SURVIVAL AND PROGNOSTIC FACTORS OF HOSPITALIZED ACUTE MYOCARDIAL INFARCTION PATIENTS IN DISTRICT OF KOTA BHARU, KELANTAN: A RETROSPECTIVE COHORT STUDY 2000-2003

by

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LIST OF ABBREVIATIONS

CVD	Cardiovascular disease
CHD	Coronary heart disease
CAD	Coronary artery disease
AMI	Acute myocardial infarction
MI	Myocardial infarction
ACS	Acute coronary syndrome
CCU	Coronary care unit
CRW	Coronary rehabilitation ward
UA	Unstable angina
NSTEMI	Non ST elevated myocardial infarction
STEMI	ST elevated myocardial infarction
CK	Creatine kinase
CKMB	Creatine kinase myocardial band
ECG	Electrocardiograph
tPA	Tissue Plasminogen Activator
LVF	Left ventricular failure
ACEI	Angiotensin Converting Enzyme Inhibitor drug
PTCA	Percutaneous Transluminal Coronary Angioplasty

CABG	Coronary Artery Bypass Graft
HKB	Hospital Kota Bharu
HUSM	Hospital Universiti Sains Malaysia
MOH	Ministry of Health
ESC	The European Society of Cardiology
ACC	American College of Cardiology
WHO	World Health Organisation
MONICA	Monitoring trends and determinants of cardiovascular disease
CI	Confidence interval
HR	Hazard ratio

ABSTRAK

TAJUK

Survival dan faktor-faktor prognostik di kalangan pesakit infarksi miokardium akut di daerah Kota Bharu, Kelantan: Kajian retrospektif kohort 2000-2003.

PENGENALAN

Penyakit infarksi miokardium akut masih merupakan masalah kesihatan awam yang utama di Malaysia walaupun telah mencapai kemajuan dari segi rawatan dan teknologi perubatan. Data setempat berkaitan prognosis penyakit ini boleh membekalkan maklumat yang penting untuk tindakan pencegahan yang efektif. Objektif kajian ini adalah untuk menentukan survival dan mengenalpasti faktor-faktor prognostik yang mempengaruhi risiko kematian pesakit infarksi miokardium akut di Kota Bharu.

METODOLOGI

Suatu kajian retrospektif kohort melibatkan 368 orang pesakit yang mengalami infarksi miokardium akut dari daerah Kota Bharu yang dimasukkan ke dua buah hospital tertiari; Hospital Kota Bharu dan Hospital Universiti Sains Malaysia dari 1 Januari 2000 ke 31 Disember 2003 telah dijalankan. Perkembangan susulan selama satu tahun selepas fasa pemilihan subjek telah dilakukan dari 1 Januari 2004 ke 31 Disember 2004. Kesemua pesakit yang memenuhi kriteria telah dipilih memasuki kajian ini. Rekod perubatan

daripada hospital dan klinik pakar telah disemak oleh seorang penyelidik. Maklumat yang berkenaan dan status survival sehingga 31 Disember 2004 telah direkodkan kedalam borang yang disediakan. Panggilan telefon juga dibuat untuk mendapatkan maklumat tentang survival sesetengah pesakit yang hidup semasa discaj tetapi tiada rekod rawatan susulan.

KEPUTUSAN

Kumulatif survival pesakit infarksi miokardium akut di Kota Bharu untuk 1 hari, 2 hari, 1 minggu dan 1 bulan adalah 91.0 (95% confidence interval (CI): 87.6, 93.5), 88.8 (95% CI: 85.2, 91.7), 86.6 (95% CI: 82.6, 89.7) dan 83.9 (95% CI: 79.6, 87.5) peratus. Manakala, kadar survival jangkamasa panjang untuk 6 bulan, 1 tahun, 2 tahun, 3 tahun dan 4 tahun selepas infarksi miokardium akut adalah 80.7 (95% CI: 76.1, 84.6), 77.5 (95% CI: 72.6, 81.7), 76.2 (95% CI: 71.2, 80.6), 71.9 (95% CI: 66.0, 76.9) and 69.2 (95% CI: 62.7, 74.8).

Berdasarkan analisa "Multivariable Cox Proportional Hazards Regression" setelah mengambilkira lain-lain faktor, didapati faktor-faktor prognostik bermakna yang mempengaruhi risiko kematian di kalangan pesakit infarksi miokardium akut di Kota Bharu adalah umur semasa diagnosa (Hazard ratio (HR)=1.03, 95% CI: 1.01, 1.06), penyakit diabetes mellitus (HR=1.60, 95% CI: 1.03, 2.46), kegagalan ventrikel kiri

(HR=2.15, 95% CI: 1.38, 3.34), rawatan trombolisis (HR=0.48, 95% CI: 0.31, 0.73) dan tempat rawatan yang pertama (HR=0.47, 95% CI: 0.24, 0.91).

KESIMPULAN

Kadar survival dikalangan pesakit infarksi miokardium akut yang dimasukkan ke hospital di Kota Bharu adalah setara dengan negara maju. Kesemua faktor yang didapati siknifikan adalah agak serupa dengan keputusan daripada negara lain, kecuali beberapa faktor yang penting seperti jantina dan ubat semasa discaj. Tempat rawatan yang pertama didapati turut mempengaruhi risiko kematian infarksi miokardum akut di Kota Bharu.

Katakunci: infarksi miokardium, survival, faktor prognostik

ABSTRACT

TITLE

Survival and prognostic factors of hospitalized acute myocardial infarction in district of Kota Bharu, Kelantan: A retrospective cohort study 2000-2003.

INTRODUCTION

Acute myocardial infarction (AMI) remains a major public health problem in Malaysia despite advances in medical management and technology. Local prognostic data on AMI will provide an essential information for effective preventive measures. The objectives of the study were to determine the survival of hospitalized acute myocardial infarction patients in Kota Bharu and identify the prognostic factors that influence the risk of death.

METHODOLOGY

A retrospective cohort study was conducted involving 368 hospitalized AMI patients from the district of Kota Bharu who were admitted in two tertiary hospital; Hospital Kota Bharu and Hospital Universiti Sains Malaysia from 1st January 2000 to 31st December 2003. Additional follow up of one year after the recruitment of the subjects was done from 1st January 2004 to 31st December 2004. All patients who fulfilled the criteria were included in the study. Hospital medical records and physician clinic records were reviewed by a researcher. The required information on variables of interest and patients'

survival status until 31st December 2004 was recorded into a data collection form. Telephone calls were also conducted to obtain the information on survival status of some patients who were discharged alive but loss to follow up.

RESULTS

The overall cumulative survival for hospitalized AMI in Kota Bharu were 91.0 (95% confidence interval (CI): 87.6, 93.5), 88.8 (95% CI: 85.2, 91.7), 86.6 (95% CI: 82.6, 89.7) and 83.9 (95% CI: 79.6, 87.5) percent for 1 day, 2 days, 1 week and 1 month respectively. The long-term survival rate for 6 months, 1 year, 2 years, 3 years and 4 years after AMI were 80.7 (95% CI: 76.1, 84.6), 77.5 (95% CI: 72.6, 81.7), 76.2 (95% CI: 71.2, 80.6), 71.9 (95% CI: 66.0, 76.9) and 69.2 (95% CI: 62.7, 74.8) percent respectively.

Based on Cox Proportional Hazards Regression multivariable analysis after adjusting other variables, the significant prognostic factors that influenced the risk of death in hospitalized acute myocardial infarction patients in Kota Bharu were age at diagnosis (HR=1.03, 95% CI: 1.01, 1.06), diabetes mellitus (HR=1.60, 95% CI: 1.03, 2.46), left ventricular failure (HR=2.15, 95% CI: 1.38, 3.34), thrombolytic therapy (HR=0.48, 95% CI: 0.31, 0.73) and first contact of care (HR=0.47, 95% CI: 0.24, 0.91).

CONCLUSION

Survival rate of hospitalized AMI patients in the district of Kota Bharu was comparable with other developed countries. All significant independent prognostic factors identified were considerably similar to other countries, except a few important factors such as gender and drugs prescribed on discharge. Interestingly, first site contact of medical care was also identified to significantly influence the risk of death of AMI in Kota Bharu.

Keyword: myocardial infarction, survival, prognostic factor

CHAPTER ONE : INTRODUCTION

1.1 CARDIOVASCULAR DISEASE

1.1.1 Global burden of cardiovascular disease

Cardiovascular disease (CVD) has emerged as the dominant non communicable disease in many parts of the world and become the major cause of morbidity and mortality worldwide (Khor, 2001). At the beginning of the 20th century, CVD accounted for less than 10 percent of all deaths worldwide. However, at early 21st century, they accounted for at least 15 million deaths or around 30% of the annual total deaths (WHO, 1998).

The Global Burden of Disease Study by Murray and Lopez, (1997) had described the CVD mortality pattern comprehensively. In 1990, CVD accounted for 14.3 million deaths, or 28.5% of the world's 50 million deaths. By 2020, CVD will account for nearly 25 million deaths or 36.3% of the estimated 68 million deaths worldwide. In contrast, the proportion of deaths attributable to communicable diseases and malnutrition is expected to drop from 28.4% to 13.6% over the same period.

Majority of the CVD deaths now are occurring in developing countries. Twice as many deaths from CVD now occur in developing countries as in developed countries. During

the period of 1985 to 1997, death due to circulatory diseases declined from 51% to 46% of total deaths in the developed countries but increased from 16% to 24% in developing countries (WHO, 1998).

Another particular concern is the relatively early age of CVD deaths in developing countries compared with those in developed countries (WHO, 2003). For example in 1990, the proportion of CVD deaths occurring below the age of 70 years was 26.5% in the developed countries compared with 46.7% in the developing countries (Reddy and Yusuf, 1998).

1.1.2 Contributing factors to global cardiovascular disease

The underlying determinants of non-communicable disease epidemics can be described by the evolution of population changes known as epidemiological transition (Gaziano, 2001). The epidemiological transition has been developed by Omran where he divided the transition into three basic ages: pestilence and famine, receding pandemics and degenerative/ man-made diseases. Olshansky and Ault had added a fourth stage so called delayed degenerative diseases. The progression of this evolution is closed linked with several parallel and interrelated transformations include demographic, economic and social transition (Levenson *et al.*, 2002). The demographic transition is characterized by declining fertility and mortality rates. Improvement of the public health infrastructure, medical care and nutrition, reduced the rates of communicable disease, malnutrition, and maternal and infant deaths which have led to increase in life expectancy and an aging

population. The economic transition is characterized by increasing per capita income while the social transition by industrialization and urbanization. The socioeconomic development and lifestyle changes have led to increase in risk factors for CVD worldwide.

In addition, globalization of food production and marketing had contributed to an evolution in dietary patterns towards increased consumption of higher-fat foods, refined carbohydrates and sweets (Ounpuu *et al.*, 2000 and Reddy and Yusuf, 1998). This diet pattern, in combination with tobacco use and decreased physical activity, led to emergence of population-wide atherosclerosis and widespread distribution of cardiovascular diseases (Beaglehole and Yach, 2003).

As the epidemiologic transition is linked to economic, social, and demographic forces, it takes place at different rates in different countries around the world (Gaziano, 2001 and Levenson *et al.*, 2002).

1.2 CORONARY HEART DISEASE

1.2.1 Worldwide Coronary Heart Disease

The most important cardiovascular diseases worldwide are coronary heart disease and stroke. Coronary heart disease (CHD) is the largest cause of death and the fifth largest in terms of global disease burden. World wide, there were more deaths from CHD (7.2 million) than stroke (4.6 million) (WHO, 1998). Murray & Lopez (1997) estimated that CHD and stroke would be the first and second causes of death globally by 2020 which

accounted for 11.1 and 7.7 million deaths respectively. They also estimated that by 2020, CHD will outnumber infectious disease as the world's number one cause of death and disability.

The WHO monitoring trends and determinants of cardiovascular disease project (WHO MONICA) which monitored the trend over 10 years in CHD across 37 population in 21 countries, demonstrated that CHD event and mortality rates vary widely between and even within countries. The greatest fall in coronary events rates in men occurred in three north European populations leading by North Karelia, Finland. Results from that project also highlighted that number of coronary events is the major determinant of this decline, whereas improved coronary and secondary care were associated with decreased event rates (Tundoe-Pedoe *et al.*, 1999).

Khor, (2001) had discussed comprehensively the cardiovascular epidemiology in Asia Pacific Region. The countries may be ranked into high, intermediate and low CVD mortality rates according to their proportion of total deaths from all causes. The high mortality categories include New Zealand, Australia, Singapore and some Pacific Islands and urban areas of China with 30-35% of total death due to CVD. The intermediate mortality category consists of rural China, Hong Kong, Japan, Korea and Malaysia with 20-30% of total deaths from CVD. Countries in the low mortality category include Thailand, Philippina and Indonesia with less than 20% of total deaths. Nevertheless, the low mortality in some countries might be due to lack of epidemiological data and underreporting of their CVD cases. The high mortality countries particularly New

Zealand, Australia and Singapore also led in CHD mortality (more than 150 deaths per 100 000 population). Countries in East Asia and South East Asia, except Singapore have lower CHD mortality rates of less than 100 per 100 000 population (Janus *et al.*, 1996). However, assessment on trend in recent decades revealed that the high mortality countries in Asia Pacific have undergone declining event and mortality rates pattern.

1.2.2 Coronary Heart Disease in Malaysia

The epidemiology of CVD particularly CHD in Malaysia was poorly known due to many reasons which include problem in standard diagnosis, coding and reporting, poor surveillance, poor statistical support and lack in good epidemiological studies (Lo, 1988). It is likely that CVD death cases in Malaysia may be underestimated, as less than half of the total deaths were medically certified and examined (Khor, 2001).

Based on available data, cardiovascular disease had risen markedly during the last 40 years in Malaysia. Since the early 1970's, cardiovascular diseases have been the leading cause of mortality in Malaysia among medically certified and inspected cases. Coronary heart disease had emerged as the most important cardiovascular disease. The increase may be partly contributed by improved method of diagnosis and reporting (Khor, 1994). However, this could indicate an actual increase in the occurrence of disease as a result of improve socioeconomic status and changing lifestyle of Malaysian population (Jeyamalar, 1991).

Cardiovascular disease ranked third in the 1950's but gradually took the first position in 1970 and continued to do so in 1989 with an increase of 16.5 times from prevalence of 1.8% in 1950 to 29.6% in 1989. On the other hand, infectious disease which was ranked first in the 1950s had fallen fourth position in 1989. Similarly, the cardiovascular disease mortality had increased from 9.2% in 1965 to 29.6% in 1989 while mortality from non cardiovascular diseases dropped from 90.8% in 1965 to 70.4% in 1989 (Khoo, 1991).

In 1955, 'Heart Disease' was not even listed as one of the 10 principal causes of medically certified death but between 1955 and 1965 it rose to second position and since 1980, has become the leading cause of death in Malaysia (Lo, 1988). The proportion of CHD deaths out of total mortality causes rose from 3% in 1965 to 11% in 1991 (Khoo, 1991 and Khor, 1994). At present, 'Heart disease and diseases of pulmonary circulation' still ranked in the first position of the 10 principal causes of death in medically certified death till year 2001. Its proportion out of total mortality generally sustained at about 16% from 1995 to 2001. In terms of trend, the mortality rate based on number of deaths in government hospital under 'ischemic heart disease' increased from 9.85 to 10.58 per 100,000 population during the same period of time (Information and Documentation System Unit, Ministry of Health Malaysia, 2002).

1.3 ACUTE MYOCARDIAL INFARCTION

Coronary heart disease or ischaemic heart disease (includes acute myocardial infarction, angina pectoris and sudden coronary death) is the single most important cause of death among hospitalized patient worldwide (WHO, 2002). Acute myocardial infarction (AMI) or heart attack is the commonest coronary heart disease with serious consequences in mortality, morbidity and cost to nation and society (Boersma *et al.*, 2003).

Over the past 30 years, the trend of AMI mortality was declining and the short-term prognosis of patients with acute myocardial infarction (AMI) have shown a steady improvement in the industrialized nations (Sytkowski *et al.*, 1996, Tundoe-Pedoe *et al.*, 1999 and Rosamond *et al.*, 1998). Additionally, recent studies reported that the long-term AMI prognosis were also tend to improve (Abrahamsson *et a*l., 1998, Capewell *et al.*, 2000 and Mahon *et al.*, 1994). The improved prognosis was attributed mainly to changing risk factor profiles and substantially due to improvement in treatment (Alpert, 1999). Some of these studies also had documented the main determinants of AMI death (Stevenson *et al.*, 1993, Abrahamsson *et al.*, 1998 and Marcos *et al.*, 1998).

Generally, the improvement in management of patients with acute myocardial infarction includes the introduction of reperfusion therapy in the 1980's and development of catheter based interventions in the 1990's (Boersma *et al.*, 2003 and Berger and Orford, 2004). In addition, chronic drug treatment has contributed to improve long-term prognosis of the survived patients (Boersma *et al.*, 2003).

Despite these advances, myocardial infarction remains a major public health problem both in developed and developing countries. For example, although CHD mortality has declined in United States, it has remained the leading cause of death in that country and acute myocardial infarction contributed the greatest rate. The estimated number of myocardial infarction in United States is 565,000 new attacks and 300,000 recurrent attack annually (American Heart Association, 2005).

In Malaysia, Acute Coronary Syndromes represent a large number of hospitalizations with 33,623 patients admissions in year 2000 (Ministry of Health, Malaysia, 2002). However, data for incidence and survival of AMI in Malaysia is sparse. Even developed countries including the United States have limited data on the incidence of CHD, since it is very difficult and expensive to collect detailed morbidity and mortality figures over an extended period of time. Nevertheless, in Singapore, where all MI in the country are systematically entered in MI registry, the incidence of MI was 104.3 per 100,000 in 1988 and show declining pattern to 82.6 per 100,000 population in 1997 (Tan *et al.*, 2002).

1.4 IMPORTANCE AND RATIONALE OF THIS STUDY

Coronary heart disease is a significant cause of morbidity and mortality in Malaysia in recent decades. Among them, acute myocardial infarction is the commonest cause of death. There is a need to take corrective action before the incidence and mortality of coronary heart disease in this country continue to increase rapidly during the next decades. Hence, research on this major disease merit continued attention.

Furthermore, the WHO MONICA project revealed coronary heart disease mortality rates vary widely between and even within countries (Tundoe-Pedoe *et al.*, 1999). It was also different when observed even in the same urban areas of one country in different racial or socioeconomic status. This strengthened the need of assessing the survival status of local communities and come up with local data that provide useful information for local effective preventive measures.

Despite advances in medical managements, myocardial infarction remains an important public health problem worldwide. Although the in-hospital mortality is reducing, unhealthy lifestyle resulted in increasing incidence of AMI especially in developing countries. The ageing community, rising prevalence of diabetes and hypertension and the improved survival of acute coronary syndromes have resulted in growing population of patients with chronic conditions (Boersma *et al.*, 2003). Further research on prognosis of AMI is warranted because AMI is inevitable in Malaysia which also experiences increasing number of patients with chronic conditions.

Studies on survival and prognostic factors of AMI are important and merit further assessment especially in Malaysia where such data are lacking. Assessment on AMI survival status may provide useful information on our underlying cardiovascular preventive action and medical care. Additionally, identification of local prognostic factors may impart more knowledge on relevant areas to improve AMI prognosis in our community.

CHAPTER TWO :
OBJECTIVES, RESEARCH QUESTIONS & HYPOTHESIS

2.1 OBJECTIVES

2.1.1 General objective

To determine the survival of hospitalized acute myocardial infarction patients in Kota Bharu and identify the prognostic factors that influence the risk of death

2.1.2 Specific objectives

1. To determine the overall survival probabilities of hospitalized acute myocardial infarction patients in Kota Bharu

2. To determine the survival probabilities of hospitalized acute myocardial infarction patients in Kota Bharu by specific subgroups in terms of demographic, co-morbidity, admission care and clinical characteristics

3. To identify the prognostic factors that influence the risk of death in hospitalized acute myocardial infarction patients in Kota Bharu

2.2 RESEARCH QUESTIONS

1. What are the overall survival probabilities of hospitalized acute myocardial infarction patients in Kota Bharu?

2. Are the survival probabilities of hospitalized acute myocardial infarction patients in Kota Bharu differ by demographic, co-morbidity, admission care and clinical characteristics?

3. What are the prognostic factors that influence the risk of death in hospitalized acute myocardial infarction patients in Kota Bharu?

2.3 RESEARCH HYPOTHESIS

1. Demographic characteristics (age, gender and race), co-morbidity characteristics (having diabetes mellitus, hypertension, previous coronary artery disease or stroke), admission care characteristics (time of symptom to admission, first medical contact of care, admitting hospital, ward of admission and year of admission) and clinical characteristics (Q wave, having left ventricular failure, given thrombolytic therapy, aspirin, beta-blocker, ACE inhibitor, statin and interventions conducted) are the prognostic factors that influence the risk of death in hospitalized acute myocardial infarction patients in Kota Bharu.

2.4 OPERATIONAL DEFINITIONS

Survival probability is defined as the probability that an individual survives longer than t (survival time). Statistically, it is also known as cumulative survival rate (Lee, 1992).

Prognosis refers to the possible outcomes of a disease and the frequency with which they can be expected to occur. Meanwhile, prognostic factors are the characteristics of a particular patient that predict the patient's eventual outcome (Laupacis *et al.*, 1994).

Hospitalization refers to patient who was admitted or warded to either coronary care unit (CCU), cardiac rehabilitation ward (CRW) or general medical ward of Hospital Kota Bharu (HKB) and Hospital Universiti Sains Malaysia (HUSM).

AMI can be defined from a number of different perspectives related to clinical, electrocardiographic (ECG), biochemical and pathologic characteristics (Alpert and Thygesen *et al.*, 2000). AMI used in this present study was defined by a combination of two out of three criteria as outlined by the WHO (Ministry of Health, Malaysia, 2001);

1.A typical clinical history of ischemic type of chest discomfort.

2.A raised and fall concentration of serum cardiac markers (include creatine kinase (CK) or preferably creatine kinase myocardial band (CKMB) enzyme).

3.A typical serial ECG changes (development of ST elevation (> 0.1 mV in standard limb leads or > 0.2 mV in two or more precordial leads) or pathological Q wave).

CHAPTER THREE: LITERATURE REVIEW

3.1 INTRODUCTION TO ACUTE MYOCARDIAL INFARCTION

3.1.1 Definition and concept

The term myocardial infarction (MI) reflects ischemic necrosis of cardiac myocytes due to prolonged inadequate blood supply produced by an acute occlusion of the coronary artery (Ministry of Health, Malaysia, 2001). The necrosis and loss of functional myocardium will result in ventricular dysfunction. Further reduce in left ventricular function can affect patient's quality of life and causes premature death (Boersma *et al.*, 2003).

Clinically, early administration of reperfusion therapy will allow more rapid restoration of coronary blood flow. Patients with MI that treated most rapidly have a lower mortality and reduce infarct size in the survivors (Berger and Orford, 2004). Severity of left ventricular dysfunction after discharge would also determine MI death after discharge (Ali *et al.*, 199). Apart from that, emerging evidences have shown that the prognosis after MI were also associated by various other factors such as age, concurrent medical illnesses and partly socioeconomic reasons (Donahue *et al.*, 1993, Miettinen *et al.*, 1998, Barakat *et al.*, 1999, Hemingway and Marmot, 1999 and Crowley, 2003).

3.1.2 Pathophysiology

Atherosclerosis underlies most CHD. The development and progression of atherosclerotic lesions is a chronic inflammatory process (Mulvihill and Foley, 2002). Risk factors such as raised plasma low density lipoprotein cholesterol, decreased high density lipoprotein cholesterol, smoking, high blood pressure and increased glucose concentration stimulate and activate the inflammatory cells including monocytes and lymphocytes via several pathways (Boersma *et al.*, 2003). These cells are rich in cytokines and growth factors, which could induce and amplify inflammation in the endothelium (Mulvihill and Foley, 2002). Consequently, continuing inflammatory process results in atherosclerotic lesion that composed of a core of lipid and necrotic tissue, covered by fibrous capsule (Davies and Bashir, 2001).

In the advanced stages of disease process, atherosclerotic plaques develop. Atherosclerotic plaques that rich in foam cells (lipid laden macrophages) are susceptible to sudden plaque rupture and hemorrhage into the vessel wall. Intraluminal thrombus formed when fissuring or disruption of the atherosclerotic plaques took place. This thrombus can superimpose on the ruptured plaque resulting in sudden partial or total occlusion of the coronary artery (Davies, 2000 and Davies and Bashir, 2001).

Transient partial occlusion, local vasoconstriction and platelet aggregates embolisation are several potential mechanisms that result in intermittent acute myocardial ischaemic syndrome of angina pectoris (Davies, 2000). However, irreversible damage to the

myocardium might occur if a coronary occlusion persists for longer than 15 minutes. Consequently, continuous occlusion of at least 4 to 6 hours or longer kills the affected myocytes resulting in myocardial infarction (Davies, 2000 and Davies and Bashir, 2001).

3.1.3 Correlations between arterial pathology and clinical presentation

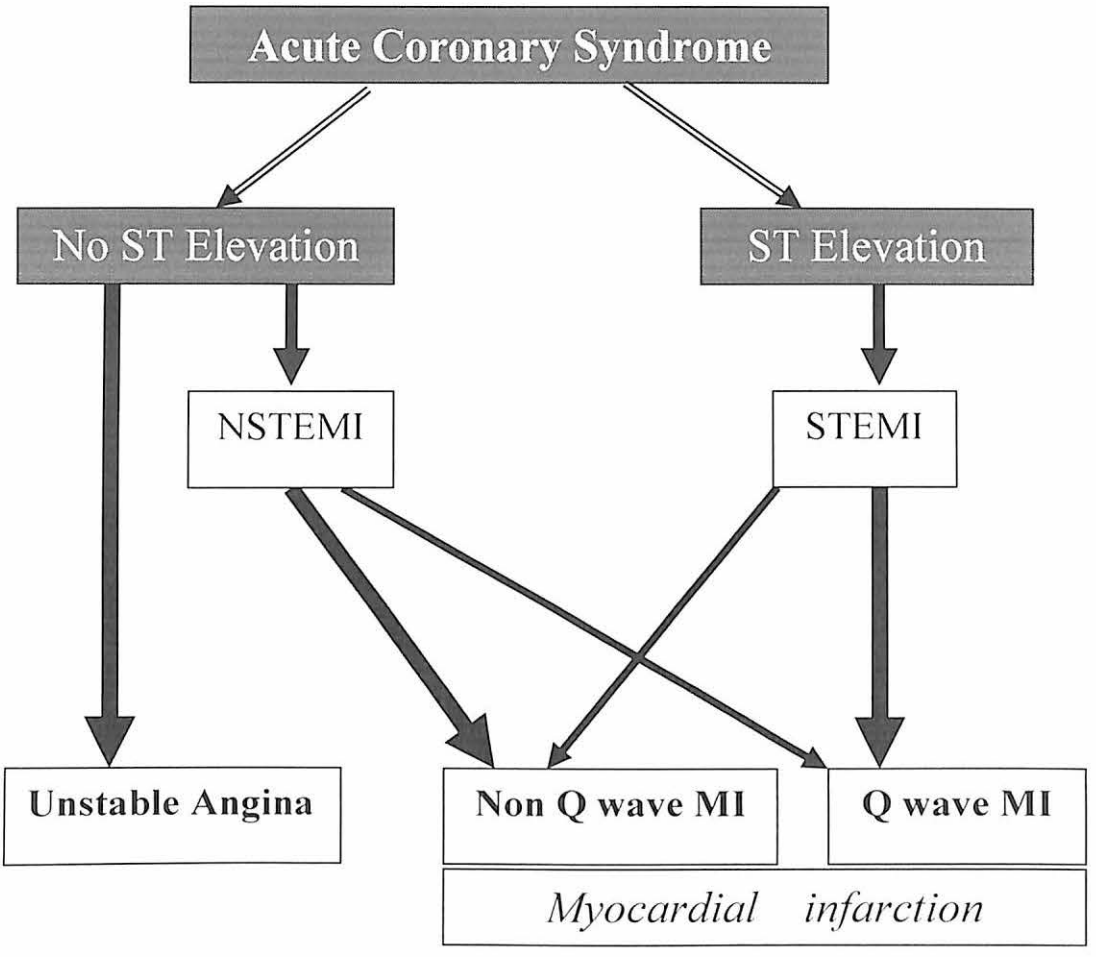
Angina pectoris is chest pain due to myocardial ischemia. Stable angina is predictable chest pain on exertion or under mental or emotional stress whereas unstable angina is chest pain that is unexpected and usually occurs at rest. Chest pain in acute myocardial infarction is due to prolonged ischemia that results in myocardial cell death or necrosis. (American Heart Association, 2005).

The pathological sequelae and progression of atherosclerosis dictates the clinical presentation. During the natural course of atherosclerosis and thrombosis, acute myocardial ischemia can be presented as a range of ischemic cardiac manifestations which is known as acute coronary syndrome (ACS).

Although imprecise, the correlations between events in the coronary arterial lumen and ECG form the basis of disease classification and management decision (Davies and Bashir, 2001). As such, ACS covers the spectrum of clinical conditions that ranges from unstable angina to non ST elevated myocardial infarction and ST elevated myocardial infarction which result from a common underlying pathophysiological mechanism (Boersma *et al.*, 2003 and Davies & Bashir, 2001).

Recently, ACS has evolved as a useful operational terminology to describe the clinical symptoms that is compatible with progress of acute myocardial ischemia at time of presentation (Ministry of Health, Malaysia, 2002). This new term is increasingly used to describe patient who present with acute myocardial infarction or unstable angina (American Heart Association, 2005).

Figure 3.1 shows clinical classifications of ACS. Most patients who have ST-segment elevation will ultimately develop a Q-wave acute myocardial infarction. Patients who have ischemic discomfort without an ST-segment elevation are having either unstable angina (UA), or a non-ST-segment elevation myocardial infarction (NSTEMI) that usually leads to a non-Q-wave myocardial infarction. The distinction between patients with UA and NSTEMI is ultimately made based on the presence or absence of a cardiac marker in blood, most commonly troponin I, troponin T or creatinine kinase myocardial nabd (CKMB). The diagnosis of NSTEMI is established if a cardiac marker is detected (Ministry of Health, Malaysia, 2002).



ST = ST segment of ECG tracing; NSTEMI = non-ST elevation myocardial infarction; NQMI = non-Q wave myocardial infarction; Q wave MI = Q wave myocardial infarction.

Source : (Clinical Practice Guidelines on Unstable Angina and Non ST elevated Myocardial Infarction, Ministry of Health, Malaysia, 2002).

Figure 3.1 : Clinical classification of acute coronary syndromes

3.1.4 Diagnosis

According to the World Health Organization, the diagnosis of acute myocardial infarction is based on the presence of at least two of the following three criteria:

A.A clinical history of ischemic type chest discomfort.

B.An evolutionary changes on serially obtained ECG tracings.

C.A rise and fall in serum cardiac markers.

(Ministry of Health, Malaysia, 2001)

3.1.4 (a) History

Chest pain due to acute myocardial infarction usually occurs at retrosternal area which lasted at least 20 minutes. The pain is usually central or in the left chest and may radiate to the jaw, neck, arm shoulder or back but occasionally may occur in epigastric region. It may be of crushing, pressing or burning in nature and usually not sharp or highly localized (Ministry of Health, Malaysia, 2001).

Diaphoresis, nausea, vomiting or light-headedness may be noted in association with chest discomfort or they may occur in the absence of chest symptoms although such pattern is atypical. Nevertheless, diabetics, elderly and females commonly present with atypical chest pain and dyspnea (Ministry of Health, Malaysia, 2001 and Berger and Oxford, 2004).

3.1.4 (b) Electrocardiographic changes

The evolutionary ECG changes of AMI include hyperacute changes of a tall peaked T wave, ST segment elevation followed by the formation of Q wave, return of the ST segment to isoelectric and T wave inversion. The presence of new onset bundle branch block in a patient with typical chest pain might indicate an infarct (Ministry of Health, Malaysia, 2001).

ECG findings were related with corresponding coronary pathophysiology. ST segment changes indicate underlying myocardial ischemia while Q waves provide evidence of the loss of electrically functioning cardiac tissue (Berger and Orford, 2004). ST elevation results from complete obstruction to coronary flow for more than one hour (Davies and Bashir, 2001). Thus, ECG finding is a valuable tool both in confirming the diagnosis of acute myocardial infarction and selecting appropriate therapy for the patient (Berger and Orford, 2004).

3.1.4 (c) Serum cardiac markers

Myocyte ischemia and necrosis results in damage to the cells and subsequently release of intracellular enzymes into the circulating blood which permit their detection as cardiac markers by blood test. The cardiac markers consist of creatine kinase myocardial band (CKMB), cardiac troponins, creatine kinase (CK), aspartate amino transferase, lactate dehydrogenase and myoglobin. Elevated values for cardiac markers should be recorded

on two consecutive blood samples to diagnose AMI (Ministry of Health, Malaysia, 2001). Cardiac troponins and CKMB are the most specific cardiac markers. CKMB takes at least 3 hours after a profound ischemia to rise above the normal level. Values for CKMB should rise and fall. In contrast, cardiac troponins levels rise soon after myocardial injury and a single raised Troponin T or I is sufficient to indicate myocardial necrosis (Berger and Orford, 2004).

3.1.4 (d) Other diagnostic modalities

Imaging techniques such as echocardiography and radionuclide techniques may be useful in identifying patients with myocardial infarction in the emergency department (Berger and Orford, 2004). These technologic advances have high sensitivity to detect very small infarcts that individual who was formerly diagnosed as having severe, stable or unstable angina pectoris might be diagnosed today as having had a small MI (Alpert and Thygesen, 2000).

Echocardiography is used to visualize regional wall motion abnormalities that occur within seconds of coronary occlusion and well before myocyte necrosis. Similarly, perfusion imaging with both thallium and sestamibi which is used to visualize cardiac tissue perfusion has been reported to be both sensitive and specific in the evaluation of patients in whom the diagnosis is uncertain. As such, both echocardiographic and radionuclide techniques are not required in patients with symptoms and ECG that evidence typical acute myocardial infarction (Berger and Orford, 2004).

The European Society of Cardiology (ESC) and the American College of Cardiology (ACC) have recently revised the definition of myocardial infarction. This new definition as shown in Table 3.1 integrated highly sensitive and specific serologic markers and precise imaging techniques.

The updated definition more accurately reflects the patient's clinical course and current scientific thinking. Application of WHO definition in clinical practice results in several patients erroneously diagnosed with non-myocardial infarction where actually irreversible myocardial damage has occurred. In addition, a sensitive detection for cardiac injury is more appropriate for purposes of risk stratification and subsequent treatment for MI (Boersma *et al.*, 2003).

However, at present, the widespread availability and standard application of the measures generating these criteria is probably limited due to its implication on individual patient, society and health resources. Additionally, the application of new and more sensitive criteria for AMI will result in the rise of recorded MI incidence and fall in the case fatality rate. Therefore, for the purpose of epidemiological monitoring, established definitions (example by WHO MONICA project) should be retained for comparison with previously collected data. At the same time, current biomarker-based definition of AMI should be applied concurrently where possible to compare with research that employ more recent standard for defining AMI (Alpert and Thygesen, 2000).

Table 3.1: Clinical Definitions of Myocardial Infarction as determined by the Joint European Society of Cardiology/American College of Cardiology Committee

Criteria for acute, evolving or recent MI

Either one of the following criteria satisfies the diagnosis for an acute, evolving or recent MI:

- Typical rise and gradual fall (Troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:

✓ ischemic symptoms;

✓ development of pathologic Q waves on the ECG;

✓ ECG changes indicative of ischemia (ST segment elevation or depression); or

✓ coronary artery intervention (e.g., coronary angioplasty).

- Pathologic findings of an acute MI.

Criteria for established MI

Any one of the following criteria satisfies the diagnosis for established MI:

- Development of new pathologic Q waves on serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarct developed.

- Pathologic findings of a healed or healing MI.

Source : (Alpert and Thygesen, 2000)

3.1.5 Treatment

The goal in the treatment of AMI is to improve the blood flow through the occluded coronary artery rapidly as to prevent injury to the myocardium. In addition, treatment aims to provide lasting restoration of coronary blood circulation.

Early management of AMI involves oral aspirin, oxygen administration, pain relief usually by intravenous morphine, stabilization of haemodynamics and assessment for reperfusion. The choices of reperfusion therapy are either thrombolytic therapy or primary / direct Percutaneous Transluminal Coronary Angioplasty (PTCA). Presently, the thrombolytic agents that available locally are Streptokinase and Tissue Plasminogen Activator (tPA). Although studies have shown that tPA is moderately superior to Streptokinase, the latter is more favorable because it is less expensive. Thus, Streptokinase is the most widely used agent locally. However, as a reperfusion strategy, primary PTCA has been shown to be more effective than thrombolytic therapy in achieving and sustaining a patent-infarct related artery. The availability of primary PTCA is however limited to only few centers in the country. It should be considered in experienced centers and the door to balloon time of less than 60-90 minutes (Berger and Orford, 2004).

Other adjunctive pharmacotherapy includes aspirin, beta blockers and ACE inhibitor (Ministry of Health, Malaysia, 2001).

3.1.6 Complication

Complications of AMI include arrhythmias, left ventricular dysfunction and others. Arrhythmias can be divided into tachyarrhythmias and bradyarrhythmias. The clinical spectrum of left ventricular dysfunction varies from asymptomatic to heart failure and cardiogenic shock (Ministry of Health, Malaysia, 2001). Chest pain post-AMI may be due to reinfarction, ischemia or pericarditis. Other identified complication is left ventricular thrombus which can lead to stroke (Berger and Orford, 2004).

3.1.7 Risk stratification post acute myocardial infarction

Risk stratification serves to identify patient who is likely to develop complication and take appropriate treatment strategies to prevent them. The high risk patients should be considered for early coronary angiography. Low risk patients should be prescribed with optimal medication and may be allowed to return to their former activities.

3.1.8 Secondary and tertiary prevention

Secondary prevention includes risk factors modifications and pharmacotherapy. Behaviour modifications such as cessation of smoking, healthy diet and increase physical activity are highly advised. Hypertension, diabetes mellitus and hypercholesterolemia should be treated optimally. The cardiac rehabilitation programme helps the AMI survivors to establish a healthier lifestyle (Berger and Orford, 2004).