CHAPTER III

MATERIALS AND METHODS

Research design overview

1. Introduction

From the results of previous study cited in Chapter II, immediate prognostic factors still have to find out. For the research design in this particular study, emphasis should be given to the area of possible predictors of unfavorable outcome (acute complications and/or acute MI) in patients with unstable angina.

2. The research question

This prospective study is intended to answer the following questions:

2.1. primary research question

What is (are) the predictor(s) of acute MI and/or acute complications in patients with unstable angina?

2.2. Secondary research questions

2.2.1. What is the natural history of patients with unstable angina admitted to ICU, Department of medicine, Chulalongkorn hospital?

2.2.2. Can we use the predictor (s) to apply for ICU admission criteria in patients with unstable angina.

3. Research objectives

The objectives of this proposed study are as follow:

3.1 To find out important variables for predictors discriminating patients with unstable angina who will be develop unfavorable outcome (acute MI and/or acute complications) from the other group.

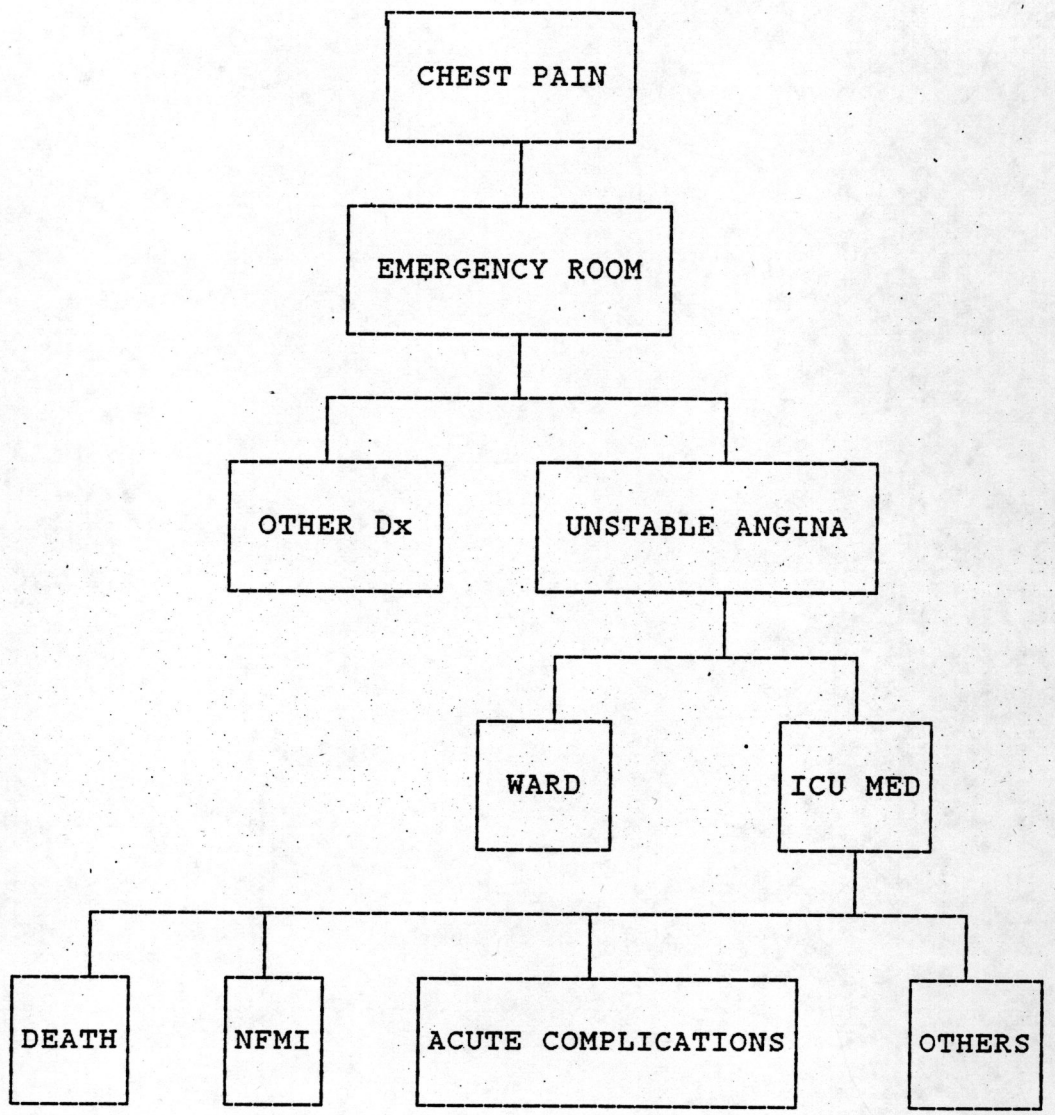
3.2 To know the natural history of patients with unstable angina in Chulalongkorn hospital.

3.3 To improve the efficacy and effectiveness of management for these patients if we knew the predictors of unfavorable outcome.

4. Brief overview of the study design

The overall study design is summarized as follow:

DIAGRAM of the study design.



NFMI = nonfatal myocardial infarction

ICU = intensive care unit

MED = medicine

The study is planned to run for approximately one year. All the patients with fulfil the inclusion and exclusion criteria will be recruited for study. They will stay in ICU, Department of Medicine, Chulalongkorn Hospital for three days or more and then transferred to wards. They will be monitored ECG, vital sign, their venous bloods will be sent for cardiac enzymes for 3 consecutive days, the same as standard 12-Leads ECG will be done for 3 consecutive days or as necessary such as developing cardiac arrhythmia. Conventional therapy with nitrates, beta-blockers and calcium antagonist will be prescribed in addition to analgesics.

The outcomes will be measured in term of mortality rate, nonfatal myocardial infarction (NFMI) and acute complications. Interview and physical examinations will be performed on the first day of admission.

5. Study Sample

The target population is that population to which the results may be applied. The target population in this study consists of all adult individuals with unstable angina in Thailand.

The population to be sampled is that population from which the sample will be actually drawn, and about which conclusions will be made. The population sampled in this study is comprised of all adult unstable angina patients admitted to intensive case unit,

Chulalongkorn Hospital, and who are eligible when inclusion and exclusion criteria are applied.

6. The sample

The unstable angina patients must fulfill all of the following criteria.

6.1 Inclusion criteria

6.1.1. History criteria : Pain [24]

6.1.1.1. Angina pectoris of new onset (less than 6 weeks)

1A. on effort

1B. at rest

6.1.1.2. Crescendo angina (increased duration, frequency of pain or decreased reponse to treatment)

2A. on effort

2B. at rest

6.1.2. Physical examination criteria

There must not be clinical signs of CHF, cardiac arrhythmia, shock or hypotension on the first admitted day.

6.1.3. ECG criteria

The attack of pain must not be associated with new or persistent Q wave on

admission.

6.2. Exclusion criteria

6.2.2. Missed diagnosis

6.2.3. The patient who had any complications before admission such as any cardiac arrhythmia, left ventricular dysfunction etc.

6.3. Criteria for acute MI

Requires two or more of the following:

6.3.1. History criteria : Angina pain is severe and prolonged more than 30 minutes

6.3.2. ECG criteria : The ECG had undergone a series of changes beginning with ST-T and T-wave changes followed by the development of abnormal Q waves.

6.3.3. Cardiac enzyme criteria : CPK, SGOT, LDH were rising in consistance with myocardial necrosis or more than two folds above the upper limit of normal values.

6.4. Sample size

Sample size calculation

$$n = \frac{(Z_\alpha + Z_\beta)^2 \; 2P \; (1-P)}{D^2}$$

$$P = {}^1/_2 \; (P_1 + P_2)$$

If P_1 = Prevalence of bad outcome of patients in group I(case)

$= 0.4$

P_2 = Prevalence of bad outcome of patients in group II(control)

$= 0.1$

Then $P = {}^1/_2 \; (0.4 + 0.1)$

$= 0.25$

$D = P_2 - P_1$

$= 0.3$

If α = 0.05 (one-sided), $Z_\alpha = 1.64$

β = 0.10 $Z_\beta = 1.28$

$$n = \frac{(Z_\alpha + Z_\beta)^2 \; 2P(1-P)}{D^2}$$

$$= \frac{(1.64 + 1.28)^2 \; 2(0.25)(1-0.25)}{(0.3)^2}$$

$= 35.53$

Sample size = 36 for each group

7. Possible bias of the study sample

The amount of patients with unstable angina are more than the amount of beds. For this reason, more severe cases may will have more chance for selection to admit in ICU than mild case.

8. Possible predictors of unfavourable outcome studied

Age[30]

Sex[32]

History of DM

History of MI

History of Hypertension

History of Angina pectoris[12]

Smoking[29]

ECG changes[27,28]

Cardiac enlargement from chest x-ray[35,39]

9. Statistical analysis

The data are presented as mean + SD, relative risk (RR) and 95% Confidence Interval of RR. The SPSS/PC+ Computer Program was used in the data analysis, which included chi-square tests.

Risk factor	Cases	Controls	Total
+	a	b	h
-	c	d	g
Total	e	f	k

$$\text{Relative risk (RR)} = \frac{a/e}{b/f}$$

$$\text{Chi-Square } (x^2) = \frac{(ad-bc)^2 k}{efgh}$$

$$95\% \text{ Confidence interval of RR} = RR^{(1 + z_{\alpha} / \sqrt{x^2})}$$