UA)

J Med Assoc Thai 2007; 90 (Suppl 1): 74-80

Full text. e-Journal: <http://www.medassocthai.org/journal>

The management of acute coronary syndrome has been changed in the recent years, especially in the group of non-ST elevation acute coronary syndrome (NSTEMI-ACS). Pharmacotherapies, such as intravenous glycoprotein IIb/IIIa inhibitors, low-molecular-weight

heparin and clopidogrel and early invasive strategy, has demonstrated their benefits in several studies⁽¹⁻³⁾. The American College of Cardiology and American Heart Association (ACC/AHA) and European Society of Cardiology guidelines recommend early invasive strategy for NSTEMI-ACS patients having one of the following recurrent ischemia, elevated troponin, new ST segment depression, congestive heart failure, depressed left ventricular systolic function, hemodynamic instability, previous PCI or coronary bypass graft (CABG)

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and ventricular tachycardia⁽⁴⁾. Furthermore, previous NSTEMI-ACS management registries as CRUSADE⁽⁵⁾ and GRACE⁽⁶⁾ that originated among developed countries has shown rate of mortality higher than clinical studies. In addition, an early invasive management strategy for high-risk patients with NSTEMI-ACS is shown to be underutilized from prospective registries that reflect “real life” management. Presently, there are no existing guidelines in Thailand; therefore, several different factors of healthcare from Western countries are being used. The degree of how much these treatments were applied and their effects on outcomes in the clinical practice in Thai population are uncertain. The purpose of the present study was to evaluate the real management strategy including the utilization of invasive management and pharmacotherapy of NSTEMI-ACS Thai patients in the absence of official clinical management guideline.

Material and Method

Patient population

Thai Acute Coronary Syndrome (Thai ACS) Registry is a large, observational prospective, population-based registry designed to collect the data of “real-life” management of patients with ACS from August 1, 2002 to August 31, 2005. The full details of methods have been published elsewhere. The strategy of treatment in each patient either conservative with medical treatment or invasive with coronary angiography and possible revascularization was at the primary physician’s discretion. This registry has recruited patients from government and private hospitals representing whole regions of Thailand. The present study protocol was approved by the institutional review boards at each institution.

Patients with non-ST segment elevation myocardial infarction (NSTEMI) or unstable angina (UA) with based on their discharge diagnosis were recruited in the present study. Patients were diagnosed with NSTEMI if presented with chest pain longer than 20 minutes, post cardiac arrest, shock, syncope, cardiogenic dyspnea with ST depression or T-wave inversion with the presence of at least one positive biochemical markers of myocardial necrosis (CK-MB > 2 folds of upper normal limit or Troponin-T or I > 0.1 ng/ml). Unstable angina was diagnosed in the patient who presented with chest pain with EKG changed and absence of positive biomarkers.

All data was retrieved from the Thai ACS registry data management center of the Thai Heart association.

Measured clinical outcomes

The endpoint was in-hospital death. The secondary endpoints were major bleeding and CVA complication or stroke.

To further understand the utilization of early invasive management strategy and the association of this strategy within hospital outcomes, patients were classified into 4 groups of intervention a) early revascularization (revascularization within 2 days), b) delayed revascularization (revascularization after 2 days) c) coronary angiogram without revascularization and d) no coronary angiogram. Patients’ characteristics and clinical outcomes were observed and compared between groups.

Statistic analysis

Statistical analysis was performed using statistical package for social sciences, version 10 (SPSS, Inc., Chicago, Illinois). Categorical variables were presented as frequencies and percentage then compared with Chi-square test or Fisher’s exact test, where appropriate. Continuous variables were presented as mean \pm 1SD or median, where appropriate and analyzed by Student’s t-test. Statistical significance was inferred at 2-sided p-value < 0.05.

Results

Five thousand five hundred and thirty-seven consecutive patients that met the inclusion criteria for NSTEMI-ACS were collected for 37 months from August 1, 2002 and August 31, 2005. Two-thirds of these patients were NSTEMI (n = 3,548) and 36 percent (n = 1,989) was UA. Demographic baselines are presented in Table 1. As expected, males were more common and more than half of the patients were older than 65 years. Hypertension and dyslipidemia were presented in about 70 percent of patients. Nearly half of the patients were diabetic. One-fourth of the patients had used tobacco.

Among these specific NSTEMI-ACS subgroups, only seventy-two percent had typical angina and nearly half were presented as heart failure (Killip II-IV) and 4.5% had cardiogenic shock. Patients with NSTEMI had more severe clinical symptoms at presentation such as heart failure, cardiogenic shock, and cardiac arrest. In-hospital management strategies are presented in Table 2.

Overall, in-hospital mortality was 9.5 percent and cardiac mortality was 6.3 percent. Patients with NSTEMI had higher mortality (about 4 times) than patients with UA (13.1% vs. 3.0%, p < 0.001). They also

Table 1. Baseline patient characteristics on admission

	Total (n = 5,537)	NSTEMI (n = 3,548)	UA (n = 1,989)	p-value
Mean age (yrs)	67.2±11.4	67.7±11.4	65.4±11.1	<0.001
Men (%)	2,992 (54%)	1,948 (54.9%)	1,044 (52.5%)	0.08
Age (yrs)				
< 45	178 (3.2%)	105 (3.0%)	73 (3.7%)	} <0.001
45-54	683 (12.3%)	402 (11.3%)	281 (14.1%)	
55-64	1,311 (23.7%)	776 (21.9%)	535 (26.9%)	
65-74	1,943 (35.1%)	1,242 (35%)	701 (35.2%)	
≥ 75	1,422 (25.7%)	1,023 (28.8%)	399 (20.1%)	
Medical history				
Diabetes mellitus	2,686 (49%)	1,788 (50.4%)	898 (45.1%)	<0.001
Hypertension	3,994 (72.1%)	2,529 (71.3%)	1,465 (73.6%)	0.08
Dyslipidemia	4,023 (72.7%)	2,536 (71.5%)	1,487 (74.8%)	0.15
Smoking	1,337 (24.1%)	880 (24.8%)	457 (22.9%)	0.13
Family history	490 (8.8%)	286 (8.1%)	204 (10.3%)	0.02
Presenting symptoms				
Typical chest pain	3,477 (62.8%)	2,085 (58.8%)	1,392 (70.0%)	<0.001
Killip class				
II	1,477 (26.7%)	1,075 (30.3%)	402 (20.2%)	} <0.001
III	634 (11.5%)	532 (15.0%)	102 (5.1%)	
IV	301 (5.4%)	277 (7.8%)	24 (1.2%)	
Cardiogenic shock	247 (4.5%)	223 (6.3%)	24 (1.2%)	<0.001
Cardiac arrest	115 (2.1%)	97 (2.7%)	18 (0.9%)	<0.001

Table 2. Invasive and pharmacotherapy in NSTEMI-ACS patients

	Total (n = 5,537)	NSTEMI (n = 3,548)	UA (n = 1,989)	p-value
Coronary angiogram	2,476 (44.7%)	1,556 (43.9%)	920 (46.3%)	0.08
Revascularization in 2 day	406 (7.3%)	266 (7.5%)	140 (7.0%)	0.06
Revascularization after 2 day	1,062 (19.2%)	711 (20.0%)	351 (17.6%)	0.06
Coronary angiogram but no revascularization	4,069 (73.5%)	2,571 (72.5%)	1,498 (75.3%)	0.06
Medication (%)				
ASA	94.4	94.6	94.1	0.36
ADP inhibitor	56.7	58.5	53.5	<0.001
Glycoprotein IIb/IIIa inhibitor	4.6	5.3	3.2	<0.001
UFH	19.5	21.3	16.4	<0.001
LMWH	68.6	72.2	62.3	<0.001

* p-value of the difference between NSTEMI and UA

had a higher rate of major bleeding and stroke than unstable angina patients (6.0% vs. 2.0%, $p < 0.001$ and 2.1% vs. 0.8%, $p < 0.001$ respectively).

Clinical characteristics and managements of patients in each group of revascularization are presented in Table 3. Patients who underwent early revascularization were younger, predominantly male,

more likely to have Killip IV heart failure and cardiogenic shock compared to the other group of patients. Patients who received only medical treatment without coronary angiogram were older, had a higher prevalence of female and had a lower use of antiplatelet and antithrombotic agents. Ninety percent of patients in the early revascularization group mostly underwent

**Table 3.** Baseline patients' characteristics on revascularization

	Revascularization in 2 day (n = 405)	Revascularization after 2 day (n = 1,019)	CAG but no revascularization (n = 1,052)	No CAG (n = 3,061)	p-value*
Mean age (yrs)	64.2±11.7	66±10.5	67±11.4	68.6±11.6	0.001
Men (%)	280 (69.1%)	578 (56.7%)	555 (52.8%)	1,579 (51.6%)	0.001
Killip II	51 (12.5%)	242 (23.7%)	268 (25.5%)	916 (29.9%)	0.001
Killip III	23 (5.7%)	90 (8.8%)	100 (9.5%)	421 (13.8%)	
Killip IV	38 (9.4%)	55 (5.4%)	39 (3.7%)	169 (5.5%)	
Cardiogenic shock	32 (7.9%)	31 (3.0%)	40 (3.8%)	144 (4.7%)	
Cardiac arrest	7 (1.7%)	18 (1.7%)	22 (2.1%)	68 (2.2%)	0.8
Medication					
ASA	388 (95.8%)	997 (97.8%)	1,002 (95.6%)	2,842 (92.8%)	NA
ADP-inhibitor	374 (92.1%)	873 (85.7%)	692 (65.8%)	1,221 (39.8%)	NA
Glycoprotein Iib/IIIa inhibitor	97 (24.0%)	122 (12.0%)	18 (1.7%)	15 (6.0%)	NA
LMWH	231 (57.0%)	812 (79.7%)	780 (74.8%)	1,977 (64.6%)	NA
Heparin	129 (31.9%)	309 (30.3%)	192 (18.3%)	451 (14.7%)	NA
PCI	372 (91.9%)	705 (69.2%)			NA
CABG	41 (8.1%)	317 (31.1%)			NA

* p-value of the difference between groups
 NA = < 0.001

Table 4. Results In-hospital outcomes based on as a function of final diagnosis

Outcomes	Total (n = 5,537)	NSTEMI (n = 3,548)	UA (n = 1,989)	p-value
Death	526 (9.5%)	466 (13.1%)	60 (3.0%)	<0.001
-Cardiac	354 (6.3%)	306 (8.6%)	48 (2.4%)	NA
-Non cardiac death	172 (3.2%)	160 (4.5%)	12 (0.6%)	NA
Major bleeding	254 (4.6%)	214 (6.0%)	40 (2.0%)	<0.001
CVA	89 (1.6%)	73 (2.1%)	16 (0.8%)	<0.001

NA = not adjust

Table 5. Results-In hospital management and outcomes based on revascularization

	Revascularization in 2 day (n = 405)	Revascularization after 2 day (n = 1,019)	CAG but no revascularization (n = 1,052)	No CAG (n = 3,061)	p-value*
Death	30 (7.4%)	65 (6.4%)	43 (4.1%)	388 (12.7%)	0.016
-Cardiac death	25 (6.2%)	42 (4.2%)	30 (2.9%)	257 (8.4%)	NA
-Non-cardiac death	5 (1.2%)	23 (2.2%)	13 (1.2%)		NA
Major bleeding	20 (4.9%)	63 (6.2%)	28 (2.7%)	143 (4.7%)	<0.001
CVA	6 (1.5%)	10 (1.0%)	11 (1.0%)	62 (2%)	0.7

* p-value of the difference between groups
 NA = not adjust

percutaneous coronary intervention (PCI), whereas patients in the delayed revascularization group underwent PCI 69 percent and coronary bypass surgery 31 percent ($p < 0.001$).

As noted, among 1,052 patients who had coronary angiogram done during hospitalization without revascularization, only 183 patients (7.4 percent) had normal coronary angiogram.

In hospital outcomes are presented in Table 4, 5. Patients who received only medical treatment without coronary angiogram had the highest mortality rate (12.7 percent compared to the other group). The in-hospital outcomes were not different between patients who received early or delayed revascularization ($p > 0.05$). Patients who underwent coronary angiogram without revascularization had less adverse in hospital events including death and major bleeding.

Discussion

Patients with NSTEMI-ACS in the authors' registry were older, had a higher prevalence of male and conventional risk factors such as diabetes, hypertension, dyslipidemia except smoking compared to the Western registries⁽⁶⁻⁸⁾. Clinical presentations were also more severe in terms of more prevalence of Killip class III and IV and cardiogenic shock. In-hospital mortality of NSTEMI-ACS patients in Thai-ACS registry (9.5%) was higher than the Western registries (1.6% in Canadian ACS registry and 4% in GRACE registry). The higher mortality could be contributed by high-risk patients' characteristics and/or the difference of managements.

Even though, NSTEMI-ACS patients in the authors' registry were in the high-risk group, but this registry showed the low rate of invasive strategy during hospitalization. Patients who received only medical treatment without coronary angiogram had the highest mortality rate. However, the proportion of patients who underwent coronary angiography (44.7%) was quite similar to GRACE registry⁽⁶⁾ (47.5%) but there was a difference in patient selection for coronary angiography. In the authors' registry, NSTEMI and unstable angina patients underwent coronary angiogram in a similar rate (43.9% vs. 46.3%, $p = 0.08$) while NSTEMI in GRACE registry had a higher rate of coronary angiography than unstable angina (53% vs. 42%). High risk patients' characteristics combined with a lower rate of coronary angiography may contribute to the higher mortality in NSTEMI patients in the authors' registry than GRACE registry (13.1% vs. 5.0%). Unstable angina patients had a similar mortality rate in these two registries (3% vs. 3%).

Although early invasive strategy has shown the benefit in randomized control trials, the benefit may be less likely to appreciate in registries. The presented patients had a coronary angiogram at some points during hospitalization. Regarding data collection, the authors could analyze only timing of revascularization. Patients with early revascularization in the authors' registry had a similar mortality with delay revascularization (7.4% vs. 6.4%, $p > 0.05$). With the higher risk of patients' characteristics but the similar rate of mortality may imply the benefit of early revascularization. Nevertheless, the higher rate of coronary bypass surgery in delayed revascularization may affect mortality in this group. Patients who received coronary angiogram without revascularization had the lowest mortality among the groups. Lesser prevalence of severe heart failure and cardiogenic shock as well as patients with normal coronary angiogram may contribute to a favorable result.

Despite previous data have demonstrated the benefit of ADP inhibitors in NSTEMI-ACS⁽⁹⁾, only 56.7% of the authors' registry patients received this medication and the majority of them were in the revascularization group. The utilization of anti-platelet glycoprotein IIb/IIIa inhibitors in patients having PCI was also less than in other registries. These may contribute to high major cardiovascular events (MACE) in the authors' study.

The present registry showed the practices in hospitals with and without on-site catheterization facilities. From ACC/AHA guideline management of NSTEMI-ACS, high-risk patients, such as NSTEMI, diabetes, congestive heart failure, or cardiogenic shock, they should proceed for urgent coronary angiography and revascularization if possible. The present results showed that in-hospital invasive strategy was associated with better in-hospital outcomes among high risk patients which also has been demonstrated in several randomized studies⁽¹⁰⁻¹²⁾ and the GRACE registry⁽⁸⁾. However, more than half of the authors' high-risk patients still were medically treated.

Conclusion

Overall mortality rate of NSTEMI-ACS patients in the present registry was quite high because patients were a high-risk population and many of them were medically treated without coronary angiography. Invasive strategy during hospitalization among high-risk NSTEMI-ACS patients is associated with a lower risk of in-hospital mortality. However, invasive strategy and intensive antiplatelet therapy were underutilized in



high-risk patients. Results from the present registry demonstrate the problem of the authors' clinical practice in the NSTEMI-ACS patient care. Therefore, the authors' suggest the implementation of a strategy of early invasive treatment and the use of more adjunctive pharmacotherapy, as recommended in the previous trials and the guidelines.

Limitation

The present study showed the highest mortality in the conservative group. The conclusion of invasive strategy was better than conservative in the present study and should be interpreted carefully because of unmeasured confounders such as the degree of ST changed from EKG, quantitative of cardiac necrosis marker, serum creatinine level, patient risk score, antiplatelet regimens and left ventricular ejection fraction. The authors' could not compare early and delayed invasive treatment during hospitalization as other clinical trials or registries due to unknown coronary angiogram timing. Further study needs to explore this issue. After hospital discharge, patients having abnormal coronary angiogram but no revascularization during admission, the severity of coronary artery disease and their long-term outcomes also need to be investigated. The predictors of outcomes were studied elsewhere in this journal.

Contributors

The Thai Acute Coronary Syndrome Registry (TACSR) was supported by The Heart Association of Thailand under the Royal Patronage of H.M. the King, Thai Health Promotion Foundation, Clinical Research Collaboration Network (CRCN), and the Health Systems Research Institute (HSRI).

Acknowledgements

The authors wish to thank the patients and their relatives, the personnel of the ICU and most of all, the research nurses who patiently and diligently assisted in all aspects of patient care and data collection and entry.

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ผลของการรักษาด้วยวิธี invasive ของผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิด ST ไม่ยก ในโรงพยาบาลจากโครงการทะเบียนผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันแห่งประเทศไทย

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การรักษาภาวะกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันเป็นโรคที่พบบ่อยทั่วโลก ในปัจจุบันได้มีแนวทางในการรักษาออกมาใช้ แต่ในประเทศไทยยังไม่มีข้อมูลแน่ชัดว่าได้ใช้แนวทางในการรักษาตามคำแนะนำหรือไม่ การศึกษานี้จึงเป็นการศึกษาดูแนวทางในการรักษาและผลของการรักษาผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิด ST ไม่ยกของโรงพยาบาลต่าง ๆ ในประเทศไทยจากทะเบียนผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลัน

วัตถุประสงค์และวิธีการ: จากทะเบียนผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันแห่งประเทศไทย ตั้งแต่ 1 สิงหาคม พ.ศ. 2545 ถึง 31 กรกฎาคม พ.ศ. 2548

ผลการศึกษา: มีผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิด ST ไม่ยกจำนวน 5,537 คน อายุเฉลี่ยเท่ากับ 67.2 ปี เป็นผู้ชายร้อยละ 54 ร้อยละ 16.9 ของผู้ป่วยทั้งหมดจัดอยู่ใน Killip class III และ IV ผู้ป่วย 3,548 คน (ร้อยละ 64.1) ได้รับการวินิจฉัยว่าเป็น non ST elevation myocardial infarction (NSTEMI) และ 1,989 คน (ร้อยละ 35.9) ได้รับการวินิจฉัยเป็น unstable angina (UA) ผู้ป่วย 2,476 คน (ร้อยละ 44.7) ได้รับการตรวจสวนหัวใจ โดยผู้ป่วยร้อยละ 16.4 ได้รับการรักษาด้วยการ revascularization ภายใน 2 วันหลังจากเข้ารับการรักษาในโรงพยาบาล และหลังจากนอนโรงพยาบาล 2 วันตามลำดับ อัตราการเสียชีวิตโดยรวมในโรงพยาบาล และอัตราการเสียชีวิตจากหัวใจมีค่าร้อยละ 9.5 และ 6.3 ผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็น NSTEMI จะมีอัตราการเสียชีวิตสูงกว่าผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็น UA ถึง 4 เท่า (ร้อยละ 13 และ 3 ตามลำดับ) ผู้ป่วยที่ได้รับการสวนหัวใจร่วมกับการรักษาด้วย revascularization หรือไม่ก็ตามก็จะมีอัตราการเสียชีวิตน้อยกว่ากลุ่มผู้ป่วยที่ได้รับการรักษาด้วยยาเพียงอย่างเดียว

สรุป: อัตราการเสียชีวิตในโรงพยาบาลของผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันชนิด ST ไม่ยกจากทะเบียนผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันค่อนข้างสูง ถึงแม้ผู้ป่วยจะเป็นกลุ่มที่มีความเสี่ยงสูงแต่น้อยกว่าร้อยละ 50 ของผู้ป่วย ได้รับการรักษาด้วยวิธี invasive แนวโน้มของการรักษาด้วยวิธี invasive จะทำให้ผู้ป่วยมีอัตราการเสียชีวิตน้อยกว่ากลุ่มผู้ป่วยที่ได้รับการรักษาด้วยวิธีการ conservative ผู้ป่วยส่วนใหญ่ได้ยาต้านเกล็ดเลือดแข็งตัวชนิดเดียว และมีผู้ป่วยจำนวนน้อยที่ได้รับ glycoprotein IIb/IIIa inhibitor ร่วมกับการรักษาด้วย revascularization