Cardiac Arrhythmias in Thai Acute Coronary Syndrome Registry

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Background: *The incidence of arrhythmic complications in Thai patients with acute coronary syndromes (ACS) has not been previously reported. The present study results will serve as the local database for future studies.*
Objective: *To evaluate the incidence of arrhythmic complications in ASC in Thai patients and to identify factors that may affect arrhythmia complications in ACS patients.*
Material and Method: *Data collected from 9,373 patients from the Thai acute coronary syndrome registry (TACSR) were analyzed. This registry includes patients who presented with ACS including ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA), within 14 days from the symptoms onset.*
Results: *395 (4.2%) patients with an ACS presented after cardiac arrest. These patients were noted to have significantly higher in-hospital mortality (50.1%). The incidence of serious cardiac arrhythmia complications in the TACSR was 16.6%. Among them, 62.7% were sustained VT/VF, 31.5% had second or third degree AV block, and 5.8% has both VT/VF and AV Block. The incidence of VT was higher in the younger age group, while AV block and arrhythmic death were higher in the older aged patients. Arrhythmias complicating ACS were associated with increased mortality risk. Congestive heart failure (CHF) within the first 48 hours, current use of tobacco and cardiac troponin elevation were associated with significantly higher arrhythmic complications during hospitalization.*
Conclusion: *Arrhythmias complicating ACS were associated with higher in hospital mortality. CHF within the first 48 hr., current tobacco use and cardiac troponin elevation were associated with significantly higher arrhythmic complications.*

Keywords: *Acute coronary syndrome, Cardiac arrhythmia, Ventricular tachycardia, AV block*

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The full spectrum of acute coronary syndrome comprises of an ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina (UA). This is a growing problem throughout the world and in Thailand. From the Thailand acute coronary syndrome registry (TACSR) mortality rates in these patients 11%, significantly higher than that in other parts of the world[1]. Serious cardiac arrhythmic complications, i.e., cardiac arrest, ventricular tachycardia /fibrillation (VT/VF), and atrio-ventricular block (AVB) were associated with a higher in hospital mortality[2-6]. Although the incidence of arrhythmic complications is decreasing and

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mortality is improving in this group of patients, the in-hospital mortality remains high. In addition, the long-term prognosis may be worsened as well[2,4].

Cardiac arrhythmias are commonly described in acute ST elevated myocardial infarction (STEMI)[1,2,4]. However, data on cardiac arrhythmias in non-ST-elevation acute coronary syndromes (NSTE-ACS) is scant[2]. Thus, it is unclear whether cardiac arrhythmias are associated with increased post ACS mortality (long term or short term). The authors analyzed data collected from the TACSR, to evaluate the extent of the arrhythmic complications of ACS, in Thai patients. Specifically, the authors analyzed the incidence of cardiac arrest, ventricular fibrillation and ventricular tachycardia, atrio-ventricular block and arrhythmic death, as well as the possible predictors of these arrhythmic events in ACS patients during their hospitalization.

Material and Method

Full details of the TARCS rationale and methods have been previously published. In brief, the Thai Acute Coronary Syndrome Registry (TACSR) subjects were recruited from 17 hospitals; 13 in Bangkok and 4 in different provinces. Three private hospitals in Bangkok and one private hospital in a regional area were included while others were government hospitals. Eight hospitals were associated with medical schools and with training programs for cardiology fellows. Consecutive subjects who presented with history of ACS were recruited into the registry. Some of these patients were transferred from other centers. The registry was begun in August 2002 and the last subject for this report was enrolled in October 2005**.** Collected variables were age, sex, a history of diabetes mellitus (DM), hypertension (HT), dyslipidemia, a family history of premature ischemic heart disease, duration of chest pain before arrival at the emergency room and associated symptoms or findings when first evaluated. Events recorded during the hospital stay included Killip's classification, markers of myocardial damage and subsequent outcomes such as dysrhythmia, stroke, (non-hemorrhagic), major bleeding including intracranial hemorrhage and bleeding which required transfusion or hemoglobin decreased more than or equal to 5 gm and deaths (cardiac and non-cardiac). All medical records pertaining to ACS treatment, including reperfusion therapy, were collected. Patients admitted to the hospital with presumptive diagnosis of ACS, (duration from onset less than 14 days) were entered into the registry. The final diagnosis for ST elevated myocardial infarct (STEMI) depended on the presence of the typical ST elevation on consecutive ECG leads or the presence of new LBBB and elevated troponin-T. The remainder was classified as NSTE-ACS, further subdivided into NSTEMI and unstable angina.

Diabetes was diagnosed when the patient's fasting plasma glucose was 126 mg/dl or higher on at least two occasions, or the patients had a history of diabetes (dietary controlled or treated with medications). Hypertension was defined as systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg or the patient was previously diagnosed with hypertension. Dyslipidemia was diagnosed when total cholesterol > 200 mg/dL or LDL cholesterol $\geq$ 130 mg/dL or HDL cholesterol < 40 mg/dL, or the patient was previously diagnosed with dyslipidemia, or was on lipid lowering agents. Smoking was defined as current tobacco use or having quit smoking less than 2 years. A positive family history included a history of a premature myocardial infarction or sudden cardiac death.

The diagnosis of a cardiac arrhythmia was made by an attending cardiologist on admission and during hospitalization. Cardiac arrest included any patients whom cardiopulmonary resuscitation was required. Serious cardiac arrhythmia included second and/or third degrees AV block, ventricular tachycardia (VT) and ventricular fibrillation (VF). Arrhythmic death was defined as death strictly resulting from ventricular tachycardia (VT) or ventricular fibrillation (VF). The present study protocol was approved by the ethics committee for human research of each participating center.

Statistical analysis

Continuous variables were expressed as mean $\pm$ standard deviation or median where appropriate, and discrete variables were presented as percentage. A univariate analysis was used to assess the relationship between each variable and in-hospital death. Multivariate analysis was employed to assess whether prognostic variables were still statistically significant when adjusted for other hospital death related variables shown by univariate analysis. A two-sided p-value < 0.05 was considered statistically significant. All analyses were performed by using Stata/SE 8.0 for windows.

Results

Cardiac arrest at presentation

The registry enrolled patients from 2003-2005. Among the total population of 9,373 patients in the Thai acute coronary syndrome registry, 395 (4.3%) presented after cardiac arrest. Among cardiac arrest

patients, 278 (70.4%) had STEMI, 98 (24.8%) had NSTEMI, and 19(4.8%) had UA (Fig. 1). Mortality among patients who presented after cardiac arrest was significantly higher 198 (50.1%) than patients without cardiac arrest (OR = 9.91, 95%CI 7.97-12.33, p < 0.001) (Table 1).

Serious cardiac arrhythmia complicating ACS

Serious cardiac arrhythmia complicating ACS was diagnosed in 1,557 patients (16.6%). Among them, 977 (62.7%), 490 (31.5%) and 90 (5.8%) were sustained VT/VF, second and third degree AV block, and both VT/VF and AV block, respectively. The incidence of serious arrhythmic complication were 1,117 (29.1%), 377 (10.6%) and 63 (3.2%) in STEMI, NSTEMI, and UA respectively. The incidence of VT/VF were 745 (19.4%), 286 (8.1%) and 63 (1.9%) in STEMI, NSTEMI, and UA respectively. Finally, the incidence of AV block were 443 (11.5%), 109 (3.1%), and 28 (1.4%) in STEMI, NSTEMI and UA respectively. Both VT/VF and AV block were associated with increased in-hospital mortality (p < 0.001) (Table 1).

For each serious cardiac arrhythmias the incidence of VT/VF was higher in the younger group of patients (p for trend = 0.01) (Table 2). Using multivariate analysis, CHF within the first 48 hr, current smoking and cardiac troponin elevation were associated with VT/VF. While female gender higher, age group, hypertension, dyslipidemia and diabetes mellitus were less likely to have VT/VF than control (Table 3, 4). AV block was associated with older age groups (p for trend = 0.004) (Table 2). Female gender, CHF within the first 48 hr, current smoking, DM and cardiac troponin elevation were associated with AVB in both univariate and multivariate analysis. While hypertension and dyslipidemia were associated with less AVB compared to control (Table 3, 4) older age was associated with higher incidence of arrhythmic death (p for trend < 0.001). Both univariate and multivariate analysis demonstrated that CHF within the first 48 hr (p < 0.001) and troponin elevation (p < 0.001) were significantly associated with

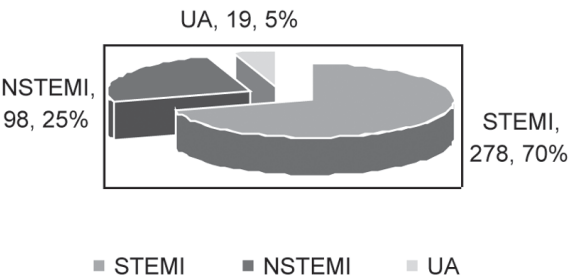

Fig. 1 Diagnosis after cardiac arrest at presentation

Table 1. Factors associated with in-hospital mortality in TACSR

	Mortality	OR (95% CI)	Age, Sex* - Adjusted OR (95% CI)	p-value*
VT/VF (n = 1,067)	512 (48.0%)	10.58 (9.17-12.22)	12.59 (10.81-14.68)	<0.001*
AVB (n = 580)	180 (31.0%)	3.51 (2.91-4.24)	3.45 (2.85-4.18)	<0.001*
CHF at present (n = 3,974)	850 (21.4%)	4.21 (3.68-4.81)	3.76 (3.28-4.32)	<0.001*
Shock (n = 871)	392 (45.0%)	8.03 (6.89-9.35)	8.25 (7.06-9.65)	<0.001*
Cardiac arrest (n = 395)	198 (50.1%)	8.20 (6.17-11.00)	9.91(7.97-12.33)	<0.001*

Table 2. Age group difference and incidence of VT/VF AV block and arrhythmic death in ACS

Age Group	Any VT/VF (%)*	Any AVB**	Arrhythmic death***
< 45 years (n = 544)	89 (16.4%)	24 (4.4%)	15 (2.9%)
45-54 years (n = 1,517)	183 (12.1%)	88 (5.8%)	29 (2.0%)
55-64 years (n = 2,227)	234 (10.5%)	119 (5.3%)	53 (2.6%)
65-74 years (n = 3,048)	339 (11.1%)	205 (6.7%)	107 (3.9%)
≥ 75 years (n = 2,037)	222 (10.9%)	144 (7.1%)	89 (5.0%)

* p for trend = 0.01, ** p for trend = 0.004, *** p for trend = 0.001

Table 3. Factors associated with VT/VF, AV block and arrhythmic death in ACS

	VT/VF n (%)	p-value	AVB n (%)	p value	Arrhythmic death n (%)	p-value
Demographic						
Sex, %						
Female (n = 3,768)	9.8% (370)	<0.001	6.8% (256)	0.046	3.5% (118)	0.650
Male (n = 5,606)	12.4% (697)		5.8% (324)		3.3% (172)	
Risk Factors, %						
CHF within 48 hr						
Yes (n = 3,947)	16.4% (651)	<0.001	7.5% (297)	<0.001	5.6% (185)	<0.001
No (n = 5,399)	7.7% (416)		5.2% (283)		2.0% (105)	
DM						
Yes (n = 4,070)	10.5% (426)	0.087	6.8% (276)	0.010	3.7% (133)	0.071
No (n = 5,141)	11.6% (596)		5.5% (282)		3.0% (140)	
HTN						
Yes (n = 5,937)	9.8% (582)	<0.001	5.4% (322)	<0.001	3.1% (167)	0.159
No (n = 3,350)	13.8% (461)		7.4% (247)		3.7% (111)	
Family history						
Yes (n = 873)	11.6% (101)	0.442	5.5% (48)	0.301	2.2% (18)	0.065
No (n = 6,890)	10.7% (738)		6.4% (218)		3.4% (216)	
Current smoker						
Yes (n = 2,923)	13.3% (388)	<0.001	7.8% (228)	<0.001	3.1% (83)	0.434
No (n = 6,215)	10.0% (624)		2.8% (332)		3.4% (190)	
Dyslipidemia						
Yes (n = 6,567)	9.7% (636)	<0.001	5.4% (352)	<0.001	2.3% (140)	<0.001
No (n = 2,147)	13.6% (291)		7.5% (161)		4.8% (90)	
Troponin elevation						
Yes (n = 6,239)	13.0% (813)	<0.001	6.8% (422)	<0.001	3.9% (101)	<0.001
No (n = 2,455)	5.8% (143)		3.6% (88)		1.6% (17)	

arrhythmic death, whereas, dyslipidemia was significantly associated with less arrhythmic death ($p < 0.001$).

Discussion

These results of serious arrhythmic complications from TACSR (n = 9,373) provided an insight into the nature of cardiac arrhythmia in ACS in the Thai population. It is not surprising that among Thais, cardiac arrhythmia is a strong predictor for in-hospital mortality (Table 1). The Global Registry of Coronary Events (GRACE) (n = 11,389) is a multinational registry following treatment of ACS on a worldwide basis. (Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, China, Columbia, Ecuador, El Salvador, France, Germany, Guatemala, Italy, Latvia, New Zealand, Panama, Peru, Poland, Portugal, Romania, Spain, Ukraine, United Arab Emirates, United Kingdom, United States, Uruguay, Venezuela)[1]. The incidence of patients who presented after cardiac arrest in TACSR is 4.2% compared with 1.5% in GRACE[6]. The in-hospital mortality in patients who presented with cardiac arrest in TACSR is also higher (50.1% vs. 28.6% in the GRACE registry) [6]. These results also support the finding from GRACE that cardiac arrest is a strong predictor for in-hospital mortality.

Overall serious arrhythmic complication in TACSR was 16.6% (the incidence of both VT/VF and AVB in GRACE was 7.7%)[1]. For patients with sustained VT/VF complicating ACS, in TACSR the incidence of VT/VF was 11.4%, (5.0% in GRACE)[1]. In-hospital mortality for sustained VT/VF was 48.0% in TACSR. Pooled data from various studies has shown that 60-days mortality varied from 20-65%, depending on the presences of VT, VF, or both[2,4].

VT/VF in TACSR has a poor prognosis. However, AVB predicts higher in-hospital mortality rate (31%) in TACSR. A similar study in the US, The Worcester heart attack study, showed that complete AV block was also associated with a significant mortality of (46.8%)[3].

Table 4. Multivariate model for VT/VF (VT/VF vs No VT/VF), AVB vs no AVB and arrhythmic death vs no arrhythmic death

	VT/VF vs No VT/VF			AVB vs No AVB			Arrhythmic death vs Survive		
	Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
Age (per 10-year increase)	0.942	0.865-0.986	0.017*	1.109	1.017-1.210	0.019	1.175	1.032-1.338	0.015
Female	0.787	0.662-0.935	0.006*	1.318	1.058-1.643	0.014	0.843	0.615-1.156	0.289
DM	0.842	0.715-0.990	0.038	1.413	1.147-1.741	0.001	1.143	0.842-1.551	0.391
HT	0.716	0.609-0.842	<0.001*	0.704	0.570-0.870	0.001	0.797	0.584-1.090	0.155
Dyslipidemia	0.815	0.689-0.965	0.017*	0.795	0.639-0.990	0.040	0.493	0.365-0.666	<0.001
Current smoker	1.198	1.008-1.423	0.041*	1.810	1.444-2.271	<0.001	0.953	0.675-1.346	0.784
Congestive heart failure	2.726	2.314-3211	<0.001*	1.342	1.092-1.648	0.005	3.057	2.210-4.229	0.001
Cardiac Troponin	1.997	1.626-2.453	<0.001*	1.668	1.296-2.148	<0.001	1.929	1.295-2.875	<0.001

Compared to the GRACE study, arrhythmic complications are more prevalent in TACSR patients with STEMI. Sustained VT/VF occurred in 19.4% of STEMI, 8.1% in NSTEMI and 1.8% in UA, compared with 10%, 4% and 2% respectively in the GRACE study population%)[1]. The incidence of AVB was higher than in GRACE, since only complete AVB was reported in GRACE, (STEMI 11.5% vs. 5%, NSTEMI 3.1% vs. 2% for and UA 1.4%vs. 1%)[1].

Data from TACSR, not surprisingly, showed that congestive heart failure within the first 48 hrs, current smoking and cardiac troponin elevation, were strong predictors for patients who were likely to develop VT/VF, AVB and arrhythmic death. Patients with hypertension and dyslipidemia had less arrhythmic complications possibly due to the protective effect of concurrent medical therapy. For different age groups, younger patients were more likely to have VT/VF while AVB and arrhythmic death was more likely to occur in older patients. However, further investigation is needed on several issues such as the effect of early beta blocker initiation in the younger ACS patients with a higher risk of VT/VF, delay or withholding beta blocker in older patients and whether early initiation of statins would decrease these fatal arrhythmias. Practically, these risk factors for arrhythmic events will be helpful to identify and monitor closely the patient at risk, since effective treatments for cardiac arrhythmias are available[7-11].

The difference of the arrhythmia complicating ACS in TACSR and other registry, may be explained by various factors; the awareness of the population on coronary artery disease, inadequate treatment of coronary risks, the delay presentation. Increased awareness of these arrhythmic complications may help direct patient referrals to focused cardiac centers where increased availability of advanced therapies will improve the patient's outcome. Finally, a national awareness campaign directed at risk factor prevention must be prioritized, as prevention of coronary disease remains the best form of treatment.

Limitations

There were several limitations in the present study. First, this has a non-randomized, observational nature. Therefore, a multivariate analysis was used in an attempt to reduce the bias inherent in this type of study. Particular steps were taken in the design of this registry to minimize bias and to reflect geographical practice patterns. Nevertheless, the project is subject to limitations that may reduce the generalization of the findings. Second, since most of the participating

hospitals were major hospitals clustered in Bangkok and major cities in the north, south and northeast of Thailand, this may reflect regional practices, facility capability, and outcomes. Patients who presented to a non-cardiac center are not represented. Third, the timing of arrhythmia, factors known to effect arrhythmic death such as, ejection fraction, concurrent atrial fibrillation and non-sustained ventricular tachycardia were not recorded. Finally, analyses of pre- and post-admission variables related to physician discretion (e.g., medications, interventions) may be strongly influenced by unmeasured confounders.

Contributors

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ภาวะหัวใจเต้นผิดจังหวะในหลอดเลือดหัวใจตีบเฉียบพลันในโครงการทะเบียนผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันแห่งประเทศไทย

ธัชพงศ์ งามอุโฆษ, ชาญ ศรีรัตนสถาวร, บัญชา ศันสนีย์วิทยกุล, ปิยะ เกษมสุวรรณ, กิตติพร อังคสุวพลา, สุกิจ แย้มวงษ์

ภูมิหลัง: *อุบัติการณ์เกิดการเต้นผิดจังหวะแทรกซ้อนในคนไข้หลอดเลือดหัวใจตีบเฉียบพลันในประเทศไทยไม่มีรายงานปรากฏจนกระทั่งปัจจุบัน*

วัตถุประสงค์: *เพื่อประเมินอุบัติการณ์เกิดการเต้นผิดจังหวะแทรกซ้อนในคนไข้หลอดเลือดหัวใจตีบเฉียบพลันที่เกิดในคนไทย เพื่อระบุปัจจัยที่อาจเป็นผลให้เกิดการเต้นผิดจังหวะในคนไข้กลุ่มนี้*

วัสดุและวิธีการ: *เก็บและวิเคราะห์ข้อมูลในคนไข้จำนวน 9,373 คน จากโครงการทะเบียนผู้ป่วยกล้ามเนื้อหัวใจขาดเลือดเฉียบพลันแห่งประเทศไทย*

ผลการศึกษา: *พบการเกิดหัวใจวายเฉียบพลันในคนไข้ 395 คน (4.2%) ซึ่งคนไข้กลุ่มนี้มีความเสี่ยงต่อการตายสูงอย่างมีนัยสำคัญ (50.1%) คนไข้ที่เกิดการเต้นผิดจังหวะอย่างรุนแรงในกลุ่ม TACSR มีถึง 1,557 คน (16.6%) ซึ่งเป็นคนไข้ ventricular tachycardia/ventricular fibrillation (VT/VF) 977 คน (62.7%) เป็นคนไข้ 2nd และ 3rd degree AV block (AVB) 490 คน (31.5%) และคนไข้จำนวน 90 คน (5.8%) พบทั้ง VT/VF และ AVB ในกลุ่มคนไข้ซึ่งอายุน้อยกว่าอุบัติการณ์เกิด VT/VF สูงกว่าในคนไข้ที่อายุมากกว่า ในทางกลับกันกลุ่มคนไข้ที่มีอายุมากกว่าอุบัติการณ์เกิด AVB และการตายจากหัวใจเต้นผิดจังหวะมีมากกว่าการเต้นผิดจังหวะแทรกซ้อนในคนไข้ หลอดเลือดหัวใจตีบเฉียบพลันมีผลทำให้อัตราการตายสูงขึ้น การเกิดหัวใจล้มเหลวภายใน 48 ชั่วโมง, คนไข้ที่สูบบุหรี่, และคนไข้ที่มี cardiac troponin สูง ส่งผลให้เกิดการเต้นผิดจังหวะแทรกซ้อนในคนไข้หลอดเลือดหัวใจตีบเฉียบพลันอย่างมีนัยสำคัญ*

สรุป: *การเต้นผิดจังหวะแทรกซ้อนในคนไข้หลอดเลือดหัวใจตีบเฉียบพลันเป็นผลทำให้อัตราการตายสูงขึ้น และมีปัจจัยหลายอย่างที่ทำให้เกิดการเต้นผิดจังหวะแทรกซ้อนในคนไข้หลอดเลือดหัวใจตีบเฉียบพลัน การเกิดหัวใจล้มเหลวภายใน 48 ชั่วโมง, คนไข้ที่สูบบุหรี่, และคนไข้ที่มี cardiac troponin สูง ส่งผลให้เกิดการเต้นผิดจังหวะแทรกซ้อน ในคนไข้หลอดเลือดหัวใจตีบเฉียบพลันอย่างมีนัยสำคัญ*