การเปรียบเทียบความถี่และระยะเวลาที่แตกต่างกันของการฝึกออกกำลังกายแบบช่วงต่อการเปลี่ยนแปลงระดับความสามารถในการออกกำลังกายในผู้ป่วยที่มีภาวะหัวใจล้มเหลวเรื้อรัง

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THE COMPARATIVE OF FREQUENCY AND DURATION IN INTERVAL EXERCISE TRAINING PROGRAM ON EXERCISE CAPACITY CHANGES IN PATIENTS WITH CHRONIC HEART FAILURE

MISS SUPA CHOMCHANG

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สุภา จอมแจ้ง : การเปรียบเทียบความถี่และระยะเวลาที่แตกต่างกันของการฝึกออกกำลังกายแบบช่วงต่อการเปลี่ยนแปลงระดับความสามารถในการออกกำลังกายในผู้ป่วยที่มีภาวะหัวใจล้มเหลวเรื้อรัง (The Comparative of Frequency and Duration in Interval Exercise Training Program on Exercise Capacity Changes in Patients with Chronic Heart Failure) อ.ที่ปรึกษา: ผศ.นพ. วสันต์ อุทัยเฉลิม อ. ที่ปรึกษาร่วม : ผศ. พญ. ดุจใจ ชัยวานิชศิริ, 88 หน้า. ISBN 974-346-636-3

การศึกษาครั้งนี้ มีวัตถุประสงค์เพื่อ ศึกษาเปรียบเทียบผลของการลดความถี่และเพิ่มระยะเวลาของการฝึกออกกำลังกายแบบช่วงต่อการเปลี่ยนแปลงระดับความสามารถในผู้ป่วยที่มีภาวะหัวใจล้มเหลวเรื้อรัง จำนวนทั้งสิ้น 26 ราย NYHA FC II-III แบ่งเป็น 2 กลุ่ม กลุ่ม A 13 คน (ชาย = 11 คน หญิง = 2 คน อายุเฉลี่ย 59 ± 7 ปี ค่า LVEF เฉลี่ย 38 ± 11 %) ฝึก 5 ครั้ง/สัปดาห์ นาน 3 สัปดาห์ กลุ่ม B 13 คน (ชาย = 11 คน หญิง = 2 คน อายุเฉลี่ย 57 ± 9 ปี ค่า LVEF เฉลี่ย 40 ± 9 %) ฝึก 3 ครั้ง/สัปดาห์ นาน 5 สัปดาห์ วิธีการฝึกออกกำลังกายประกอบด้วยการปั่นจักรยานแบบช่วง 15 นาที (ขณะปั่นหนักใช้เวลานาน 30 วินาที สลับกับระยะพักปั่นเบา 15 วัตต์นาน 60 วินาที) และเดินบนลู่กลแบบช่วง 10 นาที 3 ครั้ง/สัปดาห์ (การเดินเร็วสลับช้าในแต่ละระยะใช้เวลานาน 60 วินาที) ความหนักของการฝึกปั่นจักรยานหรืองานที่ทำได้มาจากการทดสอบด้วยวิธีของ Steep ramp test ซึ่งจะใช้เพียง 50% ของอัตรางานที่ทำได้สูงสุดจากการทดสอบก่อนและหลังการฝึกออกกำลังกายแบบช่วงจะทำการทดสอบวัดระดับความสามารถในการใช้ออกซิเจนสูงสุดของร่างกาย โดยใช้แบบทดสอบของ Ordinary ramp test ผลการวิจัยพบว่า อัตรางานที่ทำได้และความสามารถในการใช้ออกซิเจนสูงสุดของร่างกายทั้งสองกลุ่มเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ : อัตรางานสูงสุดที่ทำได้ กลุ่ม A เพิ่มขึ้นจาก 141.15 ± 53.74 เป็น 184.77 ± 65.75 วัตต์ ($p < 0.000$) กลุ่ม B เพิ่มขึ้นจาก 157.77±54.88 เป็น 204.62±59.18 วัตต์ ($p < 0.000$) ความสามารถในการใช้ออกซิเจนของร่างกายสูงสุด กลุ่ม A เพิ่มขึ้นจาก 13.32±3.77 เป็น 15.54±5.14 มล/กก/นาที ($p < 0.018$) กลุ่ม B เพิ่มขึ้นจาก 14.88 ±4.32 เป็น 17.64±4.10 มล/กก/นาที ($p < 0.000$) ภายหลังฝึกความสามารถในการออกกำลังกายทั้งสองกลุ่มเพิ่มขึ้นไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ (อัตรางานสูงสุด: $p = 0.72$ ความสามารถในการใช้ออกซิเจนสูงสุดของร่างกาย: $p = 0.54$) ผลสรุปของการศึกษา การฝึกออกกำลังกาย 3 ครั้ง/สัปดาห์ นาน 5 สัปดาห์ ทำให้ความสามารถในการออกกำลังกายเพิ่มขึ้นได้ไม่แตกต่างจากวิธีฝึก 5 ครั้ง/สัปดาห์นาน 3 สัปดาห์

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SUPA CHOMCHANG : THE COMPARATIVE OF FREQUENCY AND DURATION IN INTERVAL EXERCISE TRAINING PROGRAM ON EXERCISE CAPACITY CHANGES IN PATIENTS WITH CHRONIC HEART FAILURE. THESIS ADVISOR : ASIST PROF. WASAN UDAYACHALERM, M.D., M.Sc. THESIS COADVISOR: ASIST PROF. DOOTCHAI CHAIWANICHSIRI, M.D.,M.Sc., 88 pp. ISBN 974-346-636-3

The objective of this study was to compare the effect of different frequency and Duration of interval exercise training program on exercise capacity change in patients with chronic heart failure (CHF). Twenty-six CHF patients with NYHA FC II-III were enrolled into the study. They were divided into 2 groups. Group A (M=11, F = 2, mean age = 59 ± 7 years, mean LVEF = 38 ± 11%) underwent exercise program 5 times/week × 3 weeks. Group B (M=11, F = 2, mean age = 57 ± 9 years, mean LVEF= 40 ± 9%) underwent 3 times/week × 5 weeks. The Exercise consisted of 15 min. of interval bicycling (60-s work phases/60-s recovery phases) and 10 min. of interval treadmill walking (60-s work and recovery phases each). A steep ramp test was developed to derived maximal short time exercise capacity (MSEC) for work phases in interval bicycle raining, which used 50% of MSEC for exercise intensity. The peak oxygen consumption (peak VO_2) from ordinary ramp test were assessed before and after the training programs. The result showed that MSEC and peak VO_2 was significantly increased in both groups: MSEC: group A; from 141.15 ± 53.74 to 184.77 ± 65.75 W. ($p< 0.000$), group B; from 157.77± 54.88 to 204.62 ± 59.18 W. ($p< 0.000$), peak VO_2: group A; from 13.32 ± 3.77 to 15.54 ± 5.14 ml/kg/min ($p< 0.018$), group B from 14.88 ±4.32 to 17.64± 4.10 ml/kg/min ($p< 0.000$). Compared between group A and B, the MSEC and peak VO_2 changed were not significantly different. Conclusion: The improvement in exercise capacity of CHF patients performed interval training 3 times/week x 5 weeks was not different from the program performed 5 times/week x 3 weeks.

Program of Sports Medicine
Field of study Sports Medicine
Academic year 2000

Student's signature ……..
Advisor's signature ……...
Co-advisor's signature ……

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For the one who volunteered, I personally thank you and appreciate, your cooperation, that you all have come to exercise. And this is because of your own interest in your own health and the result that you' ll receive, and you'll have a healthy mental as well as physical. Eventhough the exercise was at a short period of time but your co-operation enable me to achieve my objectives for my studies and this is something that I always remembered.

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ACE inhibitor	Angiotensin Converting Enzyme
ATP	Adenosine triphosphate
bpm	beat per minute
Ca+	Calcium ion
CABG	Coronary artery by pass graft
cAMP	cyclic Adenosine Monophosephate
CHF	Congestive heart failure
CO_2	Carbon dioxide
cm	Centimeter
E	Epinephrine
EDD	End diastolic dimension
ESD	End systolic dimension
gm/day	gram per day
H^+	Hydrogen ion
Hr	Hour
HRr	Resting heart rate
HRm	Maximum heart rate
Hz	Hertz
K^+	Potassium ion
$L/min/m^2$	Liter per minute per meter –square
L/min	Liter per minute
LVEF	Left ventricular ejection fraction
m	Meter
m^2/min	meter –square per minute
mg/day	Milligram per day
ml/kg/min	Milliliter per kilogram per minute
mmHg	millimeter mercury
MSEC	Maximum Short Time Exercise Capacity
Na+	Sodium ion

NE	Norepinephine
NYHA FC	New York Heart Association Functional Classification
PCr	Phosphocreatine
PCO_2	Partial pressure of carbon dioxide
Peak VO_2	Peak oxygen consumption
Pi	Iorganic phosphate
PO_2	Partial pressure of oxygen
PTCA	Percutaneous transluminal coronary angioplasty
RPE	Rating perceived of exertion
s	Second
SBPm	Maximum systolic blood pressure
SBPr	Resting systolic blood pressure
VE/VCO_2	Minute ventilation for carbon dioxide
VO_{2max}	Maximum oxygen consumption
W	Watt

CHAPTER I

BACKGROUND AND RATIONALE

As the population ages, the prevalence of chronic heart failure, which currently affects 4-7 million Americans, and its incidence, presently 400,000 new case per year with 900,000 hospitalization annually, will increase (Cardiology Preminence Round Table, 1994). This is a result of the increasing prevalence and cumulative duration of hypertension and coronary artery disease with advancing age (Senni and Redfield, 1997). Chronic heart failure is the only major cardiovascular disease with an increasing prevalence and incidence. Heart failure prevalence of 1% in persons aged 50 to 59 years increase to 10% for octogenarians (Duncan et al., 1996). Currently, 13% of the population of the United States is over 65 years of age ; 21% of the population will be over 65 by the year 2030 (Redfield, 1996). Chronic heart failure is the most common diagnostic related group classification for hospitalization Medicare patients, at an estimated cost of $ 3.1 billion in 1991. Total direct health care costs for all patients with chronic heart failure is approximately $ 18 billion each year (Cohn et al., 1997). After the appearance of symptoms, the average patient with heart failure will live 5 years. If the patient has New York Heart Association (NYHA) class III or IV heart failure, he or she has a 40% chance of living 1 year. If the severity decrease, the average patient survival is 3-4 years later (Schlant and Sonnenblick, 1994).

Most heart failure is due to left ventricular systolic dysfunction characterized by a reduced left ventricular ejection fraction (generally <35-40%) and dilated (> 5-6 cm at end diastolic) left ventricle (Andrews et al.,1997). Initially the cardiac output fail to increase or may even decline during exercise or stress, and ultimately it is decrease even at rest. The usual compensatory mechanisms such as increase sympathetic adrenergic stimulation of the heart, neurohormonal activation with increase vasoconstriction etc, lead to increase in peripheral vascular

resistance at rest and number of potential mechanisms underlying the reduction in vasodilatory capacity which suggest the impairment of skeletal muscle blood flow (Hornigo et al.,1996).

Patients with chronic heart failure suffer from exercise intolerance and experience progressively worsening disability and quality of life (Coats et al., 1992). In the past decade, exercise training was withheld in patients with heart failure for fear that the stress posed by exercise would further aggravate their heart failure condition. The adverse effect of prolonged bed rest deconditioning in humans (Covertino et al. 1997), with its accompanying physical inactivity, was known to cause loss of muscle strength and exercise performance, impairment of cardiovascular and musculoskeletal function. The impairment of musculoskeletal system include changing of structure, function, morphology (Magnusson et al., 1996), decrease muscle strength and blood flow owing to increase vasoconstriction an impaired ability of arterial dilation. These abnormalities result in impaired exercise capacity but have been shown to be partially reversible by exercise training (Magnusson et al., 1996). The maximal oxygen uptake (VO_2 max) is used to evaluate exercise performance in health and disease. The degree of impairment of left ventriclar function in chronic heart failure patient dose not bear an obligatory relationship to exercise performance (Liang et al., 1992) . A number of studies have been shown that patients with severe left ventricular dysfunction can be safety entered into exercise training programs. Although left ventricle ejection fraction is less than 20% (Coats, 1994) or peak VO_2 (VO_{2max}) is less than 10 ml/kg/min (Hanson, 1994). The results indicate that exercise training is a useful tool for improving exercise capacity and decrease morbidity and mortality 20-25% (O Conner et al., 1989).

The effect of physical training in patients with chronic heart failure in other countries has been investigated in the 1970s and early 1980s but more intensively since the late 1980s. Available database in Thailand is not enough. Traditional exercise program was aerobic capacity improvement for increasing cardiorespiratory fitness. Due to low cardiac reserve, whole body physical training may not be the optimal method to train chronic heart failure patients. In daily live , the activity of cardiac patients is frequently limited because of muscular fatigue and dyspnea. Lower extremities are closely related to fundamental daily actions such as walking , sustaining posture, climbed stairs , and so on which demand both muscle strength and muscle endurance. The ideal guidelines and programs for heart failure have not yet been determined because it is unknown how to best optimize cardiovascular and skeletal muscle performance in heart failure while avoiding possible adverse effects. The most common recommended type of activity is aerobic exercise such as walking or cycling (Suzanne et al., 1999). Typically, exercise is performed in a continuous manner; however, there are some studies demonstrating that an interval method training can result in a greater increase in aerobic capacity, with minimal cardiac stress (Meyer et al., 1997(b)).

A new method of interval training, include of short work phases with high work rates, seem to be an appropriate method to stimulate both endurance capacity and muscle strength. In rehabilitation after coronary artery bypass surgery , interval training has proven to be more effective in improving exercise capacity and decrease heart rate, rate pressure product and lactate at submaximal work rates than continuous training with the same relative training heart rate (Meyer et al., 1990). Clinical experience with chronic heart failure patients also confirms the benefit of exercise training using interval methods (Meyer et al., 1996,1997 and 1998).

This method involves cycles of short (30 seconds) bursts of activity alternated by 60 seconds of recovery for 15 minutes, 5 times/week for 3 weeks. Fifty percent of maximum short time exercise capacity used as the intensity for training. This

program may be particularly useful in patients who have more peripheral muscle weakness. In Thailand the database of cardiac rehabilitation in patients with heart failure has not yet been studied, and because of the previous used interval training program require frequent training which makes it inconvenient to perform on patient in their daily lives. Therefore the purpose of this study is to compare the effects of different frequency and duration of interval training method, by decreased the frequency and increased the duration, of interval training program on exercise capacity changes in patients with chronic heart failure. These comparing has never been studied before, the mean difference of data between the previous and the current method was set by the expert opinion; professional cardiologist and physiatrist.

Objective

1. To compare the effects of decreasing the frequency and increase the duration of the interval training on the peak work rate of the patients with chronic heart failure
2. To compare the effects of decreasing the frequency and increase the duration of the interval training on the peak oxygen consumption of the patients with chronic heart failure

Research question

1. Was the decreasing of the frequency as well as increasing the duration of the interval training differently increased peak work rate in patients with chronic heart failure compare to the standard interval training program ?

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2. Was the decreasing of the frequency as well as increasing the duration of the interval training differently increased peak oxygen consumption in patients with chronic heart failure compare to the standard interval training program ?

Hypothesis

1. The decreasing in the frequency and increasing the duration of the interval training can not differed the increase in the peak work rate more than 10% from the previous program.
2. The decreasing in the frequency and increasing the duration of the interval training can not differed the increase in the peak oxygen consumption more than 10% from the previous program.

Operational Definitions

1. weeks. By using 50% of the maximum work rate; that were achieved during the steep ramp test at the beginning of the training of each week, as the intensity for 30 seconds of work phases training, and 60 seconds in recovery phases patients pedaled with 15 watts. In addition, interval walking training on treadmill 10 minutes 3 times weekly, the speed of interval walking training was adjusted according to each patient' s maximum heart rate tolerated during cycle interval training and was alternated with 60 seconds of recovery phases(low speed).
2. Frequency is defined as a number of a repetition per week
3. Duration is defined as the length of the exercise training, using the week as a unit

4. Exercise capacity is defined as the measurement of the peak exercise performance from

   : measured the peak work rate (MSEC:W) which means the performance of the muscle or muscles' strength and the endurance during exercise

   : measured peak oxygen consumption (peak VO_2 :ml/kg/min) meaning that the cardiorespiratory performance response to exercise

5. Chronic heart failure (CHF) is defined as stable clinical symptoms of heart failure at least 3 months. The assessment of the severity is classified by New York Heart Association Functional Classification

6. Left ventricular ejection fraction (LVEF) is defined as the contraction performance of myocardium to eject the blood from left ventricle which measured by two-dimensional echocardiogram. The normal level is not less than 60% which calculated from the formula

$$LVEF = \frac{EDD\text{-}ESD \times 100\%}{EDD}$$

EDD = left ventricular end-diastolic dimension

ESD = left ventricular end-systolic dimension

7. Rate of percieved exertion (RPE) is defined as dyspea or fatigue ratings with Borg scale reported by the patients during exercise testing.

ASSUMPTION

1. The studied population is the patients with stable chronic heart failure NYHA class II-III in King Chulalongkorn Memorial Hospital
2. The training program of patients with chronic heart failure performed in the exercise room, at the Physiology Building in King Chulalongkorn Memorial hospital

Expected Benefit and Application

1. The new method of the interval exercise training program can improve the exercise capacity and improve the patients' activities of daily living
2. The decreasing in the frequency and increased the duration of training is easy to generalized the performance in the real activity daily living
3. The results of training can apply for the adjunctive therapy and apply for other study

CHAPTER II

REVIEW OF THE RELATED LITERATURE

CONCEPTION AND THEORY

A. Definition

Heart failure exists when the heart is unable to pump sufficient blood to meet the metabolic needs of the body at normal filling pressure, provide the venous return to the heart is normal (Schlant and sonnenblick, 1994).

In most patients with heart failure, cardiac output is reduced due to poor left ventricular systolic function. However, left ventricular systolic function may be relatively normal in same patients. Heart failure is a syndrome identified by well-defined symptoms, signs, and/or hemodynamic finding caused by an abnormality of cardiac function that results in a relative decrease in cardiac output. Improvement in cardiac output causes a favorable alteration of the compensatory responses of heart failure, including the renal and neurohormonal response.

Cardiac output is the product of stroke volume and heart rate. Stroke volume is moderated by (Khan et. al, 1996)

- preload
- myocardial contractility
- afterload

Preload

Preload is the extent of fiber stretch during diastole and is clinically represented by the end diastolic volume. The effected ventricle may contracted well if adequately filled but more relax poorly, resulting in a diastolic dysfunction that is more prominent than the commonly occurring systolic dysfunction. An increase in ventricular diastolic stiffness impedes diastolic stretch and causes failure to adequately fill the ventricle. Conditions that alter ventricular compliance;

causing diastolic dysfunction, a decrease in preload, and thus a decrease in cardiac output.

Myocardial contractility

A decrease in myocardial contractility or systolic dysfunction is commonly caused by coronary heart disease, especially in patients with large areas of infarction. Rarely, dilated cardiomyopathy and myocarditis are implicated, and with late stage volume overload due to valvular regurgitant lesions, myocardial damage occurs, alternating in pump failure.

Afterload

Afterload is represented by left ventricular wall end systolic stress, which must be overcome to allow ejection of blood from the ventricle. An increase in afterload signifies an increase in myocardial oxygen demand.

Afterload is highly dependent on the radius of the ventricle and left ventricular end systolic pressure. In turn, left ventricular end systolic pressure is dependent on cardiac index and arteriolar resistance of impedance. A decrease in systolic vascular resistance or a fall in blood pressure is not identical with a decrease in afterload. Also, a decrease in systemic vascular resistance is not synonymous with a decrease in arterial blood pressure, as a compensatory increase in cardiac output occurs to maintain blood pressure. The peripheral systolic pressure may be maintained because of colliding reflected pressure waves, despite a fall in control systolic blood pressure.

B. Aeitiology of heart failure

Chronic heart failure may result from arrhythmia, pericardial disease, extracardiac abnormalities, valve dysfunction or disease of the myocardium. Myocardial disease causes myocardial failure also has many cause, the most common is atheromatous disease of the coronaries or dilated cardiomyopathy.

Myocardial failure, a still more narrowing circumscribes term, refers to circulatory failure caused by primary systolic or diastolic dysfunction of cardiac muscle per se. Eighty to ninety percent of patients with heart failure have symptoms due to an impairment of left ventricular function (Packer et al., 1999). The most common cause of left ventricular systolic and diastolic dysfunction are the following (Karor 1995; American Colleque of cardiology / American Heart Association Task Force Report 1995):

- Coronary artery disease
- Idiopathic dilated cardiomyopathy
- Hypertension

Coronary artery disease is the cause of heart failure in about two thirds of patients with left ventricular systolic dysfunction (Packer et al., 1999). There are several cause of both " primary " and "secondary" myocardial Failure (*Table 1*).The cause of overall heart pump failure may be classified into three main categories (Schlant and Sonnenblick, 1996):

1. failure primary related to work overloads or mechanic abnormalities,
2. failure primary related to primary myocardial abnormalities' and
3. failure related to abnormal cardiac rhythm or conduction disturbance.

Myocardial infarction may also be included as a special type of work overload. After healing of the infraction, this akinetic area dose not contribute to ventricular emptying and may even contribute to the load. Thus the entire load falls on the remaining nonischemic myocardium. This load is further increased by the increased diastolic volume, which causes wall tension to be increased for any given pressure and the nonischemic myocardium to hypertrophy in proportion to the amount of myocardium that is lost. Heart failure may ensue months or years after as a so-called ischemic cardiomyopathy that results from ventricular dilatation and reactive hypertrophy, termed ventricular remodeling, even in the absence of wall ischemia.

after as a so-called ischemic cardiomyopathy that results from ventricular dilatation and reactive hypertrophy, termed ventricular remodeling, even in the absence of wall ischemia.

Table 1 General Causes of Overall Heart Pump Failure

- Mechanical abnormalities
  - Increased pressure load
    - Central (aortic stenosis, ect.)
    - Peripheral (systemic arterial hypertension, ect.)
  - Increased volume load (valvular regurgitation, shunts, increased Venous return, ect.)
  - Obstruction to ventricular filling (mitral or tricuspid stenosis)
  - Pericardial constriction, tamponade
  - Endocardial or myocardial restriction
  - Ventricular aneurysm
  - Ventricular dysynergy
- Myocardial (muscular) abnormalities or loss of myocytes
  - Primary abnormality or loss of myocytes
    - Cardiomyopathy
    - Neuromuscular disorders
    - Myocarditis
    - Metabolic (diabetes mellitus, ect.)
    - Toxic (alcohol, cobalt, ect.)
    - Presbycardia

Possible mechanisms of myocardial failure may evolve from (Schlant and Sonnenblick ,1996)

- loss of myocytes,
- hypertrophy of remaining myocytes ,
- energy production and utilization ,
    - oxygen and energy supply
    - substrate utilization and energy storage
    - inadequate mitochondria mass and function
- ventricular remodeling,
- contractile proteins,
    - abnormal myofibrillar or myosin ATPase
    - abnormal myocardial proteins
    - defective protein synthesis
    - nonuniformity of contraction and function
- activation of contractile elements,
    - membrane Na^{+}-K^{+}-ATPase defects
    - abnormal sarcoplasmic recticulum function
        - abnormal Ca^{2+}-release
        - abnormal Ca^{2+}-uptake
- abnormal myocardial receptor function ,
    - down-regulation of beta adrenoreceptors
    - decreased β1- receptors
    - decreased G5-protein and increased G1-protein
- autonomic nervous system,
    - abnormal myocardial norepinephrine function or kinetics
    - abnormal baroreceptor function
- increased myocardial fibroblast growth and collagen synthesis,
- aging changes, presbycardia,
    - sustsined tachycardia
- miscellaneous.

C. Pathophysiology of chronic heart failure

The term myocardial failure implied that the systolic mechanical performance, or myocardial contractility per unit mass, is significantly decreased; The cardiovascular system under stress has a remarkable capacity for compensatory adaptation. Initially, however , the overall cardiac function may be maintained by the compensatory mechanisms, and the cardiac output at rest may not be abnormally decreased. The body responds to the abnormality of cardiac function and a relative decrease in cardiac output by bringing several hemostatic mechanisms into action (Khan et al., 1996) . (*Figure 1*).

Many of the adjustments and adaptation to heart failure are similar to the homeostatic mechanisms utilized by the body in response to circulatory failure from any cause. Cardiac and extracardiac physiological compensatory adjustments are activated when left ventricular function is depressed (Squires et al., 1998). These compensatory adaptations are designed to maintain an adequate cardiac output for tissue perfusion and are beneficial in the short term (day to week). However in chronic left ventricular dysfunction, these adjustments may actually contribute to progressive ventricular and vascular dysfunction, ultimately resulting in severe congestive heart failure.

<u>Cardiac adjustments</u>

Chronic myocardial failure is characterized by reduced energy consumption with reduced blood flow. Such deminished energy requirements could be interpreted as compensatory : these may contribute to a lower-rate of metabolic activity and myocyte preservation. However, in contrast to these metabolic finding is the histologic observation that hypertrophied failing myocardium is characterized by increased intercapillary distance and potential reduction in oxygen diffusion, particular in the heart failure due to coronary artery disease.

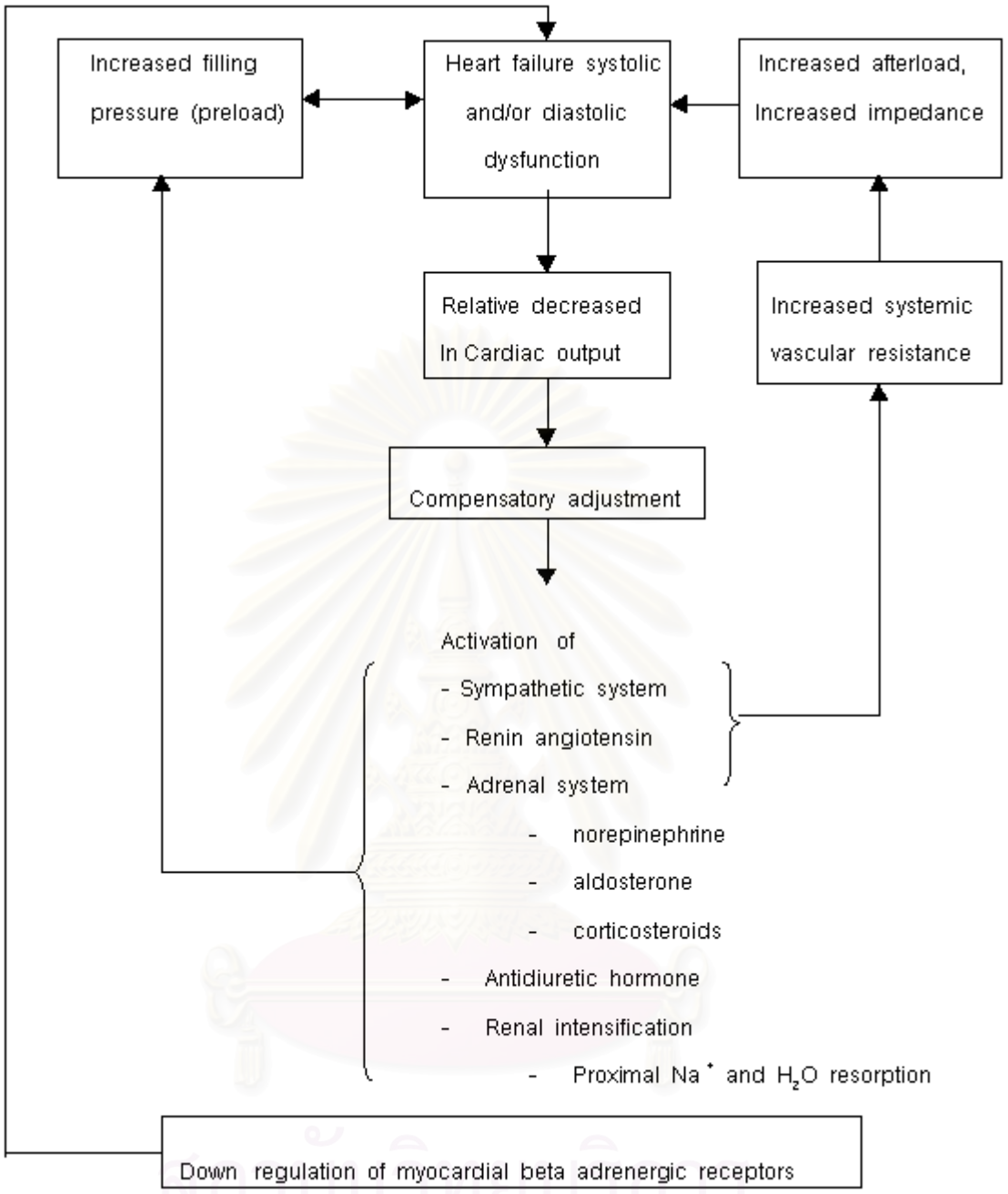

Figure 1. Pathophysiology of heart failure

The role of mitochondrial respiratory activity function in myocardial failure remains uncertain. After muscle failure ensues, the external efficiency of this augmented respiration may be diminished.

The important of myocardial energy reserves in myocardial failure is uncertain. The possibility remains , therefore, that depletion of phosphocreatine content and reduced creatine kinase activity play a role in the contractile abnormalities of chronic myocardial failure by contributing to depression of cellular energy reserves particularly in circumstances of increased demand result in depression of ATP availability of a magnitude that could explain reduced myocardial performance

Myocellular adaptation in heart failure includes changes in contractile proteins such as normal or increased myofibrillar elements, myofibril density and decreased adenosine triphosphatase (ATPase) activity. Such a change would lead to greater contractile efficiency and a reduction in energy demands on mitochondria.

The G protein system, these proteins signaling cell membrane association mediate the myocardial response to β-adrenergic stimulation by coupling the beta receptor to the intercellular formation of cyclic adenosine monophosphate (cAMP). Recent data indicate that inhibitory G proteins are increased and stimulatory G proteins are reduced in the failing human heart. This change in ratio of stimulatory to inhibitory G proteins may result in a blunted increase in intracellular cyclic AMP as a result of adrenergic stimulation and therefore, reduced myocyte Ca^{2+} influx or delayed uptake of cytosolic Ca^{2+} by the sarcoplasmic recticulum.

Data from human myocardium indicate that intracellular calcium concentrations are maintained in failing myocardium, and this suggests that altered contractile function is due to altered myofibrillar calcium responsiveness. In addition, inadequate removal of Ca^{2+} from the cytosol, reduced Ca^{2+} uptake by sarcoplasmic recticulum may also result in reduced excitation-contraction coupling.

These factors mention above caused significantly decrease in the systolic mechanical performance and increased load to the heart. To maintain an adequate cardiac output for tissue perfusion, one initial response to increased load is ventricular dilatation resulting in an increased end – diastolic volume and augmented stroke volume via the Frank – Staring mechanism. The advantage gained by this mechanism, however, is won at the price of increased ventricular wall tension. By application of the law of laplace (*Figure 2*), the untoward consequence of its sustained increased wall stress cause significant further the development of hypertrophy.

A model in which the initial acute response to increased load is increased contractility generated by augmented adrenergic drive and chamber dilatation (to achieve optimal sarcomere length). This is followed by hypertrophy, which increases the total myocardial mass. These adaptations permit maintenance of overall cardiac pump performance, at least temporarily. If excessive loading conditions become chronic, however, a phase of diminishing myocardial contractility ensues and with it a downward spiral of circulatory function and the clinical syndrome of chronic congestive heart failure.

The development of hypertrophy serves to normalize the ratio of ventricular wall thickness to chamber radius in dilated heart, that is, to minimize increases in wall stress. Overtime, additional ventricular dilatation and concentric hypertrophy may occur in response to increased wall stress, which leads to further deterioration in systolic function. Increased passive ventricular wall stiffness and slowed energy – dependent myocyte relaxation result in further diastolic dysfunction.

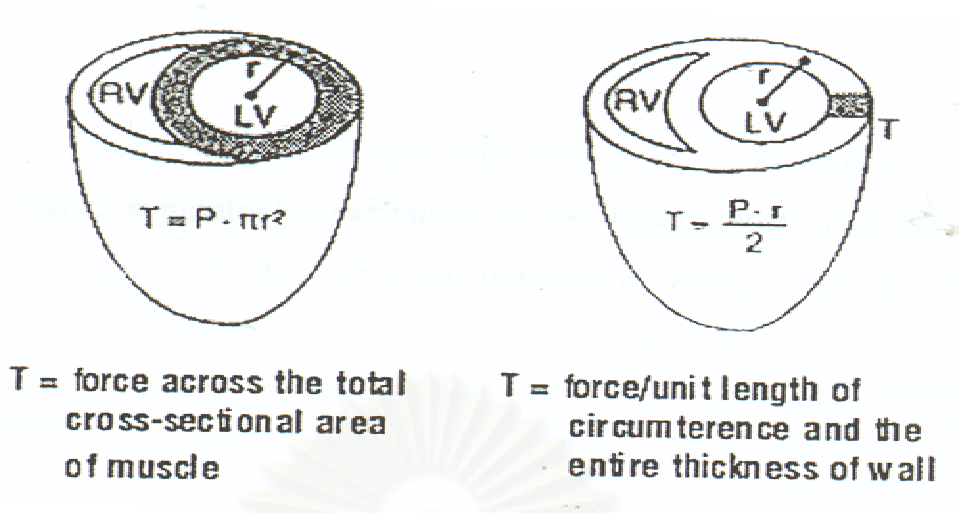

Figure 2 Two depictions of the law of Lapace, which describes the relationship among wall tension *(T)*, intraventricular pressure *(P)*, and left ventricular *(LV)* cavity radius *(r)*. *RV*, right ventricle

Extracardiac adjustment

The compensatory, homeostatic adjustments that occur when the heart fails tend to restore normal ventricular systolic pump function, although often at the price of increased diastolic pressures in the involved ventricle and the venous system filling the involved ventricle. A major compensatory mechanism is the increase in ventricular filling volume and pressured produced by an increase in plasma volume as the result of salt and water retention by the kidney.

Activation of the sympathetic nervous system and the renin – angiotensin aldersterone system is the primary extracardiac compensatory mechanism for depressed left ventricular function (Benedict et al. 1994; Kaye et al. 1995). The result is peripheral vasoconstriction mediated by neurohormonal system which changes in regional circulations occur, that result in preservation of blood flow to the brain and heart at the expense of the renal, skeletal muscle, spanchnic, and cutaneous circulation.

One of the most important acute adjustments to heart failure is a reflex increase in autonomic sympathetic excitation of the heart, most arteries and vein. Generalized arterial vasoconstriction and an increase in venous tone are produced by the increased sympathetic activity, in combination with increased plasma concentrations of NE, Angiotensin II, vasopressin , endothelium-1, neuropeptide y, and tumor necrosis factor together with reduced endothelium-dependent vasodilatation. (*Table 2*) summarized the neurohumoral changes that may occur in heart failure (Schlant et al.,1994). The increased sympathetic adrenergic stimulation of the heart is associated with an inhibition of cardiac parasympathetic activity.

Sodium and water retention by the kidney cause and increase in blood volume. The increase in vascular resistance and blood volume may be adequate to maintain blood pressure and the patient may be well compensated and asymptomatic. However, if these neurohormonal adjustments are indequate to maintain cardiac output, or if over time the neurohormonal activition worsens cardiac function, decompensation occurs and the patient develops progressive symptoms such as fatigue, dyspnea on exertion, a profoundly reduced exercise tolerance, orthopnea, paroxysmal nocturnal dyspnea, edema, and even cardiogenic shock.

Mechanisms that mediate the progression of heart failure

Although heart failure can resolve spontaneously (e.g., myocarditis) or after definitive treatment of its cause (e.g., thaimine repletion for beriberi heart disease or corrective surgery for valvular lesion), the syndrom is usually a progressive

Table 2 Neurohumorl changes in Heart Failure

Changes that increase vascular systemic resistance

- Increased sympathetic nervous system activity
  (Increased norepinephrines, epinephrine)
- Increased endothelin
- Increased arginin vasopressin
- Increased renin and agiotensin II
- Increased aldosterone
- Increased neuropeptide Y
- Increased tumor necrosis factor
- Reduced endothelial dependent vasodilatation
- Reduced calcitonin gene -related peptide
- Reduced parasympathetic nervous system activity
- Impaired baroreceptor activity
- Increased vasoconstrictor prostaglandins, kinines

Changes that decrease systemic vascular resistance

- Increased atrial natriuretic peptide
- Increased dopamine
- Increased vasodilator prostaglandins (PGI_2 , PGE_2)
- Increased vasodilator peptides,(e.g., bradykinin,kallíden)

NOTE: Changes in individual patients vary significantly and may not always be present

process, even in the absence of a new identifiable insult to the myocardium. The principal manifestation of such progression is a change in the geometry of the left ventricle such that the chamber dilates, hypertrophies, and becomes more spherical—a process referred to as cardiac remodeling. This change in chamber size not only increases the hemodynamic stresses on the walls of the failing heart and depresses its mechanical performance, but also increases the magnitude of regurgitant flow through the mitral valve. These effects, in turn, serve to sustain and exacerbate the remodeling process

Although many mechanisms, the factors that can accelerate the process of left ventricular remodeling, may be involved, there is substantial evidence that the activation of endogenous neurohormonal systems; as shown in *figure* 3 (Packer, 1992), may play an important role in cardiac remodeling and, there by, in the progression of heart failure and decreased survival (Mulder et al., 1997). Patients with heart failure have elevated circulating or tissue levels of norepinephrine, angiotensin II, aldosterone, endothelin, and vasopressin that can act (alone or in concert) to adversely affect the structure and function of the heart. These neurohormonal factors not only increase the hemodynamic stresses on the ventricle by causing sodium retention and peripheral vasoconstriction, but may also exert direct toxic effects on the heart. These effects may be mediated by changes in genetic pathways that regulate myocyte growth and death [apoptosis (Sabbah et al., 1998)]. Patients with heart failure also have increased circulating and tissue levels of cytokines (e.g., tumor necrosis factor) that may impair the viability and function of cardiac cells (Ono et al., 1998). Both neurohormonal factors and cytokines can stimulate myocardial fibrosis (Yue et al., 1998), which can further alter the architecture and depress the performance of the failing heart.

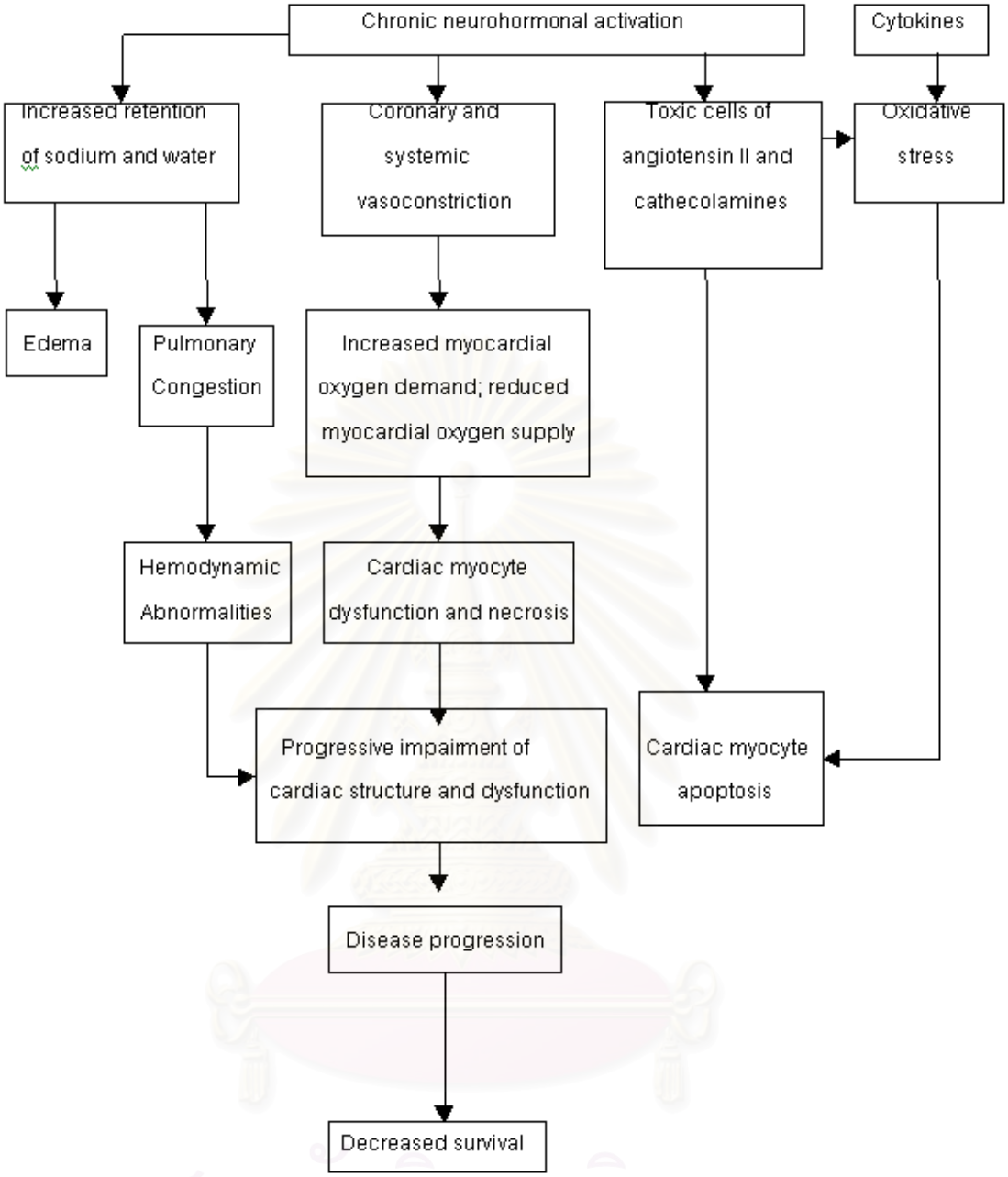

Figure 3 The effects of chronic neurohormonal activation in heart failure

on systemic and cardiovascular system

D. Clinical manifestation of heart failure

The symptoms of heart failure are;

Fatigue; These non specific but common symptoms of heart failure related to the reduction of perfusion of skeletal muscle.

Dyspnea; Often the patient with progressive systolic dysfunction gradually and unconsciously decrease his or her level of activity and denies symptoms ofexertional dyspnea in activities of daily living, thus, specific tasks performanced in daily activities must be specifically questioned. Classifying the severity of dyspnea and functional limitation in the individual patient in an objective manner to allow serial assessment.

The degree of functional disability can be estimated by either direct question or by formal exercise testing. The first approach, initially developed by the New York Heart Association (Criteria Committee, New York Heart Association, Inc In : Diseases of the Heart and Blood Vessels. Nomenclature and Criteria for Diagnosis, 1985.), assigns a numerical value Class I,II, II and IV to the amount of effort required to provoke of dyspea and fatigue (*Table 3* : Redfield, 1996).

The second approach advocated by Weber et al.(1987), categorizes patients according to their maximum exercise capacity which is evaluated by the direct measurement of oxygen consumption (Table 4) during a standardized bicycle or treadmill test. (Pina IL,1999). The severity of heart failure can also be assessed by estimating risk of death. This goal is most commonly achieved in the clinical setting by quantifying the degree of patient 's disability. When the cause of heart failure is left ventricular dysfunction, the annual mortality rate is 10% to 25% in patients with mild to moderate symptoms and 40% to 60% in patients with severe symptoms (Culiff et al., 1982, McKee et al., 1972).

Orthopnea ; Orthopnea occurs because of the redistribution of fluid from the abdomen and lower extremities into the chest causing an increase in the pulmonary capillary hydrostatic pressure, as well as elevation of the diaphragm. Patients with orthopnea must elevate their heads on several pillows at night.

Table 3	New York Heart Association functional classification
Class I	Patients with cardiac disease but without resulting limitations of physical activity. Ordinary physical activity does not causeundue fatigue, palpitation, dyspea, or angina pain.
Class II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea,or anginal pain.
Class III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.
Class IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfor. Symptoms of cardiac insufficiency of the anginal syndrome may be present even at rest. if any physical activity is undertaken, discomfort is increased.

Table 4 Functional classification for congestive heart failure based on maximal oxygen consumption (VO_2 max)

Class	Severity	VO_2 max, ml/kg/min	Anaerobic threshold, ml/kg/min	Maximal cardiac index, L/min/m^2
A	None to mild	>20	>14	>8
B	Mild to moderate	16-20	11-14	6-8
C	Moderate to	10-16	8-11	4-6
D	severe	6-10	5-8	2-4
E	Severe	<6	<4	<2
	Very severe			

Paroxysmal (nocturnal) dyspnea ; This term refers to attack of severe shortness of breath and coupling which generally occur at night, usually awaken the patient from sleep, and may be quite frightening. Though simple orthopnea may be relieved by sitting upright at the side of the bed with legs dependent, in the patients with paroxysmal noctunal dyspnea, coughing and wheezing often persist even in this position. The depression of the respiratory center during sleep may reduce ventilation sufficiently to lower arterial oxygen tension, particularly in patients with interstitial lung edema and reduced pulmonary compliance. Also, ventricular function may be further impaired at night because of reduced adrenergic stimulation of myocardial function. Cardiac asthma is closely related to paroxysmal noctunal dyspnea and noctunal cough and is characterized by wheezing secondary to bronchospasm—most prominent at night.

Cheyne – Strokes respiration ; Cheyne stroke respiration is characterized by diminished sensitivity of the respiratory center to arterial PCO_2 . There is an apneic phase, during which the arterial PO_2 falls and the arterial PCO_2 rises. These change in the arterial blood stimulate the depressed respiratory center, resulting in hyperventilation and hypocapnia, followed in turn by apnea. Chyne-strokes respiration occurs most often in patients with cerebral atherosclerosis and other cerebral lesions, but the prolongation of the circulation time from the lung to the

brain which occurs in heart failure, particularly in patients with hypertension and coronary artery disease and associated cerebral vascular disease, also appears to precipitate this form of breathing.

Cerebral symptoms ; Reduced cerebral perfusion and arterial hypoxemia, there may be alteration in the mental state characterized by confusion, difficulty in concentration, impairment of memory, headache, insomnia and anxiety.

E. Physical Examination

Abnormal hemodynamic, such as the pulse pressure may be diminished, and occasionally, the diastolic arterial pressure is elevated. There may be cyanosis of the lips and nail beds and sinus tachycardia, tachypnea , the extent of distention of the jugular veins in sitting upright. Third and fourth heart sounds are often audible but are not specific for heart failure, and pulsus alternans.

Pulmonary rales, cardiac edema, hydrothorax and ascites, congestive hepatomegaly, jaundice, cardiac cachexia may be apparent on general inspection of the patient.

Other investigation

Roentgenographic finding : The enlargement of chronic, distention of pulmonary veins and redistribution to the apices is common in patient with heart failure and elevated pulmonary vascular pressure, also, pleural effusion may be evident.

Echocardiogram is particular useful in assessing the dimensions of each cardiac chamber, abnormal contraction and relaxation, evaluation of left ventricular diastolic fillings. Ultrasound is one of the most important noninvasive techniques for cardiovascular diagnosis that provides both reliable clinical information and patient safety. Ultrasound is defined as sound above the upper threshold of human hearing (20,000 Hz). Ultrasonics, the technology of high-frequency waves through a medium. The high-frequency vibrations are created by striking an appropriate

piezoelectric crystal with alternating electric current. A short burst or pulse of high-frequency, low-intensity sound is then emitted and directed through the human body to detect boundaries between structures of different acoustic impedance. This technique is termed pulsed-reflected ultrasound.

Cardiac ultrasound presently consists of three interrelated forms: M-mode echocardiography, two dimensional echocardiography, and Doppler echocardiography. Echocardiography is thus a multidimensional and multiplanar imaging modality. Motion or M-mode echocardiography, the original ultrasonic techique developed for cardiac examination, uses a narrow ultrasound beam to depict a one-dimensional slice of the target structure. Two-dimensional echocardiography is a system for recording a spatially correct image of the heart. Two-dimensional units scan the heart in an arclike motion, resulting in cross-sectional (tomographic) slices (planes) of cardiac structures. Doppler ultrasound tracks the direction and velocity of blood flow through the heart and great vessels.

In this study has only the details of M-mode and two-dimensional echocardiography. They are based on the same fundamental ultrasonic principles. These basic ultrasonic equipment consists of an oscilloscope, a transducer, and a photographic or video recorder. The M-mode echocardiogram is obtained by using only one of the available crystals in the transducer housing to emit a single beam of sound. Two-dimensional instruments use a transducer containing one or more crystals that are mechanically rotated or electronically fired sequentially. This creates a fan-shaped, 60° to 90° image of the heart. Most modern ultrasound system integrate M-mode and two dimensional imaging in a convenient, easy to use, mobile unit. These unit can display the two-dimensional imaging alone or simultaneously with an M-mode imaging. Echocardiography provides a good quantitative assessment of wall mass. Formerly, left ventricular mass was determined by taking manual M-mode or two-dimensional measurements of septal and posterior wall thickness. Imaging parameters of global left ventricular function

are either volume-dependent or volume-independent. Volume-dependent calculations are those for ejection fraction and stroke volume. Ejection fraction traditionally uses the difference between the square of end-diastolic and end-systolic dimension divided by the square of the end-diastolic dimension. The calculation method of the volume-independent parameters of left ventricular systolic performance is the percentage of fractional shortening (%FS). This method is quick and reproducible:

$$\%FS = \frac{EDD-ESD}{EDD} \times 100\%$$

EDD = left ventricular end-diastolic dimension (millimeter)

ESD = left ventricular end-systolic dimension (millimeter)

M-mode echocardiography has been useful for determining left ventricular volumes in patients with nonsegmental disease and has been easily quantitated, since it involves only making measurements on a strip-chart recording. It is limited, however, since it was not been reliable in the presence of asynergy. Although M-mode echocardiography appears to be very sensitive for detection of true anatomic hypertrophy, two-dimensional echocardiography is superior for quantitative assessment of left ventricular mass. The reliability of quantitative two-dimensional echocardiography has been documented for both segmental and nonsegmental diseases. It thus appears superior to M-mode echocardiography for quantitative estimation of left ventricular volumes, because it directly measures all three hemiaxes, by imaging from apical as well as parasternal windows. There are several ways of calculating left ventricular volumes, including the biplane area—length method, the single—plane ellipse method, and the modified Simpson rule. The echocardiographic views of M-mode and the biplane area—length method of two-dimensional measurements are shown consequently in *figure 4 and 5.*

Electrocardiogram : No electrocardiographic findings are specific for heart failure, but the eletrocardiogram is usually abnormal in patients with significant cardiac disease.

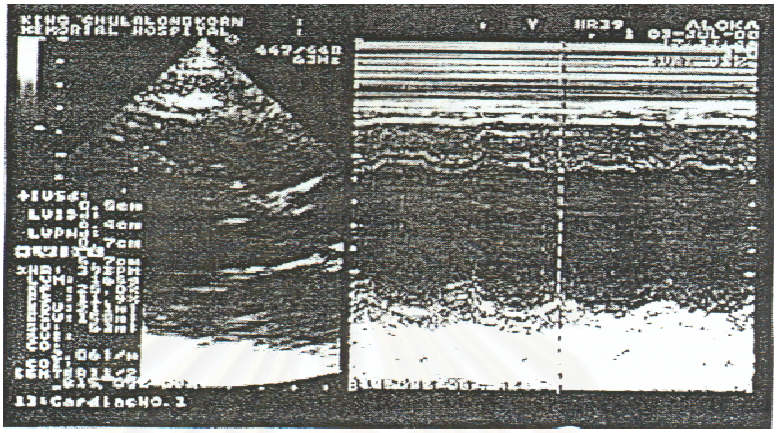

Figure 4 The echocardiographic views of M-mode for LVEF measurement

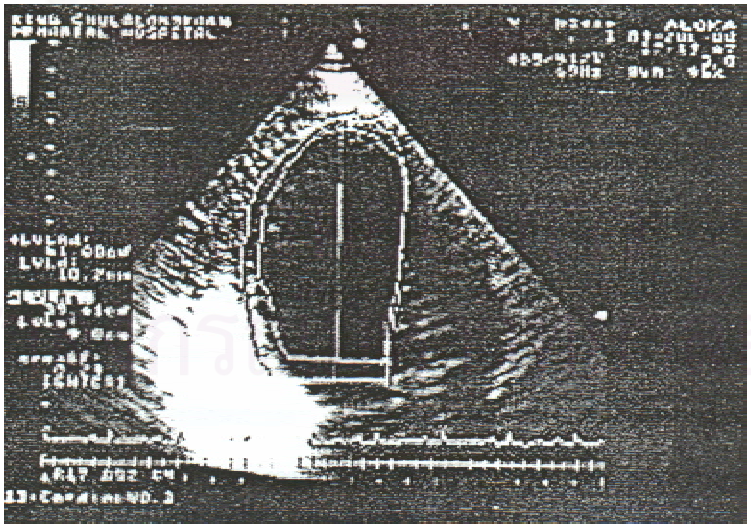

Figure 5 The echocardiographic views of two-diensional for LVEF measurement

F. General Principle of Therapy

The treatment of heart failure may be divided logically into there components (Braunwald, 1994):

1. removal of the precipitating cause,
2. correction of the underlying cause, and
3. control of the congestive heart failure state

The third component of the treatment of heart failure, i.e., control of the congestive heart failure state, may, in turn, be divided into three categories :

1. reduction of cardiac work load, including both the preload and the afterload,
2. control of excessive retention of salt and water, and
3. enhancement of myocardial contractility.

The pharmacotherapy of congestive heart failure has remained the mainstay of therapy. In most patients, first line drug therapy comprises wildly varying doses of specific pharmacotherapeutic agents from each of four classes:

1. diuretics,
2. ACE Inhibitor or other vasodilators,
3. digitalis glycosides, and
4. antithrombotic drugs.

Therapeutic interventions may improve the performance of the failing heart in 3 Ways (Packer et al., 1999). *First,* may increase ejection fraction by directly stimulating cardiac contractility. This approach (utilized by positive inotropic agents such as dobutamine and milrinone) can produce immediate hemodynamic benefits in the short term, but long-term treatment with these drugs may in crease morbidity and mortality. *Second*, drugs may increase ejection fraction by decreasing impedance to left ventricular ejection through the relaxation of peripheral blood vessels. These vasodilator interventions may relieve symptoms in the short term, but do not necessarily produce clinical benefits in the long term. *Third*, drugs may improve ejection fraction by affecting the process of cardiac

remodeling. This approach (utilized by neurohormonal antagonists such as angiotensin-converting enzyme [ACE] Inhibitors, β-adrenergic receptor blockers, and vasodilator—growth inhibitors, such as nitrates) may not produce immediate symptomatic benefits, but long-term treatment with these drugs can improve clinical status and decrease the risk of major cardiac events.

Basic principles for the medical management of the congestive heart failure include establishment of the primary cause, correction of the cause if feasible, and elimination and prevention of precipitating factors. Accordingly, though symptom relief remains a primary goal, improve survival and alteration of the natural history of the disorder have become equally important.

Adjunctive therapy

Nonpharmacologic measures are an important factor of therapy to be applied concurrently with drug intervention.

Diet: Patient with heart failure should be instructed to reduce dietary salt intake to 2 to 3 gm/day. This goal is achieved in most by eliminating table salt and food that contain excessive amounts of sodium. In patients with more severe heart failure, the sodium intake must be controlled more rigidly. Water intake may be ad libitum in all but the most severe forms of congestive heart failure. In patient with dilutional hyponatremia, restriction of water may be necessary and must be made to maintain nutritional intake and to avoid caloric and vitamin deficiencies; nutritional supplements may be in order.

Activity: For the patient with decompensated heart failure, the work of the heart must be reduced. This requires decreased physical activity. Activity may then be gradually increased as tolerated and the patient encouraged to be active within the limits of dyspnea and fatigue.

REVIEW OF THE RELATED LITERATURE

Exercise intolerance is a characteristic finding in patient with heart failure, because of both reducing exercise capacity and historic concerns that the stress of exercise would further aggravate heart function. The enrollment of these patients into an exercise training program was uncommon until the early 1990s (Span and Hurst, 1986, Cohn and Sonnenblick, 1994). Even today, exercise training is not routinely included as part of the standard clinical care for patients with heart failure. Patients with heart failure live average of 4 to 5 years (McKelvie et al., 1995), but nearly all suffer from fatigue and breathlessness that result in limited exercise capacity and poor quality of life.

In order to minimize symptoms patients with heart failure often self – restrict physical activity or deconditioning. The central hemodynamic abnormalities in heart failure are accompanied by many secondary neurohormonal, skeletal muscle, and peripheral vascular changes that may alter or attenuate the effect of exercise training. Patients with heart failure because of decreased left ventricular systolic function demonstrate large end – diastolic volumes and have little contractile reserve. It has been suggest that training in these patients may induce further increase in left ventricular end – diastolic that would increase wall tension and may be detrimental to left ventricular function and their condition would deteriorate.

The major symptoms of chronic heart failure are breathlessness and fatigue during exercise. Exploration of the mechanism of exercise limitation has tended to concentrate on the genesis of one or the other symptom. Dyspnea during exercise is poorly related to central hemodynamic variables in chronic heart failure, but the enhanced ventilatory response correlates well with the decrease in exercise capacity. Peak pulmonary capillary wedge pressure is not related to peak VO_2 or the symptoms of either fatigue or dyspnea (Sullivan et al., 1988). A close correlate of peak VO_2 in chronic heart failure is the ventilatory response to exercise. There is an increase in ventilation at a given level of

exercise (Sullivan et al., 1988), and this is well characterized by an increase in the slope of the relation between ventilation and carbondioxide production (VE/VCO_2). That is, at any given level of carbondioxide production, minute ventilation in chronic heart failure must include an explanation for the increased ventilatory response. Exercise hyperpnea is a common phenomenon in chronic heart failure, occurring at onset of exercise without evidence of arterial hypoxemia or altered CO_2 tension (Sullivan et al., 1988). The dyspnea and increased work of breathing experienced by some patients with heart failure is caused by increased dead space due to ventilation-perfusion mismatching (Myers et al., 1992), decreased lung compliance (Sullivan et al., 1990) and an increased impedance to breathing caused by chronic pulmonary venous hypertension (Mancini, 1995). Stimulation of skeletal muscle ergoreceptors induces generalized vasoconstriction and increases ventilation in chronic heart failure and may therefore from a direct link between metabolic and ventilatory abnormalities (Piepoli et al., 1996). Patients with heart failure, the ventilatory derived anaerobic threshold serves as an estimate of the beginning of excess carbon dioxide production secondary to the buffering of increasing H^+ arising from lactic acid. Thus, the hypothesis, exercise limitation by dyspnea does not explain the increase in VE/VCO_2 slope. Approximately 30% to 40% of patients with heart failure discontinue an exercise test due to dyspnea, whereas the majority of patients stop due to generalized or leg fatigue (Myers et al., 1992 and Sullivan et al,.1988). It is possible that there is a specific ventilatory signal arising from exercising muscle, which is abnormally enhanced in chronic heart failure.

The symptoms of CHF are fatigue during exercise and reduced exercise capacity. The changes seen in patients with CHF are similar to those seen in normal subjects undergoing “ detraining” with activation of the sympathetic (Cooksey et al., 1978). The generalized activation of sympathetic system seen in CHF could act as a further mediator of skeletal muscle changes, together with a possible contribution from catabolic factors and loss of anabolic function. The existence of ergoreceptors or metaboloreceptors sensitive to muscle work and transmitting to the central nervous system and enhanced by accumulation of metabolites suggests a different “ vicious cycle”. The chemically sensitive afferent fibers from

muscle drive blood pressure responses and increased ergoreceptor activity in CHF might maintain the increased sympathetic outflow, increasing peripheral resistance and reduced peripheral blood flow decreasing skeletal muscle perfusion. In turn the skeletal muscle may deteriorate further. These receptors and their afferent fibers may mediate the sensation of fatigue and possibly breathlessness.

Limiting physical activity in patients with compensated heart failure may not be unnecessary, but detrimental since it may worsen disability (deconditioning effects of inactivity). Although disuse and deconditioning are not the only cause of poor physical work capacity in patients with chronic heart failure, they play a crucial role in initiating adverse metabolic changes in skeletal muscle (Coats et al., 1992). Patients with heart failure have been found to have a lower maximal muscle strength than among healthy subjects (Lipkin et al ., 1988, Buller et al., 1991). These findings have led to the suggestion that skeletal muscle abnormalities may contribute to the impairment of functional capacity. Skeletal muscle atrophy is often observed and can occur early in the course of the disease (Lipkin et al ., 1988 and Mancini et al., 1992). Muscle atrophy may be related to diminished physical inactivity (Levine et al., 1990), and may in part be responsible for the impairment of exercise capacity. In addition, Buller and Pool-Wilson (1988) found that between comparing a healthy subject using one leg had a gas exchange pattern that use similar to patient with mild congestive heart failure.

In addition, histologic and biochemical abnormalities of skeletal muscle have long been observed in patients with heart failure. The patients were found to have a reduced percent of type I (slow twitch) (Sullivan et al., 1990), a predominant of type II (fast twitch muscle fibers) (Lipkin et al., 1988 and Sullivan et al., 1990) and a shift in fiber type distribution to type II (Drexler et al., 1992), smaller area of type IIa and IIb fibers,decrease in the number of capillaries per fibers (Sullivan et al., 1990), decrease in 3 – hydroxyacyl – coenzyme A dehydrogenase activity (Mancini et al., 1992 and Sullivan et al., 1990),a reduction in concentrations of mitochondrial enzymes succinate dehydrogenase and citrate synthase (Sullivan et

al., 1990), and cytochrome oxidase activity and mitochondrial volume density and surface density of mitochondrial cristae (Drexler et al., 1992). Mitochondrial volume density and surface density of mitochondrial cristae were significantly related to peak exercise oxygen uptake and to oxygen uptake at anaerobic threshold(Drexler et al., 1992).

The histology and biochemical changes and a reduction in the activity of oxidative enzymes suggest a switch, from aerobic to anaerobic metabolism in the skeletal muscle of patients with chronic heart failure.

A reduction in skeletal muscle blood flow is not the only factor responsible for the impairment of exercise performance in patients with heart failure. An abnormality in intrinsic skeletal muscle performance (Minotli et al., 1991) may also contribute to the reduction in exercise performance. Many studies used ^{31}P – MRS to examine muscle metabolism during exercise that found a more pronounced increase in the iorganic phosphate phosphocreatine ratio and decrease in pH (Massie et al., 1987 and Wilson et al., 1985), a reduction in phosphocreatine and pH (Massie et al., 1987 and 1988) in patients with heart failure than control subjects. The result from some studies (Nosak et al., 1987) of skinned muscle fiber and isolated muscle preparations suggest that the increase in iorganic phosphate or H_2PO_4 interferes with muscle contraction and major alteration in myosin heavy chain in skeletal muscle (Sullivan et al., 1988). Those studies would support the conclusion that in patients with heart failure there is an intrinsic abnormalities in skeletal muscle metabolic function.

The muscle hypothesis (*Figure 5*; Coats et. al, 1994) suggests new strategies for intervention. The major determinant of symptoms in chronic heart failure may be abnormality of skeletal muscle, resulting in early fatigue and an increase in the ventilatory stimulus and thus an increased ventilatory response to exercise. The evidence presented suggests that new forms of treatment focused on skeletal muscle may improve the patient's quality of life.

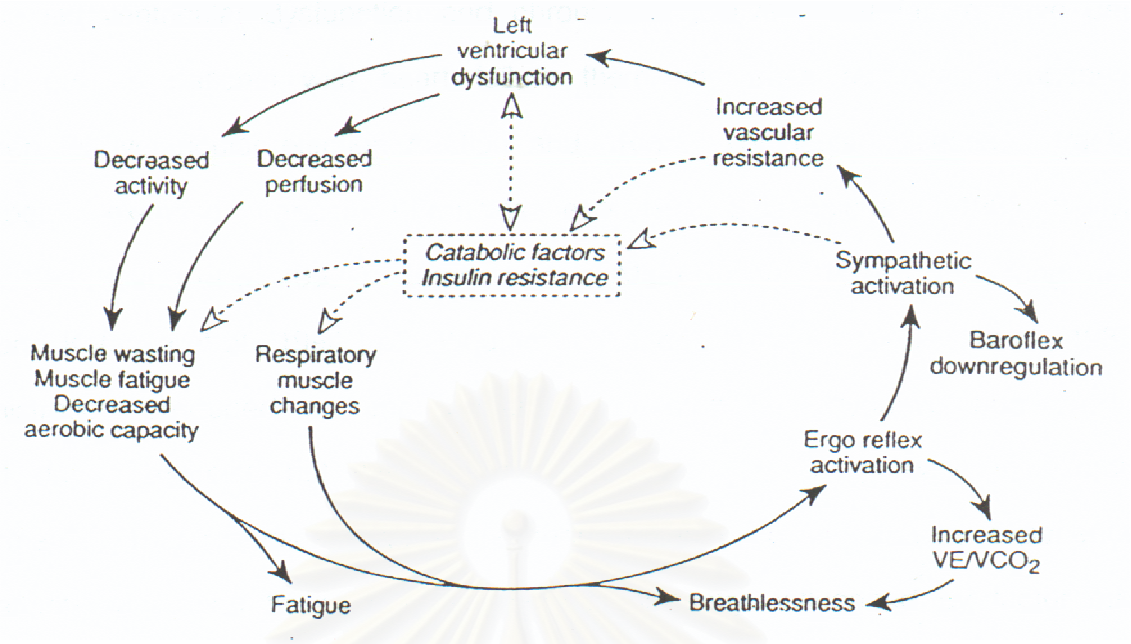

Figure 5 Muscle hypothesis in CHF. Skeletal muscle is abnormal in CHF. During exercise, muscle has a limited capacity for aerobic Metabolism, resulting in fatigue and ergoreflex activation, which causes an increases in the ventilatory response to exercise and the sensation of dyspea. Ergoreflex activation also causes sympathetic nervous system activation, with a consequent increase in afterload and a decrease in blood flow to the periphery, further exacerbating skeletal muscle abnormalities.

The first investigation of exercise training in patient with low left ventricular ejection fraction was reported by Letac and Colleagues in 1977. As part of a larger exercise training program for patients with coronary artery disease with LVEF of <45%. No changes either positive or negative in LVEF, left ventricular end-diastolic volume, or other echocardiographic indices of systolic function were found.

Since 1979, a comprehensive exercise training studies in patients with chronic left ventricular dysfunction and chronic congestive heart failure have been carried out. In patients with heart failure there has been no relation observed between left ventricular ejection fraction and Right ventricular ejection fraction and peak exercise capacity (Franciosa et al.,1979, Szlachcic et al., 1985, Sullivan et al., 1988, Liang et al.,1992). Short term (Maskin et al., 1983) and long term infusion (Kataoka et al., 1994) of dobutamine and cilazapril (Drexler et al., 1989) administration produced an improvement in central hemodynamic and cardiac output during exercise but this was not associate with an increase in exercise performance. These studies suggest the reduction in exercise capacity experienced by patients with heart failure may be more significantly influenced by factor other than poor ventricular function. Thus these investigation of exercise training in patients with chronic heart failure demonstrated the safety and potential benefits of exercise training programs.

The effects of exercise training in patients with heart failure have not only improvements in exercise capacity [measured by peak oxygen consumption (peak VO_2) or exercise duration] (Page et.al, 1994, and Sullivan et. al, 1990) but favorable changes in autonomic nervous system function; decrease in sympathetic activity and a concomitant increase in vagal activity (Coats et. al, 1992). Regional blood flow and skeletal muscle function have been observed as well. In the resent years, investigation into cardiac rehabilitation have suggested that exercise training improve peak oxygen consumption (peak VO_2) of patients with chronic heart failure.

Sullivan et al., 1988 : studied the effects of exercise training in patients with stable chronic heart failure FC I-III (EF, 24 $\pm$ 10 %). Exercise consisted of stationary bicycle riding for 25-40 minutes, walking, jogging , and stair climbing, total time about 1 hr, at a heart rate corresponding to 75 % of the peak VO_2 three to five tines per week. They found that long term exercise training increased in peak oxygen consumption and induced several important peripheral adaptations which contributed to improved exercise performance such as increase in peak muscle blood flow, increase in leg arteriovenous oxygen difference, increase systemic arteriovenous oxygen difference, and reduced blood lactate levels at submaximal exercise.

Keteyian et al., 1996 : assess a randomized control trial, the continuous aerobic exercise training program of three exercise session per week for 24 weeks (session lasted 43 minutes, three different types of equipment include motor driven treadmills, stationary cycles, rowing machines, and arm ergometers) in patients with heart failure and control group. He found that exercise training is significantly increased exercise tolerance, as measured by increase in peak VO_2 , exercise duration, peak ventilation , peak heart rate and power output in patients with heart failure than control group.

Several investigations have increased knowledge of changes that occur in skeletal muscle of chronic heart patients with habitual exercise.

Minotti and Colleagues (1990) used a wrist flexor exercise program with incremental wrist exercise testing performed pre- and post- training. Importantly, exercise training did not increase heart rate or cardiac output and constitution pure local muscle training. The trained forearm increased in endurance by approximately 260 % (no change in endurance for the untrained forearm). With incremental exercise testing, the inorganic phosphate/phosphocreatine ratio was reduced, consistent with less phosphocreatine depletion and an increase in oxidative capacity of the forearm.

Stratton et al (1994) used isometric handgrip exercise training nondominant arm two or three exercise sessions daily 7 days/week for 1 month and incremental weight pulley exercise testing in 10 patients with stable chronic heart failure NYHA FC II-IV. In the trained arm after training, maximal voluntary contraction increased 6 %. During incremental exercise duration increased 19 % and submaximal responses improved for pH and PCr / (PCr+Pi). The PCr resynthesis rate increased by 48 %, and estimated effective maximal rate of mitochondrial ATP synthesis increased by 37 % .Endurance exercise duration increased by 67 %, and submaximal levels of PCr / (PCr + Pi) improved. The PCr resynthesis rate and the effective maximal rate of mitochondrial ATP synthesis also improved. In control (untrained arm), there were no changes in any of the measured variables.

Belardinelli et al (1995) performed and eight week cycle exercise program in 27 patients with either ischemic or idiopathic dilated cardiomyopathy (exercise group, n= 18, nonrandomized control group n = 9 ; mean LVEF ~ 30 %). Graded exercise testing demonstrated a 17 % increase in VO_2 peak. Skeletal muscle biopsies of the anterolateral thigh demonstrated an increase in fiber size, an a shift in fiber type distribution from type II to type I, and increased in volume density of mitochondria.

Magnusson and Coworkers (1996) sought to train one muscle group with strengthening exercise. A single knee extension exercise, four sets of 6-10 repetitions at 80 % of maximal dynamic strength, was performed three times per week for eight weeks in five CHF patients in NYHA FC II-III (n = 11, LVEF = 5-39 %). After training, the maximal exercise intensity tolerated on the ergometer cycle was significantly raised from 99 to 114 watts. Peak dynamic knee extensor work rate after endurance training, maximal dynamic and isometric strength after strength training was increased. The crossectional area of muscle quadricep femoris increased 9 % , and the capillary per fiber ratio of muscle vastus lateralis was raised by 47% and 58 % in the endurance trained legs. The oxidative enzyme activity in muscle vastus lateralis was significantly raised above 50 % after endurance training. They concluded that specific strength and / or endurance

training of the knee extensor muscle group was raised due to changes in muscle oxidative metabolism and muscle morphology.

Ohtusbo and coworker (1997) used a repetitive isotonic right foot planter flexion exercise training. Seven patients with stable chronic heart failure, NYHA FC II-III, mean LVEF = 32 % performed six minutes of plantar flexion as one set at a rate of 40 repetitions per minute. The training routine consist of four sets per day, five to seven days per week. Before and after training, the patients' metabolic response were examined during the calf exercise test with ^{31}P-MRS and calf blood flow with plethysmography. Standardized phosphocreatine and intracellular pH decreased after training. The new Borg scale improved significantly after training. Blood flow did not change significantly.

They demonstrated that local muscle oxidative capacity is impaired, may be partly due to deconditioning, in chronic heart failure and may be improved by exercise training . These data are consistent with the concept that the majority of the increase in muscle strength and endurance resulting from exercise training in chronic heart failure is likely due to enhanced oxidative capacity of skeletal muscle metabolism.

Skeletal muscle show changes in cellular structure, depletion of phosphocreatine, alterations in oxidative capacity, and loss of muscle mass with atrophy of oxidative fibers in patients with chronic heart failure. Changes blood flow owing to increased vasoconstriction and impaired ability of arterial dilatation have also been shown to be partially reversible by exercise training. Since muscle strength has also been demonstrated to be an independent predictor of exercise capacity, both aerobic and strength exercises are required, using high exercise stimuli applied to peripheral muscles.

Until now, detailed standardized guidelines for exercise training in patients with CHF have not been established, however, some recommendations have been suggested. Exercise training method applied in previous studies were based on recommendation for fitness training or on experience from rehabilitation of coronary patients , arbitrarily modified for CHF patients. Traditionally aerobic exercise was applied by continuous training method exclusively.

A new method of interval exercise training was applied by Meyer and Colleagues (1990). The first time of interval exercise training in the rehabilitation of the patient after bypass surgery has proven to be more effective improving exercise capacity and decreasing heart rate, rate – pressure product and lactate at submaximal work rate than continuos training with the same relative training heart rate.

In daily life, most physical activities are of an intermittent type (e.g, climbing stairs, hurrying short distances for the bus, walking, sustaining posture), and demand both endurance capacity and muscle strength. As many studies affirm that the intensity of exercise training has a more pronounced affect on a subjects exercise capacity than the duration of exercise (Fox et al., 1975 and Wenger et al., 1975) Interval exercise training seems to be an appropriate method to stimulate both endurance capacity and muscle strength.

Clinical experience with chronic heart failure patients also confirms the benefit of exercise training using interval methods. In 1996 (a), Meyer and coworker studied three interval exercise modes with different ratios of work / recovery phase (30/60 s, 15 / 60s and 10 / 60s) and different works rates (50%, 70 % and 80 % of the maximum work rates achieved during a steep rump test; 3 minutes unloaded pedaling, increments of 25 watts / 10 second, during cycle ergometer exercise test) in stable chronic heart failure HYHA FC II-III, LVEF 29 $\pm$ 10 %. In all three modes VO_2 , ventilation and lactate did not increase significantly

In the random-order crossover study, Meyer and coworker (1996 (b)) assessed the effect of 3 weeks of interval exercise training and 3 weeks of activity restriction on functional capacity in 18 hospitalized patients with severe CHF (mean aged 52 ± 2 years; LVEF 21 ± 1 % half of them on a transplant waiting list). The training program consisted of interval training with bicycle ergometer (15 minutes) 5 times weekly, interval treadmill walking (10 minutes), and exercises (20 minutes), each 3 times weekly. After short – term training , patients can achieve significantly improvement in aerobic (increased work rate by 57 % and oxygen uptake by 23.7%) and ventilatory capacity (delayed onset of ventilatory threshold , decreased in slope of ventilation / carbon dioxide production by 14.6 %, and ventilatory equivalent of carbon dioxide production by 10.3 %) and symptomology (decreased heart rate (7.3%), lactate (26 %), and ratings of perceived leg fatigue and dyspnea (14.5 % and 16.5 %). Independently of the random order, data after activity restriction did not differ significantly from data measured at baseline.

In 1997(b), Meyer and Colleaques assessed the interval training program (Same as the previous study in 1996(b)) in 18 males patients with stable CHF aged 52 ± 2 years as a result of dilated cardiomyopathy (N= 9) and coronary heart disease (N=9) . Half the patients were on the heart transplantation waiting list. Eight patients were in NYHA class II and ten in class III. At rest ejection fraction was 21±2 % and cardiac index was 2.2 ± 0.2 /.m^2 .min^{-1}. The maximum work rate achieved from steep rump test increased weekly. There was no significant change in heart rate, blood pressure, and ratings of perceived exertion (RPE) using a Borg Scale. Mean lactate concentration indicated an overall aerobic range of training intensity. The performed training work rate was more than doubled (240 %) while cardiac stress was lower (86 %) when compared steep ramp test with the commonly used submaximum intensity levels of 75 % peak VO_2 from an ordinary ramp test. Values of norepinephrine and epinephrine as well as of RPE corresponded to those measured at 75 % peak VO_2. They concluded that the cardiopulmonary and neurohormonal responses to the interval training were similar to those for 75% of VO_2 peak, although, the work interval intensity was 240% higher.

Meyer and colleaques (1998) sought to assess the safety of interval exercise training in 11 men with chronic heart failure(LVEF～ 37±3 %) with respect to left ventricular(LV) function compare with control group. Radionuclide ventriculography was used to assess LV function during interval exercise training(IET) and steady state exercise

training (SSET) and during works versus recovery phases, at temporally matched times between the fifth and the sixteenth minutes of IET and SSET. During the course of both IET and SSET there was a significant increase in LV ejection fraction, accompanied by increased heart and cardiac output. The magnitude of change in LV ejection fraction during IET was similar to that seen in controls and SSET. Both ejection fraction and the clinical status in patients remained stable during IET. These investigators reasoned that the interval training approach would stimulate skeletal muscle adaptation with the high intensity work interval while minimizing cardiac and metabolic stress and because of interval exercise training appears to be as save as steady state exercise training or continuous training with respect to LV function. Thus interval exercise training method at relatively high intensities appears to be more benefit and with no greater LV stress in chronic heart failure patients than continuous exercise training method. Detailed standardized guidelines for exercise training in patients with chronic heart failure in Thailand have not been established. Therefore in the current study want to assess the benefit of the interval exercise training in the Thai patients with chronic heart failure as a result of ischemic cardiomyopathy (coronary artery disease).Because the previous interval training program (5 times/week x 3 weeks) required frequent training this make it inconvenient to perform on patient in their daily lives. The comparing effects of the different frequency and duration; decreasing the number of frequency practice in each week (3 times/week) and increase duration (5 weeks) of the current method, of the interval training from the previous method has not been studied yet. Thus, this study want to compare the effect of both interval training program on the changes in exercise capacity by measured peak work rate and measured peak oxygen consumption in patients with chronic heart failure.

CHAPTER III

RESEARCH METHODOLOGY

The study procedure was approved by the local ethics committee of Medicine Faculty of Chulalongkorn University. Patients were recruited at King Chulalogkorn Memorial Hospital and invited to participate in the study. Before entered the program, all patients gave written informed consent to participate in the study. The interview were done by one investigator (cardiologist).Two dimensional echocardiographic examinations at baseline and at completion of the study were carried out by one cardiologist, using 3 times repeated measurement and calculated for the average of LVEF, and the exercise test by the same group of investigators. Before and after training, patients were weighed and height for baseline variables and were measured flexibility by sit and reach for assessment of musculoskeletal and joint coordination of back from the calisthenics with stretching exercise. The results of the baseline examinations and the type of the program of training for each patient were not known to the investigators when the end of examinations were performed, and all data were blindly evaluated.

RESEARCH DESIGN

The current study was an experimental design. The all procedure of exercise training performed at the exercise laboratory room 107, Physiology Building, Medicine Faculty of Chulalongkorn University in Chulalongkorn Memorial Hospital. The duration of experiment was about one year. The experimental design was shown as figure 7.

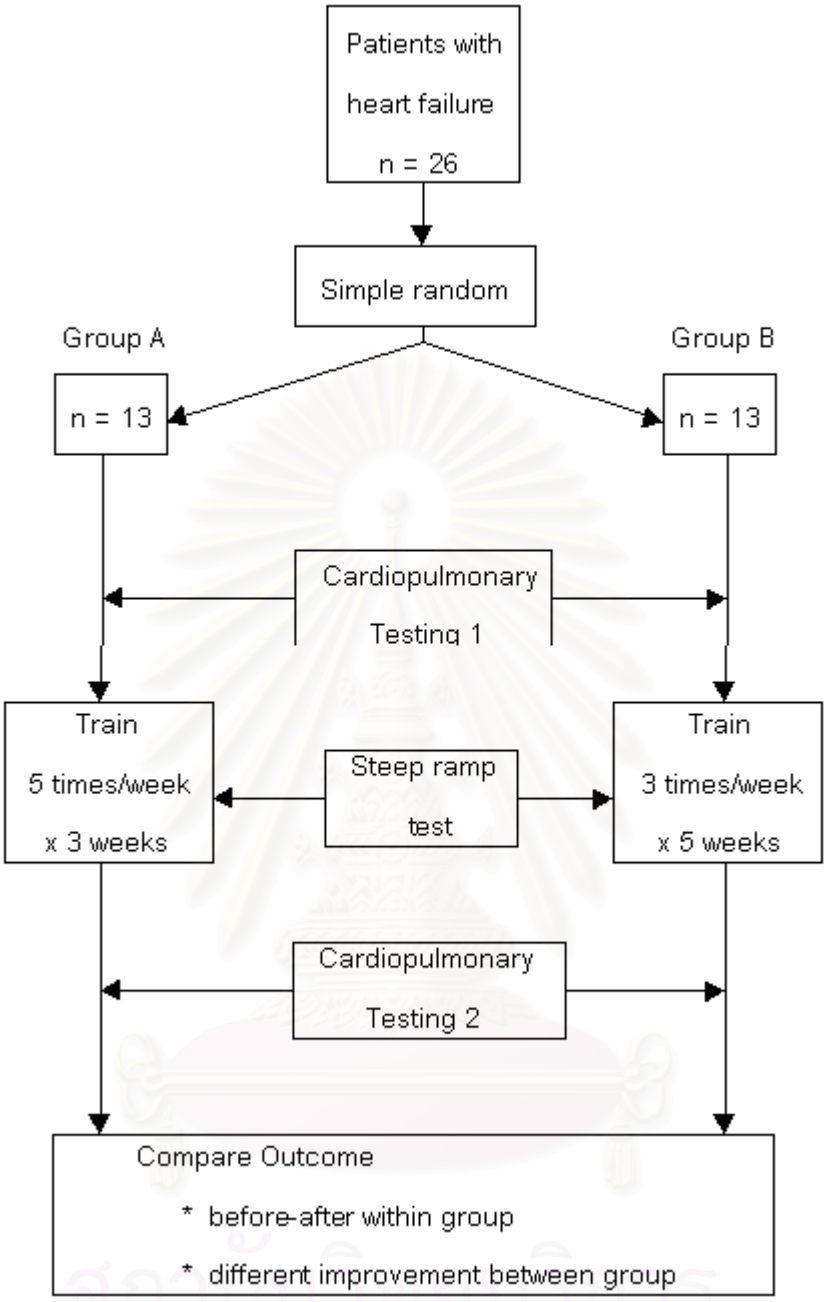

Figure 7 Experimental design

POPULATION

The study included 26 patients with NYHA FC II-III chronic heart failure due to coronary artery disease (ischemic cardiomyopathy). The patients were simple randomly divided into 2 groups. Group A (n=13; M=11, F= 2) underwent exercise training 5 times/week × 3 weeks. Group B (n=13; M=11, F=2) underwent 3 times/week × 5 weeks. The criterion for inclusion and exclusion included:

The inclusion criteria

1. Ischemic cardiomyopathy with NYHA FC II-III
2. Both sex aged between 40-70 years old, last 3 months stable chronic heart failure patient due to ischemic heart disease
3. LVEF was in between 20-60 %
4. Electrocardiographic was in normal sinus rhythm
5. Patients have never been entered exercise training program before this study
6. Long-term medication, which was not changed during the study period

The exclusion criteria

1. Unstable angina
2. Decompensated congestive heart failure
3. Acute myocarditis or pericarditis
4. Deep vein thrombophlebitis
5. Recent systemic or pulmonary embolism
6. Uncontrolled hypertension
7. Resting ST displacement was more than 3 mm.
8. Uncontrolled atrial and ventricular arrhythmia
9. Acquired third degree heart block

10. Uncontrolled diabetes miilitus

11. Neutological/Orthopedics disease limited exercise

MATERIALS

1. A weighing Scale (Yamato DP - 6100 GP)

2. A Scale for height

3. Echocardiography (Two dimensional)

4. Flexibility scale

5. Dyspnea and fatigue Borg scale

6. Cardio tachometer (Polar Sport Tester, Polar electro Oy FIN-90440, Finland)

7. Electrocardiographic monitor (Quinton Instrument CO, Q4500)

8. A noninvasive blood pressure monitor (Quinton instrument CO, model 412)

9. Oxygen and carbondioxide gas analyzer (Quinton Metabolic Cart; QMC)

10. Bicycle ergometer (Corival 400)

11. Treadmill (Quinton instrument CO, Q 55 Series 90)

Long – term medication, which was not changed during the study period, included

Group A : ACEI - Enaril (0.25 – 5 mg once daily)

- Cozaar (50 mg once daily)

: Vasodilator - Isosorbide dinitrate (2 to 3 times, 20-30 mg/day)

- Ismo (once daily/ 20 mg)

- Hydralazine (75-150 mg/day , 3 times / day)

: Digoxin (0.125-0.25 mg once daily)

: Betablocker - Prenolol (25-50 mg once daily)

- Carvidilol (6.25 mg/day , 2 times)

: Diuretic - Lasix (40 mg/day , once daily)

- Modiuretic (5 mg/day, once daily)

- Aldactone (25 mg/day , once daily)

: Antihypertensive drugs - Cardil SR 120 (120 mg/day , once daily)

- Vastarel (6 mg/day , twice daily)

- Herbessor (30 mg/day , once daily)

Group B : ACEI - Enaril (5-20 mg/day , 1-2 times)

: Vasodilator - Norvasce (10 mg , once daily)

- Isordil (30 mg/day , 3 times)

- Ismo (20 mg/day , once daily)

- Hydralazine (25 mg , 3 times/day)

: Digoxin (0.25 mg , once daily)

: Betablocker - Metroprolol (50-100 mg/day , once daily)

Prenolol (50 mg/day, once daily)

: Diuretic - Aldactone (25 mg , once daily)

- Lasix(40 mg, once day)

- HCTZ (50 mg , once daily)

DATA COLLECTION

Exercise testing program

1. Steep ramp test for skeletal muscle strength and endurance

A steep ramp test on bicycle ergometer performed with 3 minutes unloaded pedaling, work rate increments of 25 watts every 10 second, stopped when patients could not maintain 60 revolutions/min. for achieved maximum short time exercise capacity (MSEC). MSEC (watts: W) was the primary outcome variables.

2. Ordinary ramp test with a Quinton Metabolic Cart for cardiopulmonary endurance measurement.

After overnight fasting and before administrating medication or at least 2 hours after a light breakfast in the morning the day testing, cardiopulmonary exercise testing using upright bicycle ergometry was carried out before the start of training and the day after the training program was completed. Cardiopulmonary exercise measurements were obtained during the ordinary ramp cycle test. Starting with 3 minutes unloaded, work rate was increased by 12.5 w/min. During exercise, subjects breathed through a mouthpiece and a 1- way attached a mass spectrometer. A breath-by-breath analysis of total body oxygen consumption and carbon dioxide production were performed, using a cardiopulmonary gas exchange system Quinton Metabolic Cart (QMC) model. This allowed on-line measurement of metabolic gas exchange and ventilation every 5 seconds. Continuous 12 leads ECG registration with computerized ST analysis was performed, as well as blood pressure measurement, registration effort, chest pain and dyspnea, according to the Borg scale. Before each test, the system was calibrated by gases at the standard and/or body temperature and pressure (dry), and volume by a 3 L syringe. Heart rate, blood pressure, Oxygen uptake (VO_2 ; L/min, ml/kg/min), and exercise time was the secondary variables as shown in figure 7.

Exercise Training Method

The training program was 5 times/week ×3 weeks in Group A and 3 times/week ×5 weeks and consisted of interval bicycle ergometer training and interval walking training on a treadmill , and stretching exercise. Before each session training patients were instructed to gently warm – up exercise with calisthenics, generally lasting 5 to 10 minutes. Training session were supervised by continuous monitoring of heart rate and rhythm, ratings of leg fatigue and dypsnea by Borg scale, which translated to Thai by Wongphaet et al., (1998) as shown in figure 8, and for other possible complaints such as vertigo or chest pain. Blood pressure were measured before beginning and during bicycle training and after exercise by cuff method. Patients remained on medication during the exercise training procedure. Before each session, patients were weighed, auscaltated for well-being. Exercise testing and training were performed between 8 and 12 am. All patients had received ordinary medication 2 hours before training and were recommended not to train at home during the study.

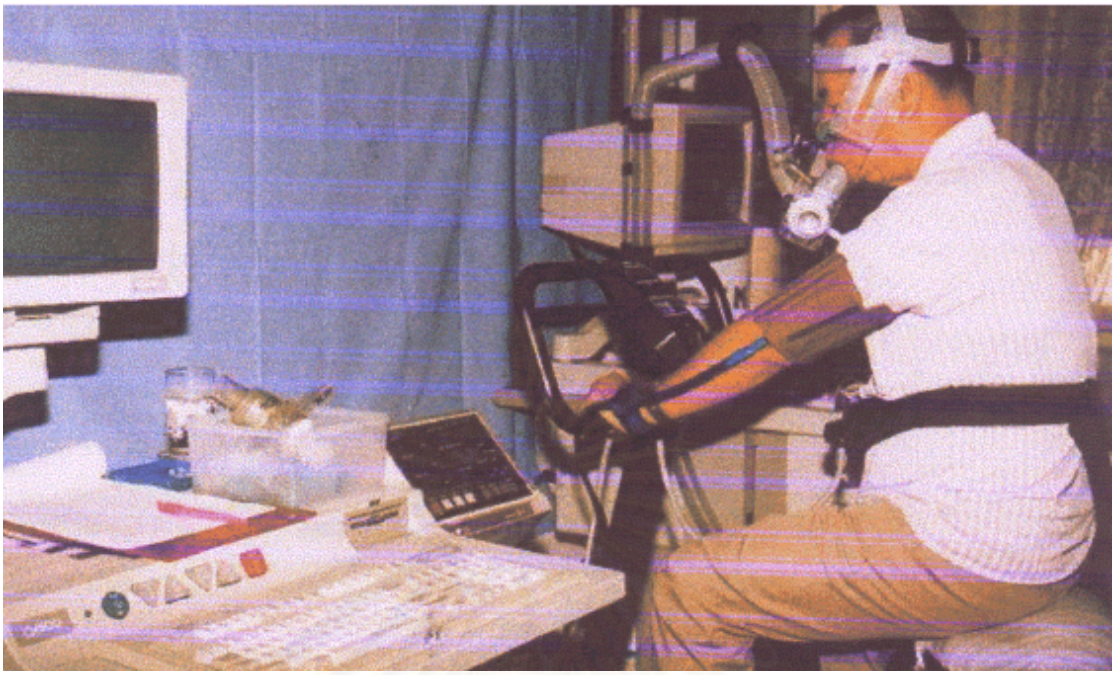

Figure 7 Cardiopulmonary exercise testing: Ordinary ramp test

Figure 8 Rating perceived of exertion: Borg scale

Bicycle ergometer training, 15 minutes, employed phases of 30 seconds and recovery phases of 60 seconds. Exercise intensity for work phases was derived from a steep ramp test. We chosed 50 % of the maximum work rate (MSEC), during interval training. In recovery phases , patients pedaled with 15 watts. The steep ramp test was repeated at the beginning of each training week for group A but every 5 sessions in group B to adjust exercise intensity for the following week as shown in figure 10.

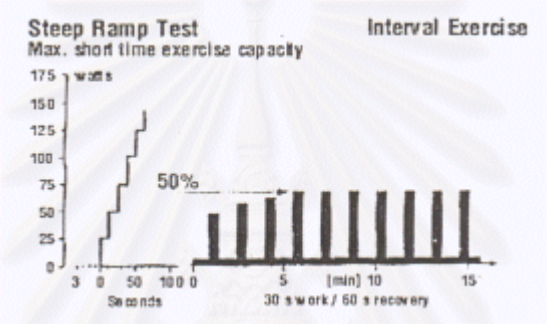

Figure 10 Intensity for bicycle interval training obtained from steep ramp test

Walking training on a treadmill performed 3 times weekly for 10 minutes each using an interval method. Sixty seconds of work phases (group A : mean speed 2.76 mph, range 1.9-3.7 mph, group B : mean speed 2.98 mph, range 2.2-3.7 mph during the last week of training), adjusted according to each patients maximum heart rate tolerated during cycle interval training, was alternated with 60 seconds of low speed (mean speed 0.8 mph) of recovery phase

STATISTIAL ANALYSIS

The data in this study were statistically analyzed using the SPSS/window (Statistical Package for the Social Service) program. Data presented as mean $\pm$ SD. The student t-test for paired samples was applied to compare measured MSEC during the first and the last training week and to compare measured peak VO_2 before and after training program of the 2 groups. An ANCOVA was applied for the differences of MSEC and peak VO_2 between 2 groups. Two tailed P values < 0.05 were considered significant.

CHAPTER IV

RESULTS

Baseline Variables:

Table 5 summarized the general characteristics of both groups. No significant different in clinical characteristic were observed. The aetiology for heart failure was ischemic cardiomyopathy: angiographically verified coronary artery disease; in group A: single vessel = 5, double vessel = 6, triple vessel = 2 patients. Group B: single vessel = 4, double vessel = 6 , triple vessel = 3 patients. Exercise training was well tolerated by all patients. No patient had to refrain from participation in exercise training because of acute deterioration in clinical status. No adverse training-related side effects were reported by the subject. The medication used in patients was shown in *table 6.*

Maximum short time exercise capacity(MSEC)

MSEC changes within group: Changes in effect variables with exercise training were shown in *table 7*, There were no significantly changed in resting heart rate, maximal heart rate, systolic blood pressure, and Borg scale in both groups, but exercise duration was significantly increased. Maximum work rates (MSEC) was significantly increased; as shown in *figure 10*, from the first to the last training week; group A from 141.15 $\pm$ 53.74 to 184.77 $\pm$ 65.75 watts ($p < 0.000$), group B from 155.77 $\pm$ 54.88 to 204.62 $\pm$ 59.18 watts ($p < 0.000$). The mean tested duration in group A was increased from 3.57 $\pm$ 0.22 to 4.14 $\pm$ 0.26 min. ($p < 0.000$), and group B was 4.02 $\pm$0.22 to 4.19 $\pm$ 0.23.($p < 0.000$).

Cardiopulmonary function

VO_2 changes within group: After training VO_2 peak was increased from 13.32 ±3.77 to 15.54 ± 5.14 ml/kg/min (p< 0.018) in group A and group B was in creased from 14.88 ± 4.32 to 17.64 ± 4.10 ml/kg/min (p < 0.000). Other variables summarized in *table 8* and showed in *figure 12.*

Comparison of MSEC and peak VO_2 between group:

Both MSEC and peak VO_2 after training of the two program was increased not significantly differenct: MSEC; p = 0.72, VO_2 peak; p = 0.540 (Figure 13 and 14). Although baseline peak work rate and peak VO_2 between group was significantly different (p< 0.000 both).

Body weight, LVEF, flexibility post training

Post training, body weight and LVEF was not change but improvement in NYHA Functional class and flexibility as shown in *table 9*.

Table 5 Patients' characteristics

Variables	Group A (n = 13)	Group B (n = 13)
Age (years)	59 ± 7	57 ± 9
Sex (n)	M = 11, F= 2	M = 11, F= 2
BW (Kgs)	65.48 ± 10.90	65.08 ± 13.34
Ht (cms)	163.46 ± 5.13	163.46 ± 5.96
Duration of disease	3 mo.-12 years	3 mo.-16 years
NYHA class (n) II	11	12
III	2	1
EF (%)	38 ± 11	40 ± 9
PTCA (n)	7	11
CABG (n)	3	2

Data are expressed as mean ± SD

BW = body weight, Ht = height,

NYHA = New York Heart Association Functional Classification

EF = ejection fraction,

PTCA = Percutaneous Transluminal Coronary Angioghraplasty,

CABG = Coronary Artery Bypass Graft

Table 6 The medication used in patients with chronic heart failure

Medications	Group A (n)	Group B (n)
Digoxin	2 (15.38%)	1 (7.69%)
Vasodilators	6 (46.15%)	4 (30.78%)
ACE Inhibitors	6 (46.15%)	7 (53.85%)
β - Blocker	4 (30.78%)	5 (38.46%)
Diuretics	3 (23.08%)	3 (23.08%)
Antihypertensive	4(30.78%)	-

Table 9 Body weight, LVEF, NYHA functional class, and flexibility post training

Variables	Group A	Group B
Body weight (kgs)	65.48±10.90	64.68±13.13
LVEF (%)	41±9	40±12
NYHA FC (n) II → I	11	12
III → II	2	1
Increased flexibility (cms)	4.35±3.18	5.69±4.47

Table 7 Steep ramp test variables

Variables	Group A			Group B		
	First week	Last week	%Change	First week	Last week	%Change
MSEC (W)	141.15± 53.74	184.77±65.75 [1]	+30.9	155.77±54.88	204.62±59.18 [1]	+31.36
HRr (bpm)	77.85±11.38	77.46±11.12	-0.5	72.69±13.83	75.38±16.87	+3.7
HRm (bpm)	104.62±9.09	109.15±8.94	+4.33	106.85±17.91	11.922±0.52	+4.74
SBPr (mmHg)	112.85±14.91	108.00±15.81	-4.3	123.92±16.90	119.23±10.75	-3.78
SBPm (mmHg)	141.38±25.17	140.15±20.64	-0.87	148.00±23.69	147.31±18.87	-0.47
Duration (min)	3.57±0.22	4.14±0.26 [1]	+7.18	4.02±0.22	4.19±0.23 [1]	+7.12
Borg scale	14.69±0.85	15.00±0	+2.1	14.61±1.12	14.92±0.28	+2.1

Data are expressed as mean ± SD

MSEC = maximal short time exercise capacity,

HRr = resting heart rate, HRm = maximal heart rate,

SBPr = resting systolic blood pressure,

SBPm= maximal systolic blood presure,

t = $p < 0.001$: significantly differences within group

- = percent decreased, + = percent increased

Table 8 Cardiopulmonary variables pre-post training in group A and B

Variables	Group A			Group B		
	Pre-training	Post-training	% Change	Pre-training	post-training	% Change
HRr (bpm)	77.5±11.9	73.4±12.7	- 5.3	77.9±13.7	73.7±15.0	- 5.3
HRm (bpm)	120.9±16.9	121.9±16.7	+ 0.82	123.5±15.6	126.0±18.1	+ 2.02
SBPr (mmHg)	116.8±15.3	108.7±12.4	- 6.9	123.8±17.6	110.4±34.1	- 1.9
SBPm (mmHg)	154.8±24.6	157.5±28.7	+ 1.74	169.2±23.9	167.0±28.0	+ 1.3
Duration (min)	6.16±0.004	7.01±0.19 t	+ 11.52	6.45±0.24	7.21±0.17 **	+ 8.8
Work rate (Watts)	96.2±32.03	111.5±32.3 t	+ 16	105.8±38.40	123.1±29.7 **	+ 17
VO_2 peak (L/min)	0.88±0.30	1.02±0.40 *	+ 15.9	0.98±0.40	1.14±0.41 t	+ 16.32
(ml/kg/min)	13.32±3.77	15.54±5.14 *	+ 16.7	14.88±4.32	17.64±4.10 t	+ 18.55

Data are expressed as mean ± SD.

HRr = resting heart rate, HRm = maximal heart rate

SBPr = resting systolic blood pressure

SBPm = maximal systolic blood pressure

VO_2 peak = peak oxygen consumption

* = $P < 0.05$, ** = $P < 0.01$, t = $P < 0.001$

- = percent decreased, + = percent increased

Maximum short time exercise capacity (MSEC: W)

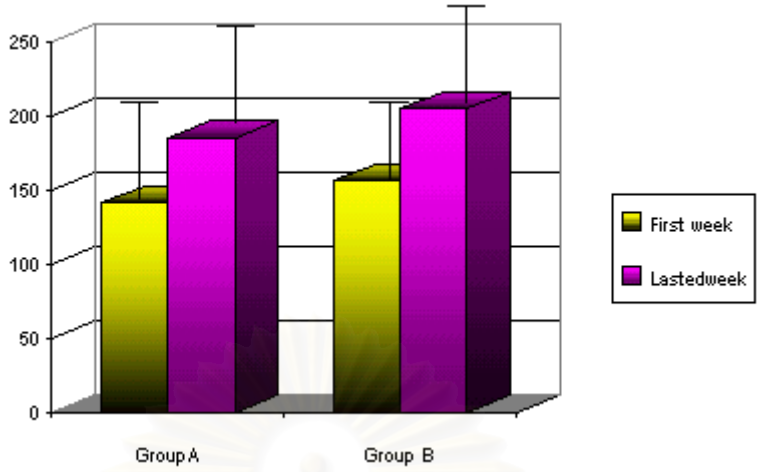

Figure 11 Comparison of maximum short time exercise capacity within group

Peak VO_2 (ml/kg/min)

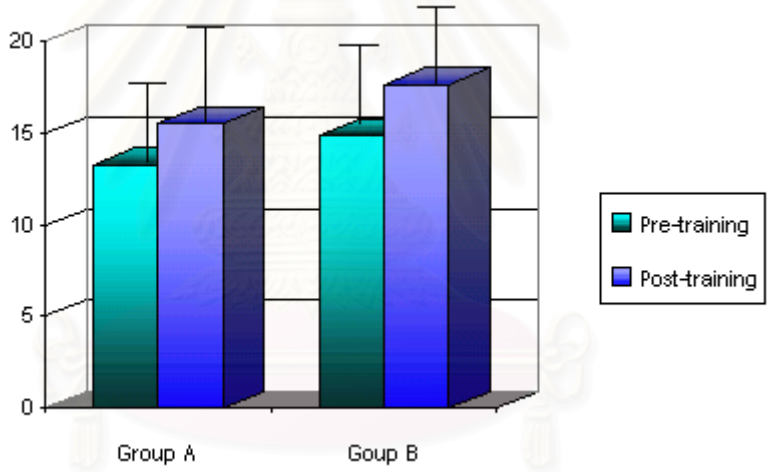

Figure 12 Comparison of VO_2 peak before and after training within group

Maximum Short Time Exercise Capacity (MSEC: W)

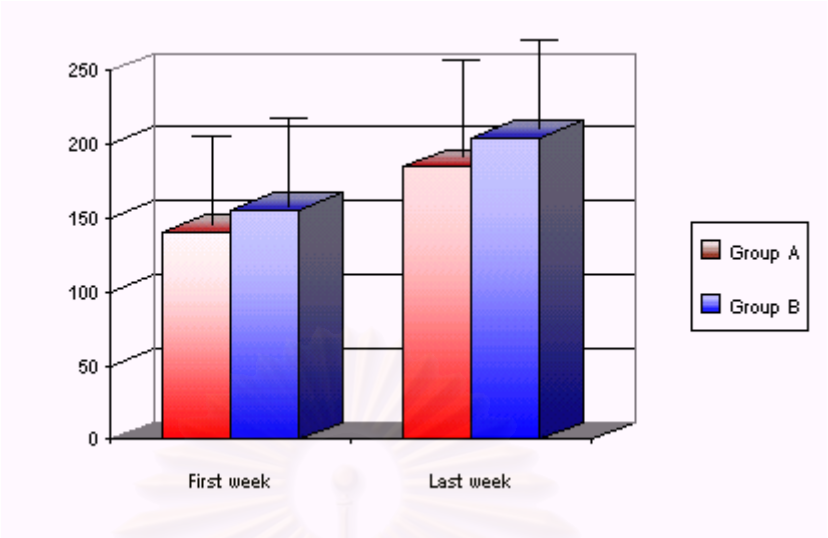

Figure 13 Comparison of maximum short time exercise capacity between group A and B

Peak VO_2 (ml/kg/min)

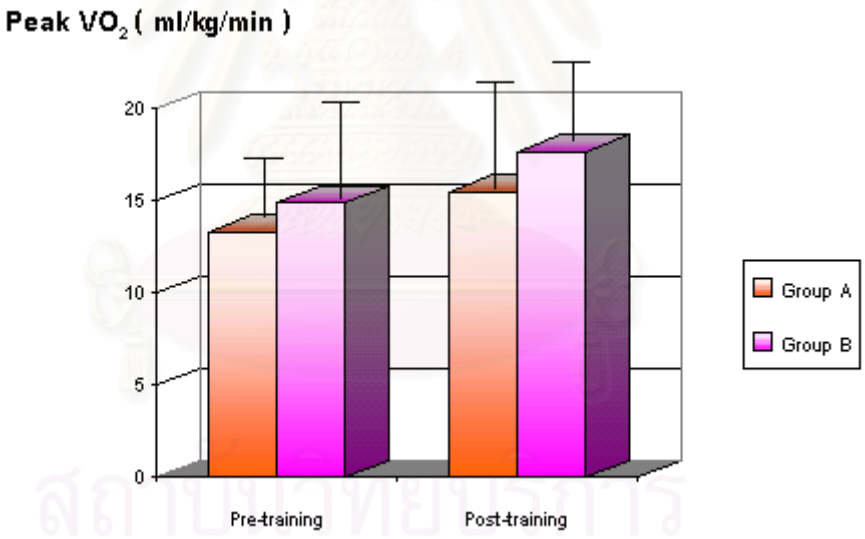

Figure 14 Comparison of VO_2 peak before and after training between group

CHAPTER V

DICUSSION AND CONCLUSION

Discussion

Most patients with heart failure are characterized by reduced cardiac output, increased peripheral vascular resistance from increased sympathetic activity activation, and impaired vasodilatory capacity owing to decreased maximal skeletal muscle blood flow. These resulted in impairment of muscle endurance. In addition, decreased skeletal muscle mass or loss of muscle strength was known as the results of physical inactivity or deconditioning . All of these abnormalities resulted in impaired exercise capacity but have been seen to be partially reversed by exercise training.

In the current study, improvement in exercise capacity was increased in both group, measured by peak work rate (MSEC) and peak VO_2, after interval exercise training same as the study of Meyer et al (1996(b) and 1997(b)). It demonstrated that MSEC was increased 43.62 watts (group A = 30.9%) and 48.85 watts (group B = 31.36%). The peak VO_2 in group A was increased by 2.22 ml/kg/min (16.7%) and group B by 2..76 ml/kg/min (18.6%). Interval exercise training in patients with heart chronic heart failure may be better than the continuous method. Meyer and coworkers (1990) found that in rehabilitation after coronary bypass surgery, interval exercise training has proven to be more effective in improving exercise capacity and decreased heart rate, rate-pressure product and lactate at submaximal work rates than continuous training with the same relative training heart rate. In 1997, they also studied in patients with heart failure and found that the performed peak work rate was more than doubled(240%) while

cardiac stress was lower (86%) when compared during interval exercise than during ramp bicycle exercise at 75% peak VO_2.

The interval exercise training method consisted of short work phases and recovery phases. In the study of Meyer and coworkers (1996) demonstrated that short term training of only 3 weeks resulted in a marked delay of ventilatory threshold. The amount of improvement in oxygen uptake was similar to that reported after 24 weeks of training in patients with moderate heart failure. The reduction of lactate after 3 weeks of training was remarkable relative to that seen in training programs lasting much longer. Along with these benefits, the reduction in perception of leg fatigue and dyspnea was probably due to an increased exercise capacity of the peripheral muscles.

Patients with heart failure seem to have a decreased capacity to produce energy in skeletal muscle. Despite the high rate of anaerobic energy production, this, together with skeletal muscle under perfusion, results in a markedly decreased capacity to produce energy in the exercising leg muscles. As patients with chronic heart failure are characterized during exercise by a rapid decline of phosphocreatine, reduced aerobic capacity, the high rate of lactate accumulation, and decreased muscle strength. Interval exercise could help overcome the premature muscle fatigue seen during high work rate training and prepare patients for coping with activities of daily living. In the study of Meyer et al (1996), work rates in the 30 s. work phases/ 60 s. recovery phases, which metabolic stress did not increased significantly during the first and last work phase, and blood lactate displayed no appreciable lactacid strain. Obviously phosphocreatine was sufficient to meet the major part of energy requirement in this mode. Similar findings have been reported for interval test in healthy subjects when the duration of the work phases was below 30 s. (Astrand et al., 1960). In addition, heart rate and systolic blood pressure stabilized during this exercise mode test, as is characteristic for aerobic exercise by continuous method test. Furthermore plasma norepinephrine

(NE) and epinephrine (E) levels stabilized during in this mode, as was seen in aerobic training by continuous method in coronary patients when compare to interval training (Meyer et al., 1990). RPE was significantly increased, but was remained within the range of values considered " very light to fairly light " on the Borg scale.

In each work phases HRmax and SBPmax were the same and decreased to nearly baseline in recovery phases. These results are similar to Meyer et al. (1996 and 1997(b)) which may be explain by less stimulation of sympathetic activity from interval training and Borg scale or RPE during training was not more than 15. It has been shown that anaerobic threshold usually occurs at a Borg scale of 13 to 15 (somewhat hard to hard). (Suzanne et al., 1999). It implied that this type of training did not have too much metabolic and cardiac stress. In addition, maximal heart rate training achieved from steep ramp test was 60-70% (group A) and 60-65% (group B). As in the recommendation of Suzanne and coworkers (1999), heart rate can also be used to guide exercise intensity. Patients should aim for 60 to 80% of their maximum heart rate as determined at stress testing or at the heart rate corresponding to an RPE of 13 to 15. During training in the current study, the abnormalities symptoms such as chest discomfort, cardiac arrhythmia, and lower systolic and diastolic blood pressure were not found in all patients. They could tolerate well and complete the program successfully.

Interval exercise training seems to be an appropriate method to stimulate both endurance capacity and muscle strength. The steep ramp test enables one to determine maximum short time exercise capacity (MSEC) which partially reflects anaerobic capacity and leg muscle strength. These have previously shown that this intensity resulted in a marked increase of exercise capacity with only 3-4 weeks of interval training (Meyer et al., 1996 and 1997). But difference from Willenheimer et al. (1998), patients with mild to moderate heart failure performed interval training on a cycle ergometer: 90 seconds exercise and

30 seconds rest, at 80 % of maximal intensity over a period of 4 months. The exercise time was gradually increased from 15 minutes twice a week to 45 minutes three times a week from week 7. Compared with controls, there were significant improvements in maximum exercise capacity only by 7 watts. These might resulted from the more intensity and too long time of work phases along with shorten of recovery phases which could have more stress on cardiac function. And because of those studies did not reevaluate the ejection fraction post training, which reflect the effect of training on cardiac function.

Furthermore interval training shown to have the ability to improve peripheral muscle power without cardiac overloading the central circulatory capacity. In 1998, Meyer et al. found that in CHF patients the magnitude of change in LV ejection fraction during interval exercise training was similar to that seen in controls without complications. Because interval exercise training appears to be as safe as steady state exercise training with respect to LV function. With all these benefits, interval exercise training can be recommended for patients with a low ejection fraction, NYHA FC II-III, to apply higher peripheral exercise stimuli and with lower LV stress than during steady state exercise training.

LVEF was not change significantly through out the study while the severity reported with NYHA functional class was decreased in both groups. This supported that the high work rates and short work phases of interval exercise training can improve peripheral muscle strength and aerobic capacity and produce the no further workload to the failing heart. Some studies, Obermann and coworkers (1995), found that high intensity exercise training; 85% of max. VO_2 in sedentary men with coronary artery disease significantly increased rest-peak LVEF from 6.20% at base line to 6.54% in 6 months and 6.73% at 12 months without adverse effects. It is possible that high intensity interval exercise training could improve LV function if it was trained for longer period.

By fact, the more frequent training can improvement exercise capacity better than that one with less frequent training. But improvement in exercise capacity resulted from interval program performed 3 times/week was not significantly different from the program performed 5 times/week (MSEC: $p = 0.72$, peak VO_2 : $p = 0.54$). Same as some studies using interval training showed that training 2 days per week resulted in VO_{2max} changes similar to those observed when training 5 days per week (Fox et al., 1973). In other studies for which total exercise volume was held constant, there were no differences in VO_{2max} improvements when training frequency was 2 versus 4 or 3 versus 5 days per week (Sydney et al., 1972). The improvement in peak VO_2 may be cause from increased muscle strength by increased peak work rate, skeletal muscle oxygen extraction, and oxidative enzyme capacity (Magnusson et al., 1996). As was the case with training duration, more frequent training is beneficial if the training is performed at a lower intensity. In an experiment of Moffat and coworkers (1977) supported that improvements in VO_2max nearly identical regardless of the 3-day-per week training schedule. As generally recommendation of frequency for improved aerobic capacity of American Sports of Medicine should be performed 3-5 times/week. This finding suggest that perhaps the stimulus for aerobic training is closely tied to the intensity and total work accomplished and not to the sequence of training. The improvement in exercise capacity occurred after the second week of strength training and two months post endurance training. But in the second week, endurance training can increased 20-30% of VO_{2max} (McArdle et al., 1996). An adjustment of intensity (MSEC) for training in the following training week was increased every week (group A) and every 5 session (group B). Group A was increased in the second week and group B increased in the third training week while equally controlled the number of total exercise session (group A: 5 times x 3 weeks = 15 sessions, group B : 3 times x 5 weeks = 15 sessions), training intensity, speed and the total number of walking on treadmill (9 times).

Conclusion

The improvement in exercise capacity of CHF patients performed interval training 3 times/week x 5 weeks was not different from the program performed 5 times/week x 3 weeks. Both interval program could improve muscular strength by 30.9% in group A and 31.36% in group B, improve aerobic capacity by 16.7% in group A and 18.6% in group B, and decreased functional class by one level.

Suggestion

The patients were hospitalization during the period of study by Meyer et al. (1997(b)) to performed exercise 5 times/week because of high risk patients. This rehabilitation program has to do under supervisor and monitoring in the hospital. There are some limitations and difficulty to perform this program in our out patients basis. It makes the patients inconvenient to travel from home to the hospital 5 days or 3 days/week with an increased cost and interfere with patients works. Therefore this program may apply to be the hospital plus home based by decreasing frequency, such as 2 times/week at hospital and light exercise (walking, jogging, stair climbing etc.) at home. Further study should compare the program performed 2 versus 3 times/week and search for the appropriated training intensity and duration which is harmless and adapt to be the only home program.

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APPENDICES

APPENDIX A

Characteristic of group A

SEX	AGE	HT	BW(kgs)		FLEXIBILITY(cm)		LVEF(%)	
	(year)	(cms)	PRE	POST	PRE	POST	PRE	POST
M	63	165	71.7	72.50	+2	+8	30	36
M	50	167	69.40	68.44	-5	+6	49	49
M	52	160	58.59	55.20	-6	-3	48	50
F	54	156.5	68.62	68.25	+8	+9.5	42	44
M	65	169	79.64	79.15	-2	+2.5	59	51
F	64	157	57.16	56.88	+20	+20	39	41
M	63	168	63	63.94	-1	+6	23	40
M	47	161	50.60	50	+2	+11	26	49
M	72	167	58.80	58	-7	+1	51	45
M	55	168	70.52	69.86	-12	-10	28	25
M	61	154	50.78	51.18	+11	+14	36	33
M	61	167.5	63.60	62.85	+7	+11.5	25	23
M	62	165	88.50	87.95	-10.5	-8.5	43	45

Pre = Pre-Training

Post = Post-Training

APPENDIX B

Steep ramp test data of group A

SEX	HRr			HRm			SBPr			SBPm		
	1	2	3	1	2	3	1	2	3	1	2	3
M	98	92	95	114	118	117	118	120	119	136	153	137
M	86	77	74	106	104	113	100	90	90	131	147	140
M	62	55	61	100	113	114	128	115	109	136	147	142
M	85	64	72	102	97	100	80	80	81	87	90	92
M	64	59	73	121	126	120	126	126	108	161	151	152
F	80	87	88	112	110	113	129	129	126	164	166	167
M	88	86	71	104	106	105	106	119	134	143	158	146
M	84	82	78	105	107	106	116	120	120	160	150	150
F	72	65	67	108	108	101	106	92	109	172	155	156
M	60	54	69	83	84	93	106	104	104	135	145	128
M	76	88	84	98	105	109	120	120	120	150	140	140
M	72	75	76	100	90	103	100	90	90	100	100	110
M	85	93	99	107	125	125	132	130	94	163	176	162

1 = The day before training of the first week

2 = The day before training of the second week

3 = The day before training of the third week

APPENDIX C

Steep ramp test data of group A (next)

SEX	MSEC(W)			ET(seconds)			Borg scale		
	1	2	3	1	2	3	1	2	3
M	140	164	180	235	244	248	15	15	15
M	125	148	162	229	235	247	15	15	15
M	125	170	180	230	248	253	12	15	15
M	100	110	110	223	227	227	15	15	15
M	220	140	250	268	232	300	15	11	15
F	70	70	80	204	208	212	15	15	15
M	250	275	300	280	290	300	14	15	15
F	100	120	140	221	228	239	15	15	15
M	150	175	225	240	250	270	15	14	15
M	200	220	230	260	268	272	15	15	15
M	125	178	195	220	241	258	15	15	15
M	80	90	100	220	229	230	15	15	15
M	150	220	250	247	262	242	15	15	15

APPENDIX D

Ordinary ramp test data of group A

SEX	HRr		HRm		SBPr		SBPm	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M	81	83	146	142	139	116	180	196
M	67	56	97	101	106	113	142	151
M	72	67	106	100	106	108	160	156
F	78	77	129	128	140	110	190	160
M	89	62	104	108	126	128	152	168
F	82	84	121	129	138	111	186	184
M	66	65	149	150	122	111	171	178
M	86	62	124	117	104	83	124	93
M	52	59	135	148	115	120	151	178
M	71	76	132	120	99	90	148	150
M	98	94	119	121	103	103	128	133
M	86	85	107	109	100	100	110	120
M	80	84	103	112	120	120	170	180

APPENDIX E

Ordinary ramp test data of group A (next)

SEX	VO_2 (L/min)		VO_2 (kg/ml/min)		WR(Watts)		ET(seconds)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M	1.31	1.37	18.3	19.1	125	150	454	498
M	1.06	1.44	15.2	21.1	125	150	468	520
M	1.06	1.38	18.0	25.1	125	125	427	461
F	0.85	0.85	12.2	12.2	100	100	363	370
M	1.22	1.80	15.2	22.5	125	150	436	532
F	0.58	0.61	10.3	10.8	50	75	277	312
M	1.24	1.09	19.7	17	125	150	470	497
M	0.41	0.53	8.2	10.3	50	75	283	331
M	0.78	0.92	13.3	15.8	100	100	368	413
M	0.61	0.72	12.2	14.0	75	100	315	365
M	0.75	0.85	10.7	12.2	75	100	340	399
M	0.51	0.52	7.9	8.2	50	50	300	310
M	1.06	1.22	11.9	13.7	125	125	396	455

APPENDIX F

Characteristic of group B

SEX	AGE	HT	BW(kgs)		FLEXIBILITY(cm)		LVEF(%)	
	(years)	(cms)	Pre	Post	Pre	Post	Pre	Post
M	43	168	84.78	83.20	0	+3	55	45
M	55	172	77.98	76.14	-2	0	33	28
M	55	162	64.62	62.00	+12	+16	34	34
F	59	153	47.56	47.15	+11	+16	25	35
M	46	170	91.46	91.70	-5	+5	54	72
F	63	154	55	56.20	+2	+9	37	39
M	62	157	44.52	44.28	-15	+3	39	32
M	42	167	61.34	59.34	-16	-9.5	48	53
M	67	164	60.00	60.80	-12.5	-7	42	38
M	63	165	61.72	61.90	-10	-4	42	45
M	63	167.5	66.56	67.80	-16	-16	32	30
M	66	160	66.20	64.65	+5	+9	35	32
M	56	165.5	64.30	65.70	-18	-15	40	43

APPENDIX G

Steep ramp test data of group B

SEX	HRr			HRm			SBPr			SBPm		
	1	2	3	1	2	3	1	2	3	1	2	3
M	74	90	88	128	125	128	150	160	130	190	190	165
M	68	72	70	104	111	108	140	120	114	170	150	160
M	70	60	56	113	98	108	120	120	119	141	141	131
M	99	100	100	109	110	100	144	130	120	160	160	150
M	64	64	66	92	116	120	100	90	100	115	99	132
F	84	92	78	127	116	131	128	120	118	149	135	134
M	98	101	113	139	138	151	128	119	123	163	168	188
M	72	84	71	108	110	118	120	124	126	142	140	145
F	68	70	75	80	86	88	120	116	118	133	136	144
M	50	64	80	101	103	114	100	100	100	101	95	120
M	64	62	58	115	106	126	97	90	122	134	111	136
M	62	62	57	91	88	83	130	120	120	160	150	140
M	72	66	68	82	83	80	134	140	140	166	159	170

APPENDIX H

Steep ramp test data of group B (next)

SEX	MSEC(Watts)			ET(seconds)			Borg scale		
	1	2	3	1	2	3	1	2	3
M	130	165	185	231	248	258	15	15	14
M	145	175	185	238	249	254	15	15	15
M	250	270	300	278	292	297	11	15	15
M	125	150	170	229	238	248	15	14	15
M	140	175	210	233	251	264	15	15	15
F	80	110	145	213	223	235	15	15	15
M	250	280	325	280	292	300	15	15	15
M	150	180	200	238	252	247	15	15	15
F	80	80	120	212	212	220	15	15	15
M	150	160	180	238	239	252	15	15	15
M	225	250	270	270	280	288	14	15	15
M	150	175	180	242	250	251	15	15	15
M	150	166	190	243	247	255	15	15	15

APPENDIX I

Ordinary ramp test data of group B

SEX	VO_2 (L/min)		VO_2 (ml/kg/min)		WR (Watts)		ET (seconds)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M	1.85	2.19	21.8	25.7	175	175	591	595
M	0.88	1.04	11.1	14.3	100	125	372	429
M	0.97	1.01	14.9	15.7	100	125	385	453
F	0.37	0.75	7.7	16.3	50	100	290	368
M	1.61	1.73	17.3	18.9	175	175	544	564
F	0.50	0.60	9.2	10.8	50	75	300	325
M	0.96	1.12	21.4	25	100	125	415	434
M	1.03	1.06	16.9	17.6	125	125	427	441
M	0.91	1.14	15.9	18.9	100	150	382	500
M	0.81	0.95	13	15.3	75	100	355	365
M	0.76	0.94	11.5	15.1	100	100	366	388
M	0.98	1.07	14.9	16.5	100	100	397	414
M	1.15	1.28	17.9	19.2	125	125	431	441

APPENDIX J

Ordinary ramp test data of group B (next)

SEX	HRr		HRm		SBPr		SBPm	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
M	80	53	148	119	120	109	190	179
M	97	78	120	102	146	120	182	160
M	60	75	106	136	90	105	127	121
F	84	83	131	144	128	129	161	158
M	97	101	128	132	111	138	183	199
F	88	89	127	139	141	140	159	195
M	81	72	134	151	120	126	183	203
M	82	85	123	122	98	100	138	120
M	61	67	122	135	116	103	134	149
M	56	51	107	104	142	120	170	150
M	68	56	97	91	134	130	203	160
M	88	83	150	141	144	128	190	197
M	70	65	112	122	120	130	180	180

BIOGRAPHY

Miss Supa Chomchang was born on July, 1969 in Udornthani, Thailand. She graduated bachelor of science in nursing from Thai Red Cross Nursing Collage in 1992. She has worked for nine years in Cardiovascular-Thoracic surgery Intensive Care Unit (ICU CVT) at King Chulalongkorn Memorial Hospital.