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Physiology of Aerobic Exercise and its Role in Coronary Artery Disease

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The role of exercise to improve quality and longevity of life has been an area of great controversy over the centuries. Its importance as a cultivator of good health has varied considerably during different periods of medical history. In the the last two decades its importance has resurged. This change was spearheaded by cardiology giants none less than late Drs. Paul Dudely White, Samuel Levine and Tinsley Harrison. All of them were strong advocates of the benefits produced by regular exercise on cardiovascular function. Accordingly they put this belief into actual practice. It was a common sight to see Dr. White bicycling on the streets of Boston regularly right upto the last days of his life. He died at a very ripe age of 96. But before he died he was able to convince the cityof Boston to designate the track on which he used to bicycle as a bicycle track which is now named after him. Drs. Levine & Harrison were firm advocates of early cardiac rehablitation following a myocardial infraction and were mostly responsible for the trend which has resulted in early mobilization of such patients.

This changing out look has produced a new trend particularly in the western societies where jogging, bicycling, tennis etc. has become a regular norm of modern day living. This has resulted in a mush room growth of health clubs gymnasiums and other such facilities all over the western countries. It is not an uncommon sight in these countries to see men & women in their track suits jogging in subzero weather. This at times have resulted in unpleassant surprises including loss of external genitalia in males due to frost gangrene. This trend and other factors like giving up smoking, reducing intake of high cholesterol diet, and maintaning normal weights along with better treatment facilities have been the probable factors responsible for a reduction 20% in the mortality of ischemic heart disease in the last two decades in the U.S. With this back ground scenario, I intend to review this subject in the light of the available scientific data.

PHYSIOLOGY OF EXERCISE:

The capacity of human body to perform a physical activity depends on three major factors.

1. Capacity for energy out put.
2. Neuro muscular function.
3. Psychological factors.

1. CAPACITY FOR ENERGY OUTPUT:

This is dependant on oxygen (O_2) demand, and its supply to the body thus becomes an important factor in patients with cardiovascular disease. Later on two other important factors which can help with chronic adaptation are the skeletal muscles and the O_2 transport system of the body.

Skeletal muscle has a greater metabolic range than other organs and the metabolic rate may increase 50 folds from rest to maximal exercise. Aerobic capacity or maximal oxygen uptake (Vomax) is defined as the level of O_2 uptake which can not be increased further with workload in an individual. Accordingly during any activity lasting over few minutes, O_2 supply to the muscle, which in turn is dependant on the status of the lungs and the cardiovascular system, is the main limiting factor.

2. SKELETAL MUSCLE FUNCTION:

Activities of shorter duration are supported by anaerobic mechanism and are not O_2 dependant. Pulmonay status in the absence of significant lung disease and high altitudes is not an important limiting factor either. The role of cardiac out put as the main determinant of limiting physical activity has also been challenged by the physiologists recently. The main emphasis is now on the ability of the muscle to utilize oxygen. Other peripheral mechanism are also important and probably play a significant role to

maintain the muscular activity. However it is evident that high aerobic capacity of the muscles can only be maintained if adequate O_2 is delivered to the muscles by adequate cardiac out put. Energy source during the muscular activity varies with the type of acticity. Minor activities use high energy phosphate like ATP & creatine phosphate (C.P.) However, these stores are so small that they are depleted during a 100 meters dash. Thus during continuing activity these stores have to be replenished. This takes place via oxidative i.e. aerobic or glycolytic or anaerobic pathways. Glycogen, glucose and free fatty acids (F.F.A) and to some extent the aminoacids are the main fuels. Breakdown of glucose by aerobic pathway to CO_2 & H_2O produces 10 times A.T.P. energy as compared to anaerobic channels which produces pyruvate & lactate by fermentation or anaerobic method. It is thus quite obvious that in order to maintain the high energy aeroboic system in various muscles adequate O_2 supply is essential.

Carbohydrates (CHO) and F.F.A. are used in equal proportion during rest where as F.F.A. are the main source during steady state exercise. As level of exercise exceeds about 70 % of the maximal capacity CHO utilization increases progressively.

Role of F.F. A. as a fuel is advantageous condidering the size of the fatty stores (Table I). It is also evident that the glycogen content of the muscle are the main limiting factor during continuing activity beyond a certain level. Anaerobic metabolism of glucose & glycogen is the main source of energy during early period of exercise when A.T.P. & C.P. stores have been exhausted. This metabolism is also a main source of energy during supramaximal levels of exercise and is evident from the fact that arterial lactate levels show a steep rise as the work load increases beyond a certain level. However, this metabolism can be used only to a certain level and produces a maximum energy of 30 K Cal. The exact mechanism of this metabolic limitation is still uncertain. The role of lactate as a direct toxant is doubtful but it does produce acidosis which in turn inhibits glycolysis and contractility thus producing fatigue.

MAXIMAL OXYGEN UPTAKE:

This is a stable & highly reproducible parameter in an individual. It can be expressed as L/min or ml/Kg/min. (Mets) and is the accepted unit of measurement when used as an index of cardiovascular function. It varies with body size, age, sex and physical training.

TABLE–1

ENERGY STORES MEASURED AS KILOCALORIES AVAILABLE FOR MUSCULAR WORK

ATP	1.2
Creatine phosphate	3.6
Glycogen	1,200
Fat	50,000

Body weight = 75 Kg. (165 lbs); muscle weight = 20 Kg. (44 lbs). From Astrand and RodahI with permission.

BODY SIZE:

When expressed in ml/Kg/min, the value of O_2 uptake in an obese person is much smaller and is the result of obesity rather than poor functional status of his cardiocascular system.

AGE:

The peak is usually seen betwen age 15-20 years and there is progressive decline with advancing age. A 60 years old person has two third of the value compared to some one aged of 20. This decline is unavoidable even if the individual has been a regular athelete through his forties and fifties. However, his uptake will be higher as compared to his inactive counter parts.

SEX:

There is no difference between the sexes during early child hood. However, girls show an abrupt fall of 20-30 % between the age 12-14. Subsequently the pattern of O_2 uptake is the same as that of men.

PHYSICAL ACTIVITY:

There is enough evidence that physical activity improves O_2 uptake. A 20-30 % drop in the uptake can occur if a young healthy person is put to bed rest for three weeks. On the other hand increase in the physical activity involving major muscle will improve this value. This increase is dependant on many factors including severity, duration and frequency of exercise as well as the age and the genetic predisposition of the individual. There

is improvement in the circulatory system and the pump performance, though no conclusive evidence exists supporting mechanical improvement in the isolated heart muscle.

A healthy normal 20 years old man is capable of increasing his VO_2 max with exercise to 40 ml/Kg/min i.e. about 13 times the resting level without previous physical training. This figure can be increased by another 30-40% by strenous physical training. However, professional atheletes and olympic medalists are capable of increasing their VO_2 max by over 100 %. It is thus obvious that such exceptional increase is only possible in certain individuals who have certain exceptional genetic pre-dispositions.

CARDIOVASCULAR RESPONSE TO EXERCISE:

There is a four fold increase in the cardiac out put with maximal exercise in a healthy average young normal man. This is primarily achieved by three fold increase in the heart rate. Stroke volume however varies and depends on position and degree of exercise. The change in the heart rate and O_2 uptake has linear relationship during submaximal exercise thus heart rate can be conveniently used to assess the level of O_2 uptake instead of doing a more cumbersome measurement of VO_2 max. Average maximal heart reat is 190/min in a 25 years old healthy man and it declines at a rate of ¾ beat/min/year. Similarly there is a three fold increase in the extraction of O_2 during submaximal exercise. This is achieved by redistribution of the blood to the exercising muscles as shown in the diagram. Systolic blood pressure shows a steady increase during exercise where as the diastolic usually drops as a result of decreasing peripheral vascular resistance. Accordingly the mean arterial pressure increase only by 20 mm Hg with maximal exercise.

Changes in the cardiovascular system during exercise are brought about by central nervous styem as well as local regulatory mechanisms. This includes reduction in the parasympathetic tone and increase in the sympathetic tone resulting in increased inotropicity of the myocardium. Release of metabolites released by the conracting muscles are also important in the auto regulation of blood flow. A typical maximal data for a young normal sedentary subject, a marathon running champion and a patient with damaged myocardium is shown in table 2.

TABLE–2

TYPICAL MAXIMAL DATA IN A PATIENT WITH MODERATELY SEVERE CORONARY HEART DISEASE (LEFT VETNRICULAR DYSFUNCTION BUT NO ANGINA PECTORIS), A NORMAL SEDENTARY SUBJECT AND A LONG-DISTANCE RUNNER.

	Oxygen uptake (L./min.)	Heart Rate (eat/min.)	Stroke Volume (ml	Cardiac Output (L./min.)	Total A-V 02 Difference (ml./100 ml)
Patient	1.5	175	50	8.8	17.0
Sedentary normal man	3.0	190	100	19.0	15.8
Runner	5.6	180	180	32.5	17.0

There is a linear relationship between the heart rate and work load. Thus heart rate provides an index of relative work load during exercise. A work load of 25 % of the maximum capacity will produce an increase in 50 % of maximum heart rate for that age. However, patients with various heart diseases have a less predictable response and this is made more unreliable if the patient has artial fibrillation or is receiving drugs which are likely to affect the heart rate. In patients with angina the heart rate response is normal before the onset of myocardial ischemia or symptom of angina. However, the range of the heart rate at which symptoms and ischemic ST changes develop in various individual is quite variable.

CORONARY CIRCULATION:

The myocardial oxygen demand is dependant on;

- Heat rate
- Force of ventricular contractility
- Tension in the ventricular wall

External work or stroke work is the product of ventricular stroke volume and mean aortic or pulmonary artery pressure as the case may be. Stroke volume does not produce significant change in the myocardial 02 demand, systolic pressure is closely related to the wall tension. Thus external work of the myocardium has no significant affect on the myocardial oxygen demand when the internal work of the myocardium is being taken into account.

Contractile state is an important factor for O_2 onsumption. However it has an inverse relation with the ventricular volume and thus as it increases, the O_2 demand is not much affected.

During exercise increased O_2 demand of the skeletal muscles is met mostly by an increase in the skeletal muscle blood flow as well as increased extraction of O_2 from the circulating blood. In contrast the myocardium is already extracting a much larger O_2 fraction at rest and is thus dependant entirely on increased blood flow in the coronaries during exercise. Further more myocardium is uanble to utilize the anaerobic metabolic channels. Therefore, the myocardial O_2 uptake is almost equal to the myocardial O_2 demand and is closely related to coronary blood flow and product of heart rate and systolic blood pressure which is thus and index of internal work of the heart, ignoring the contractility and volume of the heart. Patients with angina of effort usually have a well defind threshold or HR x Pressure product at which the symptoms appear. Coronary blood flow increases from 60 ml/100 gm of left ventricular myocardium to 300 ml/100gm with exercise in normal persons. This increase is affected by arteriolar resistance and coronary lumen. In patients with coronary artery disease (C.A.D.) though the resting perfusion may be normal, areas of regional hypoperfusion can be easily seen during exercise due to reduction in the blood flow.

Role of exercise in C.A.D. is not yet established as a definitive preventive measure. Accordingly inactivity is not as high a risk factor as hypertension, smoking & hypercholesterolemia. Various studies carried out by different workers have some practical problems making interpretation of the data difficult. Following types of studies can be carried out to study the effect of aerobic exercise on reducing the risk of C.A.D.

A. CLINICAL

- Retrospective studies
- Prevalence studies
- Prospective studies
- Rehablitation studies
- Autopsies studies

B. ANIMAL

C. EXERCISE AFFECTING OTHER FACTORS . .

Prevalence studies record the manifestation of a disease in a population. Perspective studies are carried out on a cohort of individuals who are followed through to determine the subsequent development of disease. Both these studies have their limitation mostly because of premorbid job shift which will obviously bias the result. Further more there are serious limitations as to how to quantitate activity levels with various jobs in term of actual energy consumption. Brand & Paffenbarger in two studies conducted on S.F. longshoreman publishd in 1976-1977 came out with some important conclusion. In the first study using a sophisticated multiple logistic risk analysis approach, he grouped risk to year units of age and activity so as to minimize the effect of premorbid job transfers. He found risk to be inversely related to actitvity level at work particularly in younger age group. By further extrapolation of the data he concluded that relative risk drops from low acitivity and plateau at about 2.5 cal/min (2 Mets) and to drop further at 5.5 K cal (4 Mets). In the second study using a cohort analysis technique they assessed job activity and six personal characteristics and effect of traditional risk factors like smoking, cholesterol, hypertension etc. on C.A.D. In the younger age groups, less active workers had three fold increase in the risk. This risk increased to 20 times if smoking and hypertension were also added to this group. Wilhelmsen in a perspective study published in 1976 on men born in Gothenberg Sweden and living to the age of 50 concluded that inactivity during leisure time but not at work was weak risk factor. His data thus suggest that physical activity has some role as a coronary risk factor. Cooper has reported an inversrelation between the physical fitness and resting heart rate, body fat, cholesterol, triglycerides glucose and systolic blood pressure. His data thus suggests that physical fitness is related to low coronary risk factors.

Data from rehablitation studies following myocardial infarction is not without controversies, since only those patients with uncomplicated infarcts are usually subjected to rehabilitation programme. The randomized studies conducted over the last decade so far in this regard have shown improvement in mortality ranging from 20.6 % to 37.0 % in all except one study. These studies are based on supervised exercise programme consisting of 2-4 sessions/ week of 20-60 minute duration. (Table 3)

TABLE–3

SECONDARY PREVENTION WITH PHYSICAL TRAINING (PREVIOUS RANDOMIZED CONTROLLED TRIALS)

Trial	N	Intervention	Follow up (Months)	Mortality(%) Control	Mortality(%) Intervention	Effectiveness (%)
Sweden (1968-72)	315	Supervised exercise, 3 X / Week	48	22.3	17.7	26.6
Finland (1969-72)	298	Supervised exercise, 2-3 X/Week	12	21.9	17.1	21.9
Finland	380	Dialy home exercise	29	14.0	10.0	28.6
Canada (1972-78)	733	Partially supervised exercise, 2-4 X/Week	48	7.3	9.5	30.0
United States (1974-79)	651	Supervised exercise, 3 X/Week	36	7.3	4.6	37.0

Effectiveness = Control mortality – intervention mortality X 100 control mortality

There is also data on reduction of arteriosclerosis with exercise by modifying factors like;

1. Weight reduction and lean body mass.
2. Changes in lipid profile and increase in HDL.
3. Improved Glucose tolerance.
4. Minimal B.P. changes and lower diastolic B.P.
5. Modification of personal behaviour.
6. Reduced platelets adhesiveness and increased fibrinolysis.
7. Reduced adrenogenic response to stress.

ANIMAL STUDIES:

Various animal studies old and new have confirmed the following changes after chronic exercise.

1. Myocardial hypertrophy(with one hour of exercise 5 times/WK)
2. Increased myocardial capillary to fibre ratio (30 minute exercise 2/week)
3. Increase in coronary artery size (one hour exercise per week)
4. Improved cardiac performance.
5. Changes in myocardial mitochondria and metabolic enzyme.

To sum up then it is believed that regular aerobic exercis by

A. Hemodynamic changes
B. Morphologic changes
C. Biochemical changes
D. Indirect modification of risk factor can alter the risk of coronary artery disease. Further more regular aerobic exercise.

- Lowers resting heart rate
- Lowers H.R. & Systs. B.P. at any submaximal work load.
- Increases C.O. & VO_2 max
- Brings faster return to normal H.R. after exercise.
- Improve CO_2 metabilism

Slower H:R., lower H.R. x B.P. Product for any work load and longer diastolic periods are factors that reduce myocardial oxygen demand and improve coronary perfusion, resulting in improved threshold for angina or myocardial ischemia.

Exercise prescription, therefore has to be planned keeping in mind all the factors discussed above. Unfortunately, a certain amount of morbidity is unavoidable as a direct result of the exercise it self. This morbidity which is directly releted to the duration, level and physical conditioning of the individual consists of musculo skeletal trauma, as well coronary events particularly if the individual was not assessed properly before an exercise was

advised. It is therefore mandatory that every person should be assessed individually before he or she embarks on a regular exercise. This is more so if the person is over 30 years of age and has not been actively involved in an exercise training.

I have no doubt in my mind that exercise is beneficial for every one and more so following a coronary event provided it is advised and carried out under certain discipline. With increasing incidence of C.A.D. in our country and with more and more younger people being affected by this disease, it is only mandatory that the medical community should get involved in this aspect of medicine, by organizing cardiac rehablitation centres around the country and to educate the public in this regard. This will go a long way to restore and improve vitality, self confidence and over all quality of life of our patients following a coronary event or cardiac surgery. Such patients will be more productive and independant and will fullfil their obligation to their family, profession and the country, in a more befitting manner.

REFERENCES

1. Gollnick, P.D., and Hermansen, L: Biochemical adaptations to exercise. Anaerobic Metabolism (Vol. 1), in Wilmore, J.H.(ed): Exercise and Sport Sciences Reviews. *Academic Press, New York,* 1973; 1-43.
2. Holloszy, J.O.: Biochemical adaptations to exercise. Aerobic metabolism (Vol. 1), in Wilmore J.H. (ed): Exercise and sport Sciences Reviews. *Academic Press, New York,* 1973; 45-71.
3. Saltin, B., Blomovist, G., Mitchell, J.H. et al.: Response to exercise after bed rest and training. *Circulation,* 1968; 38: (Supply); 1-78.
4. Wohl, A.J., Lewis, H.R., Campbell, W., et al: cardiovascular function during early recovery from acute myocardial infarction. *Circulation* 1977; 56: 931-4.
5. Froelicher, V., and Oberman, A.: Analysis of epidemiologic studies of physical inactivity as risk factor for coronary artery disease. *Prog. Cardiovasc. Dis.* 1971; 15: 41-42.
6. Froelicher, V.: animal studies of effect of chronic exercise on the heart and atherosclerosis. *A review. Am. Heart* J. 1972; 84: 496-9.
7. Froelicher, V.: does exercise conditioning delay progression of myocardial ischemia in coronary athehrosclerotic heart disease? Gardiovasc. *Clin* 1977; 8: 11.
8. Paffenbarger, R., Hale, W., Brand, R., et al.: Work-energy level, personal characteristics, and fatal heart attack: a birth-cohort effect. *Am. J. Dpidemiol.* 1977; 105 : 200-205.
9. Wilhelmsen, L., Tibblin, G., Aurell, M., et al.: Physical activity physical fitness and risk of myocardial infarction. *Adv. Cardiol.* 1976; 18 : 217-221.
10. Cooper, K., Pollock, M., Martin, R., et al.: Physical fitness levels vs. selected coronary risk factors. *J.A.M.A.* 1976; 236 : 166-169.
11. Wilhelmsen, L., Sanne, H., Elmfeldt. D., et al.: A controlled trial of physical training after myocardial infarction. *Prev. Med. 1975;* 4:491-294.
12. Bell, R., Andrasmussen, R.: Exercise and the myocardial capillary-fiber ratio during growth. *Growth* 1974; 38: 237-240..
13. Leon, A., And Bloor, C.: The effect of complete and partial deconditioning on exercise-induced cardiovascular changes in the rat. *Adv. Cardiol* 1976; 18:81-84.
14. Cohen, H., Yipintsoi, T., Malhotra, A., et al.: Effect of exercise on coronary collateral function. *Am. J. Cardiol.* 1977; 39: 362.365.