CHAPTER I
INTRODUCTION

Exercise training has assumed a major role in both the primary and secondary prevention of disease. It can prevent the illness as well as decrease the duration of illness. Studies have shown that exercise augments a positive effect on fibrinolytic system. Effects of exercise are increased fibrinolytic activities which are dependent on the exercise intensity and the duration. In coronary artery disease (CAD) patients, exercise training has presumed a major role in increasing physical performance, lifting the angina threshold in patients with symptomatic CAD, and improving myocardial perfusions.

Fibrinolysis is the mechanism involved in fibrin degradation through the proteolytic action of the serine protease plasmin (Collen and Lijnen 1991). This enzyme originates from the activation of proenzyme plasminogen by tissue plasminogen activator (t-PA). Tissue plaminogen activator is released into the circulation from the endothelium and rapidly inactivated by the endothelial type plasminogen activator inhibitor (PAI-1).

Impaired fibrinolysis may result from either low t-PA or elevated PAI-1 levels. It plays an important role in the development of CAD, and it is related to long-term mortality (Rocha and Paramo 1994; Juhan-Vague and Alessi 1993).

Tissue plasminogen activator is a serine protease of about 70 kd and composes of a single polypeptide chain of 527 amino acids (Pennica et al. 1983). t-PA antigen levels in human plasma at rest range between 3.4 $\pm$ 0.8 ng/ml and 6.6 $\pm$ 2.9 ng/ml. This level increases about three folds by exhaustive physical exercise (Rijken et al. 1983).

Plasminogen activator inhibitor-1 is a single-chain glycoprotein of about 52 kd and consists of 379 amino acids. In healthy individuals, highly variable plasma levels of both PAI-1 activity and antigen were observed. PAI-1 activity

ranges between 0.5 and 47 IU/ml. PAI-1 antigen in plasma ranges between 6 to 85 ng/ml (Kruithof et al. 1988). Activated PAI-1 is synthesized in platelets as well as endothelial cell (Sprengers et al. 1986; Kooistra et al. 1986). PAI-1 binds rapidly to t-PA forming a stable complex with a 1:1 ratio (Lindahl et al. 1990). The active form of PAI-1 is unstable, with a half-life of 30 minutes (Kooistra et al. 1986).

The development of CAD involves hyperplasia of arterial smooth muscle, the formation of fatty streaks, atheroma, plaque rupture, and ultimately thrombus formation and vessel occlusion (Fuster et al. 1992). This development of disease suggests the importance of environmental influences and interactions between genes and the environment (Michaels 1966).

Prospective and case-control studies have indicated that many of the proteins involved in coagulation and fibrinolysis that might contribute to a thrombotic tendency are related to the development of CAD. The suppression of fibrinolysis was due to high plasma concentrations of PAI-1 and increased plasma concentrations of factor VII, fibrinogen, and von Willebrand factor which are associated with the development of myocardial infarction (Heinrich et al. 1994).

Cardiac rehabilitation is a combination of services that helps patients with cardiovascular disease improve their functional abilities, particularly their tolerance for physical activity, decrease their symptoms; and achieve and maintain optimal health. Accumulating evidence indicates that exercise might favorably modify several of conventional CAD risk factors including blood lipid, obesity, blood pressure and insulin levels (Lavie et al. 1993; Chen et al. 1994).

It is generally accepted that physical exercise enhances the fibrinolytic activity and induces changes in some hemostatic parameters. An increase in t-PA activity and decrease in PAI-1 levels have been described in healthy

subjects following long-term exercise training (Streiff 1994; Gris et al. 1990). It has been suggested that exercise could favorably influence the clinical course of patients with CAD through a reduction of PAI-1 levels (Rydewski and Sakata 1990; Estelles et al. 1989). As shown in figure 1.1 higher intensity exercise would enhance more fibrinolytic function (Weiss et al. 1997).

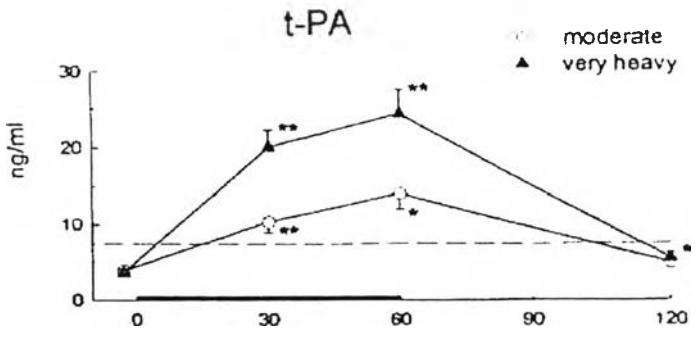

Figure 1.1 Changes of fibrinolysis following moderate and very heavy exercise in healthy male.

The aim of this study was to evaluate the influence of a cardiac rehabilitation program on fibrinolysis in patients with CAD.

1.1 Research Question

Are there any changes in fibrinolysis in CAD patients participating in 8 weeks of cardiac rehabilitation at light-moderate level program ?

1.2 Objectives of this study

To demonstrate the effects of cardiac rehabilitation program at light-moderate level for 8 weeks on fibrinolytic system as follows.

1. Effect of cardiac rehabilitation on plasma t-PA activity, t-PA antigen, PAI-1 activity, PAI-1 antigen.

2. Comparison of the fibrinolytic response to light -moderate exercise between acute training and 8 week period training.

1.3 Assumptions

The study population was CAD patients in Thammasat University Hospital and King Chulalongkorn Memorial Hospital. The subjects were male at age of 40-70 years, non-diabetic, with controlled lipid profile at the normal range.

1.4 Operational Definitions

1. **Coronary artery disease** is the stenosis or obstruction of coronary artery vessels. It is consisted of 2 groups of stable angina and acute coronary syndrome that includes unstable angina, myocardial infarction.
2. **Fibrinolysis** is the mechanism to degradation clot in blood vessel to prevent and decrease the obstruction of vessel.
3. **Cardiac rehabilitation program** is the process to train CAD patients. It consists mainly of aerobic exercise training at light - moderate level for 8 weeks. Each session of the program consists of 10 minutes warm up, 30 minutes walking on the treadmill with intensity of 60-65% VO_{2peak} and 10 minutes cool down. The heart rate, blood pressure, and rating of perceived exertion (RPE) were monitored during the training period.

1.5 Expected Benefits of the study

1. More knowledge will be gained regarding the effect of exercise cardiac rehabilitation program at light - moderate intensity on the changes of fibrinolysis in patients with CAD.

2. This cardiac rehabilitation program will be prescribed to CAD patients in order to enhance the function of fibrinolytic system.