Chapter 2

Acute Coronary Syndrome

Epidemiology of cardiovascular diseases

Cardiovascular diseases (CVDs) are the first leading cause of death in the world,[1,2] with an estimated 17.5 million CVD deaths in 2012, representing 31% of all global deaths (approximately 56 million global deaths).[3] Of these deaths, an estimated 7.4 million were due to coronary artery disease (CAD) and 6.7 million were due to stroke.[4] Worldwide, CAD is projected to be the first leading cause of mortality and disability in 2020,[2,5,6] and in 2030, with 13.4% of total deaths.[7] In Thailand, CAD was the second leading cause of mortality in 2005 (7.8%) following stroke (10.7%);[8] CAD is ranked as the fourth leading cause of death among males (7.3%) and second among females (8.6%).[8]

Epidemiology data in the field of cardiovascular diseases in Thailand are quite limited especially the risk factors of cardiovascular disease. A well-known study on risk factors of cardiovascular disease in Thais is the Electricity Generating Authority of Thailand (EGAT) Study.[9,10] The EGAT study involved employees at EGAT. This started in 1985 where 7,824 eligible employees aged between 35 and 54 working at EGAT in Bangkok were invited to be part of a cross-sectional study to explore cardiovascular risk factors of Thais. Each employee was invited by letter. A total of 3,499 (2,702 males and 797 females) agreed to enrol in the study. Participants were asked to complete a self-administered questionnaire for cardiovascular risk factors and underwent an oral glucose tolerance test as well as a physical examination. They also were asked to give blood samples. Lipid profiles levels including total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were also measured. In 1997 and 2002, the participants were asked to repeat these examinations again.[9,10]

In 1997, a report over 12 years of follow-up on the changes in levels of vascular risk factors was released. They found the associations of baseline risk factors with vascular death. Over this follow-up time, mean levels of risk factors were increased including total cholesterol, high density lipoprotein (HDL) cholesterol, body mass index, diastolic blood pressure (DBP), and systolic blood pressure (SBP). During follow-up, vascular diseases were the most frequent cause of death (n = 46), were

positively associated with baseline age, SBP, DBP, smoking, diabetes, male sex, and total cholesterol, but were negatively associated with HDL cholesterol.[10]

In 2002, after 17 years of follow-up, another report of the EGAT study revealed that the major cause of death among men was cardiovascular disease, while cancer was the major cause of death among women. Total cholesterol and low-density lipoprotein cholesterol were found to have a negative relationship with liver cirrhosis mortality. The EGAT study also found negative associations between HDL-C and CVD mortality (RR = 0.59; 95% confidence interval [CI], 0.39-0.93), coronary heart disease mortality (RR = 0.36; 95% CI, 0.17-0.75) and all cause-mortality (RR = 0.68; 95% CI, 0.54-0.87). HDL-C is considered as a vital risk factor for CVD in middle-class urban Thais.[9] Triglycerides were not associated with mortality in the EGAT study.[9]

In short, the EGAT study revealed risk factors of cardiovascular disease among Thais worsen substantially over the follow-up time of more than 10 years. However, the EGAT study had a limitation in their study population which were workers in only middle class, well-educated and urbanized individuals. In addition, the association of independent risk factor of LDL-C on cardiovascular events has not been found in the EGAT study.

Acute coronary syndrome

The clinical presentations of CAD include silent ischaemia, stable angina pectoris, unstable angina, myocardial infarction (MI), heart failure, and sudden death. Acute coronary syndrome (ACS) is a life-threatening complication of CAD, mostly resulting from atheromatous plaque rupture.[11-13] Fissuring or rupture of these plaques results in promoting platelet aggregation and adhesion and the formation of intracoronary thrombus.[14] ACS encompasses ST segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI), and unstable angina (UA).[11,15] Chest pain is the leading symptom initiating the diagnostic and therapeutic cascade. The electrocardiogram (ECG) and biomarkers such as troponin are used to differentiate and classify patients in one of three groups: STEMI, NSTEMI, or UA. Patients presenting with STEMI are found with total occlusion of the infarct artery,

which can be detected by the ECG showing the ST-elevation.[16] Patients presenting with UA and NSTEMI are similar with regard to their pathophysiologic origins as well as clinical presentations, but the severity differs.[12] A diagnosis of NSTEMI can be accomplished when the ischemia is severe enough to cause sufficient myocardial damage to release detectable amounts of a biomarker of myocardial injury into the circulation. The most common biomarkers are troponins T or I, or muscle and brain fractions of creatine kinase (CK-MB). In contrast, UA is diagnosed when no such biomarker has been released in the circulation after the initial onset of ischemic chest pain.[12] Figure 2.1 shows the spectrum of ACS.

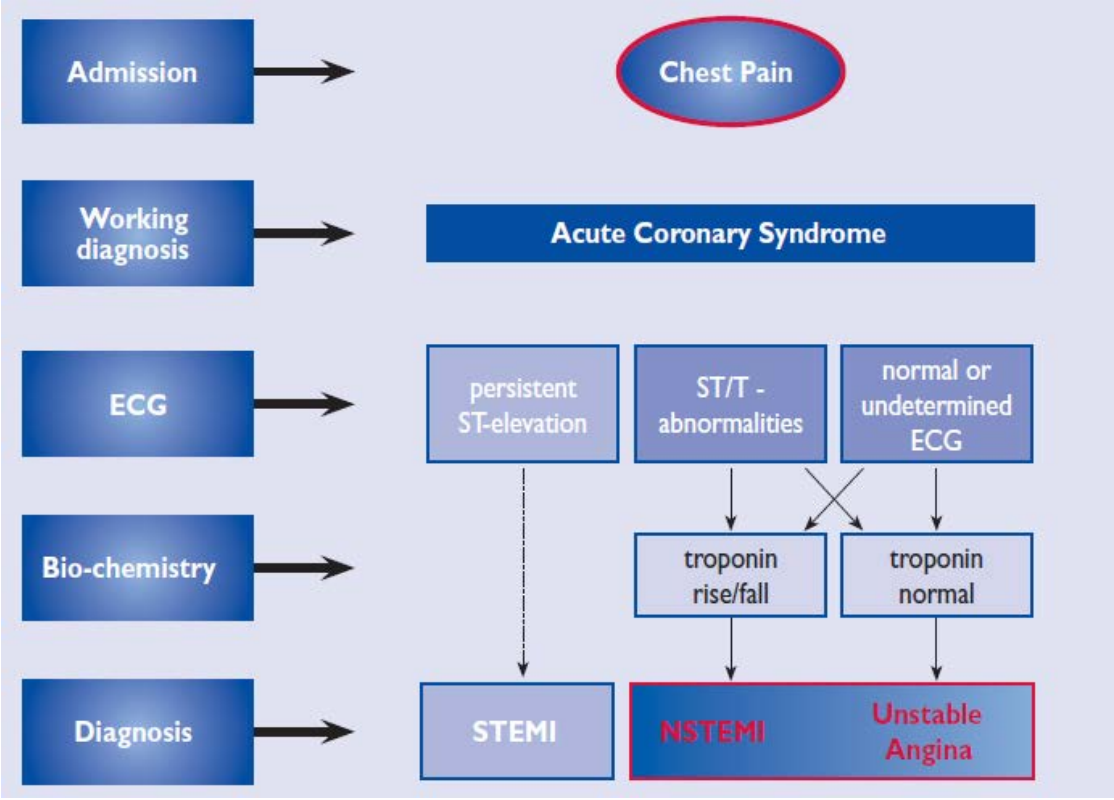

Figure 2.1 The spectrum of acute coronary syndrome.[11]
Abbreviations: ECG, electrocardiogram; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction;
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Etiology / Pathophysiology / Pathogenesis[12-14,17]

ACS is caused primarily by atherosclerosis. Atherosclerosis is the ongoing process of plaque formation (or known as atherosclerotic plaques), the underlying cause of CAD. Endothelial dysfunction, inflammation, and the formation of fatty streaks play important roles in the formation of atherosclerotic plaques. Atherosclerosis progresses throughout a person's lifetime finally manifesting itself as an acute ischemic event.

Several coronary risk factors influence this process, including dyslipidaemia, diabetes, hypertension and smoking.[13,17,18] The endothelium of the blood vessel can be damaged by these risk factors and lead to endothelial dysfunction. Endothelial dysfunction plays crucial roles in initiating the atherosclerotic process.[12,13,17] After the endothelium has been damaged, the inflammatory cells, especially monocytes, migrate into the subendothelium by binding to endothelial adhesion molecules. In the subendothelium, monocytes undergo differentiation and become macrophages. Low-density lipoprotein (LDL) also penetrates into the arterial wall and is oxidized and digested by macrophages. After digestion oxidized-LDL, macrophages transform into foam cells and cause the formation of fatty streaks. Then the activated macrophages will release chemo attractants and cytokines. These will perpetuate the process by recruiting additional macrophages and vascular smooth muscle cells at the site of the plaque. The stability of atherosclerotic plaques varies. The characteristics of vulnerable plaques include but are not limited to: a thin fibrous cap, large lipid-rich necrotic core and increased plaque inflammation. After either endothelial erosion or plaque rupture, the subendothelial matrix is exposed to the circulating blood. This exposure leads to platelet adhesion, activation and platelet aggregation, and the subsequent formation of a thrombus[12-14,17]

The pathogenesis of ACS involves a complicated relationship among the inflammatory cells, the endothelium, and the thrombogenicity of the blood. Important factors in controlling the degree of thrombus formation and prone to plaque rupture are the lipid and tissue factor contents of the plaque, the blood flow in the area, the severity of the plaque rupture, the degree of inflammation at the site, and the patient's antithrombotic and prothrombotic balance. [9-11, 14]

However, a nonatherosclerotic aetiology (such as thrombo-embolism, congenital anomalies, dissection, trauma or arteritis) can cause ACS, but is very rare,[11] but beyond the scope of this thesis.

Risk factors of ACS

A number of modifiable risk factors, e.g., cigarette smoking, dyslipidemia (elevated LDL or total cholesterol or reduced HDL cholesterol), diabetes mellitus, hypertension, physical inactivity and obesity (BMI greater than or equal to 30 kg/m^2) and non-modifiable risk factors, e.g., sex, age and family history of premature cardiovascular disease are associated with the development of atherosclerosis and the risk of presenting acute coronary syndrome.[11,19-21]

Elevated LDL-C as a major risk factor for ACS

Elevated low-density lipoprotein cholesterol (LDL-C) has been strongly associated with the risk of developing coronary artery disease (CAD).[19] Several studies have revealed the benefit of lowering LDL-C with statin therapy associated with reduced incidence of cardiovascular events.[22-24] Lifestyle modifications such as body weight control, physical activity, dietary intake and smoking cessation also lower the risk of cardiovascular disease,[18] but this is beyond the scope of this thesis.

Statin therapy in ACS

Evidence of statins in secondary prevention has been unequivocally established.[23,24] Specific trials, e.g., the MIRACL study and the PROVE IT–TIMI 22 study, have proved the advantage of early and intensive statin therapy.[25,26] The meta-analysis of trials comparing more- and less-intensive LDL-C reduction with statins demonstrated that more-intensive statins, as compared with less-intensive statins, resulted in reduced risks of cardiovascular death, ischemic stroke, nonfatal MI, and coronary revascularization. Data from some specific trials[25,27,28] and meta-analysis recommend routine early use of prompt and intensive statin therapy among patients presenting with ACS. Therefore, guidelines endorse that patients following an acute coronary

syndrome should receive statin therapy soon after being diagnosed, irrespective of initial LDL-C levels.[11,18,20]

Statin therapy should be started as soon as possible during hospitalization because this increases the adherence to statin therapy of patients after discharge. Statins should be given at high-intensity doses, as it is associated with early and sustained clinical benefits.[18] The goal of treatment is an LDL-C level of <1.8 mmol/L (<70 mg/dL). Patients at increased risk of side-effects from statin therapy, e.g., patients with hepatic or renal dysfunction, with previous side-effects of statins, patients likely to have interaction with essential concomitant therapy and the elderly, should be given lower-intensity statins.[18] Lipid levels should be re-evaluated 4–6 weeks after ACS to determine LDL-C goal attainment of patients as well as to monitor for safety issues; then the dose of statins can be adjusted accordingly.[18]

Mechanism of action[18]

The mechanism of statins to reduce cholesterol is through decreasing synthesis of cholesterol in the liver; statins competitively inhibit hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase activity. When intracellular cholesterol concentration decreases, this induces low-density lipoprotein receptor (LDLR) expression on the hepatocyte cell surface, resulting in increased extraction of LDL-C from the blood and a decreased concentration of circulating LDL-C and other apo B-containing lipoproteins including TG-rich particles. [18]

Beyond the lipid lowering effect, statins are believed to have pleiotropic effects. These pleiotropic effects include improving endothelial function of arteries, reducing vascular inflammation, and decreasing platelet aggregability and thrombus formation.[29-34]

Efficacy in clinical studies

Well established research has documented that lowering LDL-C with statins results in reduced incidence of mortality and morbidity from coronary heart disease (CHD) in both primary and secondary prevention.[15,35-40] Efficacy of statins in patients at varying degrees of risk of CHD events and differing ranges of serum cholesterol levels have

been investigated in several landmark trials.[15,35-40] Thus, statin treatment has been shown to provide morbidity and mortality benefits in a wide range of patients.

The first clinical trial to show the efficacy of statins in secondary prevention in patients with CHD was the Scandinavian Simvastatin Survival Study, or the 4S study, in 1994. A total of 4,444 patients with CHD, i.e., angina pectoris or previous MI, were randomized to receive simvastatin or placebo. Their baseline serum cholesterol levels were 215-312 mg/dL (5.5-8.0 mmol/L). After the median follow-up period of 5.4 years, the mean change in LDL-C was -35%, with only few adverse effects. Treatment with simvastatin was associated with an absolute 4% reduction and a 30% relative risk reduction in all-cause death (p=0.0003). CHD mortality (42%), major coronary event (34%), and coronary revascularization (37%) were also reduced significantly in the simvastatin group compared with the placebo.[41]

Following the 4S study, more major clinical trials have shown the benefit of statins in CHD patients such as the Heart Protective Study. This study conducted in patients at high risk of cardiovascular events, and the patients were randomized to either the simvastatin or placebo arm. The study showed that simvastatin was associated with decreased risk of clinical outcomes. In patients randomized to simvastatin, the results revealed the risk in all-cause mortality, major vascular events, major coronary events, nonfatal stroke, and cardiovascular revascularization were decreased by 13% (p =0.0003), 24% (p<0.0001), 27% (p<0.0001), 25% (p<0.0001), and 24% (p<0.0001), respectively, as compared with the placebo arm.[42] Other studies also support statins are associated with reduced cardiovascular risk, e.g., the TNT study.[43]

Evidence supporting early and intensive statin therapy after acute coronary syndrome

RCT studies

For patients at very high risk of suffering recurrent cardiovascular events such as patients with ACS, most randomized controlled trials (RCT) excluded these patients from the study. Three major randomized controlled trials demonstrated the role of statins after ACS on clinical outcomes: the Myocardial Ischemia Reduction with

Aggressive Cholesterol Lowering (MIRACL),[25] A-to-Z,[27] and Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT-TIMI 22)[26] trials.

MIRACL[25]

The MIRACL trial, the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering study, was the first clinical trial showing the reduced recurrent ischemic events in patients treated with intensive statin in early period soon after a diagnosis of ACS. Within 24-96 hours of hospitalization, 3,086 patients with non-ST elevation ACS were allocated randomly to either atorvastatin 80 mg or placebo.[25] The primary endpoint in this study was defined as a composite of death, nonfatal MI, cardiac arrest with resuscitation, or recurrent symptomatic ischemia requiring emergency rehospitalisation at 16 weeks. The mean LDL-C at baseline was 124 mg/dL (3.2 mmol/L). In patients allocated to atorvastatin, LDL-C was decreased from 124 mg/dL to 72 mg/dL (1.9 mmol/L), showing a 42% reduction compared with placebo. A primary endpoint was found in 14.8% of patients treated with atorvastatin and 17.4% in patients receiving placebo (RR 0.84; 95% CI 0.70 - 1.00; p = 0.048). The risk of death, nonfatal MI or cardiac arrest between the atorvastatin and placebo group did not significantly differ. This trial suggested the advantage of early management with intensive statin in ACS patients; however, safety and efficacious in long-term intensive statin therapy, as well as the benefits over less intensive statin drugs should be further investigated.

PROVE IT-TIMI 22[26]

The PRavastatin Or atorVastatin Evaluation and Infection Therapy–Thrombolysis In Myocardial Infarction 22 (PROVE-IT–TIMI 22) trial was conducted among 4,162 patients with ACS, within 10 days of admission of an ACS, to compare between a moderate statin regimen (pravastatin 40 mg/day) and an intensive statin regimen (atorvastatin 80 mg/day). The ACS patients were randomized to receive either pravastatin to achieve LDL-C goal of ≤100 mg/dL or atorvastatin to achieve LDL-C goal of <70 mg/dL.[26] The primary endpoint included composite outcomes: stroke, revascularization (performed at least 30 days after randomization), unstable angina requiring rehospitalisation, MI, and death from any cause. Patients were followed up

for 2 years on average. The median LDL-C achieved was significantly lower (p<0.001) in the atorvastatin group, 62 mg/dL (1.60 mmol/L), compared with the pravastatin group, 95 mg/dL (2.46 mmol/L). At 2 years, the primary endpoint was 22.4% in the atorvastatin group and 26.3% in the pravastatin group. This reflected a 16% reduction in the HR in favor of atorvastatin (HR 0.84; CI 0.74–0.95; *p* = .005). The benefit occurred as early as 30 days, and was consistent over time. Although approximately two thirds of the patients treated with atorvastatin 80 mg achieved LDL-C ≤70 mg/dL, benefits might be associated with even lower levels. Patients in the PROVE IT-TIMI 22 study, treated with atorvastatin 80 mg/day, showed evidence of a graded association between ranges of achieved LDL-C (≤40, >40–60, >60–80, and >80–100 mg/dL) and prognosis. The best prognosis was found in those with an LDL-C level ≤40 mg/dL.[44]

A to Z[27]

A to Z (Aggrastat to Zocor) was conducted among 4,497 ACS patients to compare early initiation of an intensive statin regimen, simvastatin 40 mg/day for 1 month followed by simvastatin 80 mg/day , with delayed initiation of a less intensive statin regimen, placebo for 4 months followed by simvastatin 20 mg/day.[27] The primary endpoint was a composite outcome: cardiovascular death, nonfatal MI, readmission for ACS, and stroke. Patients were followed up for at least 6 to 24 months. The primary endpoints were 14.4% in the early initiation of intensive simvastatin and 16.7% in the less intensive statin regime (HR 0.89; 95% CI 0.76-1.04; *p* = 0.14). Cardiovascular death occurred in 4.1% and 5.4.% of the 2 groups, respectively (HR 0.75; 95% CI 0.57-1.00; *p* = .05). No differences were found in other individual components of the primary endpoint. The primary endpoint from 4 months through the end of the study was significantly decreased in the simvastatin group (HR 0.75; 95% CI 0.60-0.95; *p* = .02), but no differences were found between the two groups during the first 4 months (HR, 1.01; 95% CI 0.83-1.25; *p* = 0.89).

Meta-analysis

In addition to randomized controlled trial studies, meta-analyses showed the benefit of statin therapy in reducing the risk of cardiovascular disease.[23,24] A meta-analysis of 26 randomized controlled clinical trials involving approximately 170,000 patients has

shown a consistent proportional association between reduced LDL-C levels and reduced major vascular events (nonfatal MI, coronary heart disease [CHD] death, stroke, and revascularization).[24] For every 38.6 mg/dL (1 mmol/L) reduction in LDL-C with statin therapy, major vascular events were reduced by 22% (Rate Ratio (RR) 0.78; 95% CI: 0.76–0.80; P <0.001) after a mean follow-up of approximately 5 years of statin therapy compared with placebo or less efficacious LDL-C–lowering therapy.

How to select the optimal statin therapy for each patient

Each statin at maximal recommended doses differs in the LDL-C reduction capacity. Evidence shows that the clinical benefits of statins depend on the degree of LDL-C reduction but does not depend on the type of statin; thus, statin used for each patient should reflect the extent of LDL-C lowering required to reach the target LDL-C in that patient. [24,45] The following scheme has been proposed by the 2013 ESC/EAS guidelines on how to select statins for each patient:[18]

- Assess the total cardiovascular risk in each patient
- Engage the patient's decisions on the management of cardiovascular risk
- Determine the LDL-C goal for the patient according to the risk level, e.g., the LDL-C goal of <70 mg/dL is required for patients presenting with ACS
- Calculate the percentage of LDL-C reduction required to achieve that target
- Select a statin that can provide this LDL-C reduction (by average)
- Because the response to statin therapy varies from patient to patient, up-titration to reach goal is required
- Consider combination therapy if the selected statin cannot attain the goal.

The details above are only the general criteria for selecting a statin for a patient. The variability of each patient, such as concomitant treatments and drug tolerability, will play important roles in selecting the desired choice of medicine and dose.

Side effects and interactions[18]

Statins differ in their absorption, bioavailability, plasma protein binding, excretion and solubility. Simvastatin is a prodrug, while other statins are administered in the active form. The absorption rate of each statin varies from 20 to 98%. Some statins, except pravastatin, rosuvastatin and pitavastatin, undertake significant hepatic metabolism by cytochrome P450 iso-enzymes (CYPs); these enzymes are found mostly in the liver and gut wall. Although statin therapy can prevent cardiovascular disease, responding to statin treatment and experiencing the incidence of adverse effects vary from patient to patient.

Muscle

Stain therapies are usually well tolerated, and serious adverse events are infrequent. Myopathy is found to be the most serious adverse event related to statin treatment, which could progress to rhabdomyolysis, culminating in renal failure and death. Patients with complex medical problems, or with multiple medications, or in aging patients, particularly women, are more likely to experience myopathy. Approximately 5–10% of patients in clinical practice experience myalgia (without CK elevation). Patients should be educated on quickly reporting unexpected muscle pain or weakness. Nevertheless, patients complaining of myalgia without CK elevation can continue the statin if they can tolerate their symptoms. If they cannot tolerate the symptoms, the statin should be stopped.

Liver

Clinicians assess hepatocellular damage by the level of alanine aminotransferase (ALT) and aspartate aminotransaminase in blood plasma. All significant statin trials usually monitor these measures. Elevation of hepatic transaminases is dose dependent and occurs in 0.5–2.0% of statin-treated patients. An increase of three times the ULN of these enzymes on two occasions is a meaningful elevation. It has not been determined whether transaminase elevation associated with statins constitutes true hepatotoxicity. Development to liver failure is very rare.

Type 2 diabetes mellitus

Treatment with statin is associated with a 9% increased the risk of incident diabetes.[46] However, the absolute cardiovascular disease risk reduction in high risk patients outweighs the possible adverse effects of a very small increase in the incidence of diabetes.[46]

However, in our retrospective studies, the side effects of statin therapy as well as interactions with statin therapy are beyond the scope of our studies.

Registries of ACS patients in Thailand[47,48]

The registry of ACS patients is established to collect data of patients presenting with ACS. For example, the Global Registry of Acute Coronary Events (GRACE) is a well-known international registry of ACS patients worldwide. This registry tracks in-hospital and long-term outcomes of ACS patients.[49] Due to concerns that ACS is a serious life-threatening condition, two prospective registries of ACS have been established in Thailand. The first ACS registry named, "The Thai ACS Registry (TACSR),"[47] was established in 2002, and later the second registry named, "The Thai registry in Acute Coronary Syndrome (TRACS),"[48] was established in 2007. Their aims are collecting data related to ACS in the Thai population through a networking of hospitals all over Thailand. These include the data of ACS patients in Thailand such as epidemiology, initial management, practice, and outcomes, e.g., inhospital mortality rate, 6-month and 12-month mortality rate. These useful data from many parts of Thailand will support the evidence-based practices and may help to develop guidelines for Thais.[47,48]

The first Thai ACS registry involved 17 hospitals and 9,373 patients, whereas the second ACS registry involved 39 hospitals and 2007 patients. Characteristics of hospitals, patients and use of medications between the two registries are compared in Tables 2.1, 2.2, and 2.3. In general, the outcomes in the second registry were better than that in the first registry. For example, in-hospital mortality was decreased from 12.6% to 4.8%. This was also true for all spectrums of ACS: UA, NSTEMI, and STEMI. A big difference seen in the STEMI patients was that mortality rate was significantly reduced from 17.0% to 5.3%. In addition, NSTEMI patients decreased mortality rates from 13.1% to 5.1%. Nonetheless, the first and second registry differs in some points

that should be considered. For example, informed consent forms need to be obtained from patients included in the second registry.

In addition, the second registry showed the improvement of pharmacological treatment for ACS patients in all medications compared with the first registry, especially aspirin and statin. A total of 93% of ACS patients were treated with statins at second registry compared with 80% at first registry (Table 2.3).

Table 2.1 Characteristics of hospitals at first and second registry of patients with ACS in Thailand

	1st registry (2002-2004)	2nd registry (2007-2008)
Hospitals in the registry	17	39
Location		
Metropolitan, n (%)	13 (76.5%)	16 (41.0%)
Government, n (%)	10 (58.8%)	10 (25.6%)
Private, n (%)	3 (17.6%)	6 (15.4%)
Regional government, n (%)	4 (23.5%)	23 (59.0%)
Government, n (%)	3 (75%)	22 (56.4%)
Private, n (%)	1 (25%)	1 (2.6%)
Hospital beds, median (IQR)	755 (418-1,110)	602 (100-2,279)
CCU beds, median (IQR)	6 (5-8)	6 (0-22)
Admission of ACS per year, mean (range)	275 (150-400)	428 (150-1,140)
Cardiac catheterization, n (%)	16 (94.1%)	22 (56.4%)
Emergency on call for primary PCI, n (%)	11 (64.7%)	17 (43.6%)
Open-heart surgery, n (%)	16 (94.1%)	22 (56.4%)

*Modified from[48]

Table 2.2 Characteristics of patients with ACS at first and second registry in Thailand based on diagnosis at discharge

	UA		NSTEMI		STEMI		Total	
	1st registry (n=1,989)	2nd registry (n=241)	1st registry (n=3,548)	2nd registry (n=664)	1st registry (n=3,836)	2nd registry (n=1,102)	1st registry (n=9,373)	2nd registry (n=2007)
Mean age (y)	65.8	65.5	68.0	67.1	62.2	60.9	65.2	63.5
±SD	±11.0	±11.6	± 11.6	± 11.9	± 12.8	±13.0	± 12.3	±12.8
Male (%)	52.5	54.4	54.9	58.7	68.1	75.7	59.8	67.5
Presenting symptom								
Typical angina (%)	84.2	85.1	71.7	81.6	82.0	91.7	78.6	87.6
Atypical angina (%)	13.1	13.7	15.7	14.2	10.0	5.8	12.8	9.5
Shock (%)	1.2	5.8	6.3	9.5	16.3	16.3	9.3	12.8
Cardiac arrest (%)	0.9	0.4	2.7	2.0	7.3	3.8	4.2	2.8
Risk factors								
DM (%)	45.5	46.5	50.9	57.4	37.2	47.6	44.2	50.7
HT (%)	73.9	74.7	71.7	70.2	51.4	49.8	63.9	59.5
Dyslipidaemia (%)	78.4	88.4	76.7	83.4	72.5	8.9	75.4	83.2
Smoking (%)	23.4	15.9	25.3	22.0	42.7	41.8	32.0	32.1
Family Hx of CAD	10.3	8.7	8.1	8.4	10.0	10.0	9.3	9.3
Referring (%)	25.1	33.2	31.4	42.5	54.2	54.0	39.5	49.3

*Modified from[48]

Abbreviations: STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; UA, unstable angina; DM, diabetes mellitus; HT, hypertension; CAD, coronary artery disease

Table 2.3 Medications during admission

Medications	UA		NSTEMI		STEMI	
	1st registry (n=1,989)	2nd registry (n=241)	1st registry (n=3,548)	2nd registry (n=664)	1st registry (n=3,836)	2nd registry (n=1,102)
Aspirin (%)	94.1	98.8	94.6	98.6	95.2	99.5
Statin (%)	81.7	92.5	81.5	91.4	77.5	96.1
ACEI (%)	55.3	54.8	57.5	58.3	59.4	66.6
ARB (%)	11.2	12.0	8.8	11.6	5.3	6.3
Beta-blocker (%)	71.9	71.8	61.6	62.4	58.3	59.2
ADP inhibitor (%)	53.5	75.9	58.5	83.4	60.4	97.8
LMWH (%)	62.3	75.5	72.2	87.1	50.7	56.7
Unfractionated heparin (%)	16.4	21.6	21.3	28.5	28.3	39.5
GP IIb/IIIa (%)	3.2	2.5	5.3	4.5	19.5	19.5

Modified from[48]

Abbreviations: STEMI, ST- elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; UA, unstable angina; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; GP, glycoprotein

Table 2.4 Hospital outcomes, 6-month mortality, and 12-month mortality

	UA		**NSTEMI**		**STEMI**		**Total**	
	1st registry (n=1,989)	2nd registry (n=241)	1st registry (n=3,548)	2nd registry (n=664)	1st registry (n=3,836)	2nd registry (n=1,102)	1st registry (n=9,373)	2nd registry (n=2,009)
CHF (%)	27.4	28.6	56.2	50.3	44.1	27.1	45.1	34.9
CHF after 48 h (%)	2.9	3.3	5.5	2.6	7.8	2.4	6.0	2.5
Serious cardiac Arrhythmia (%)	3.2	3.3	10.6	7.5	29.1	17.1	16.6	12.2
Heart block	1.4	1.7	3.1	1.7	11.5	6.2	6.2	4.1
Ventricular arrhythmia	1.8	1.2	8.1	1.2	19.4	8.8	11.4	6.8
Both		0.4		0.3		2.1		1.3
Stroke (%)	0.8	0	2.1	0.3	2.5	1.6	2.0	1.2
Ischemic	0.8	0	1.7	0.8	1.9	0.9	1.6	0.7
Hemorrhagic	0	0	0.1	0	0.6	0.7	0.3	0.4
Both		0		0.2		0		0.1
Unknown		0		0.2		0		0.1
Major bleeding	2.0	1.7	6.0	4.1	7.9	5.3	5.9	4.4
Length of stay (days)								
Mean ± SD	8.6±8.8	6.4±6.6	11.8±12.6	8.8±9.7	9.4±12.3	6.7±7.5	10.1±11.8	7.4±8.3
Median	6.0	4.2	8.0	5.6	6.0	4.9	6.8	5.0
Death								
In-hospital	3.0	1.7	13.1	5.1	17.0	5.3	12.6	4.8
Cardiac	2.4	1.7	8.6	4.4	14.7	4.4	9.8	4.1
Non-cardiac	0.6	0	4.5	0.8	2.2	0.8	2.8	0.7
6-month		9.5		18.9		12.1		14.1
12-month		13.8		25.0		14.1		17.7

Modified from[48]

Abbreviations: STEMI, ST- elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; UA, unstable angina; CHF, congestive heart failure

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