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# **Integrate Acute Cardiovascular Adjustments to Exercise: Impact of Exercise Type and Population Characteristics**

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*Sport is For Your Life,  
Your Life is For You,  
Sport is You.*

*Dedicated to All Those who in The Sport also recognize the Values Of:  
Health, fitness And Competition.*



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Cap1: “ General Introduction”





## **Hypothesis**

We worked on the hypothesis that the metabolic and cardiovascular responses to different kinds of exercise activities may be to some extent related to gender, age and health condition. Our approach, at substantial difference with most data in the literature, was holistic, including in the same sessions different physiological measurements and testing on the same individual different exercise modalities. Once outlined peculiar patterns we will suggest specific training programs.

## **Introduction**

The project started from the expected opportunity to test some female patients with Chronic Heart Failure (CHF F) and to compare them with older and young females. We had already tested a training project with CHF MALE (CHF M) in, and the good results had given the idea to try with women, in order to study and compare males and females with this pathology.

If we rapidly check the results, we can affirm that CHF subjects can limit muscle degenerations and social isolation by increasing independence and daily life activity, with an equilibrate combination of resistance and aerobic exercise. The new aspect was that also force training could be suggested to this kind of patients, in order to increase their muscle mass, to ease supporting many life actions and therefore improve their independence, in total respect of human integrity and safety. The possibility to perform a combined training leads to better cardiovascular functions and an increased muscular strength.

We started with testing 3 CHFF only; thereafter, it became really impossible to proceed with further candidates, because the session tests worried them, but they were very often involved in domestic affairs or the cardiologists did not give their permission, based on clinical state.

So we quit this starting point, and we carried on the comparison between male and female in young and elderly subjects, in order to clarify sex and age differences with a large view on the physiological parameters, that can explain some different adaptations to the exercise and help in the physical training planning. In a second stand it was possible to study pathology in collaboration with the Hospital, Diabetes, which became the substitute for cardiovascular disease.

It is clear that nowadays most of the population is made up of older people, and this is a fact growing because life expectancy is continuously stretched. So we will always have more to do with degenerative diseases, aging, cardiac disease, obesity, diabetes etc that typically accompany the person during his/her lifespan. Here the role of physical activity comes into play: as already well documented, it can change lifestyle and give precious years of independence, and autonomy, while slowing both pathological and psychological degeneration. However it is very important to detail what happens during training to the body of an elderly person in order to facilitate the improvement.

The strong positive value of aerobic exercise for the cardiovascular component is well-established, but evidence that the exercise of weight training can benefit in some way was still inconsistent, even if it is sufficiently demonstrated that it slows muscle degradation, limits possible falls, increases muscle volume etc ... All this, however, has not been thoroughly studied, with distinction per gender and age.

Actually sex and age differences have a big relevance in medicine and sports. In literature there are already many studies about these diversities, but most studies were performed with different modality and subject groups <sup>(1, 2, 3, and 4)</sup>. We considered an advantage, leading to more realistic results, to gather all parameters together, in individual subjects. Moreover functional evaluation in sports sciences needs to integrate the whole response to exercise. When somebody is performing any kind of exercise, his organism works at the same time with infinity of cooperative components, and this amazing organization can be damaged by the presence of some inefficient mechanism, due to of wrong lifestyles, ageing, and pathology. Therefore, for each trainer it can be really important to clearly know what happens to the body when it is working in a specific way, in order to choose the correct intensity, frequency and duration of exercise sessions.

## **GROUPS**

### **Young**

Young healthy subjects may be taken as the gold standard for definition of physiological adjustments to exercise. It is therefore logical to compare results obtained with other groups with results in the young.

### **Aged**

With advancing age, there is a gradual reduction in physical strength and the ability to sustain strenuous physical exercise and daily life activity. Elderly people lose muscle mass and gain body fat, so exercise is especially important for them, since it can prevent these changes while improving flexibility, cardiovascular function etc... It also improves their mood and feeling of overall wellbeing. ACSM have published guidelines for the physical activity recommendations that derived from analysis of the relationship between physical activity and morbidity and mortality outcomes. The suggestion for elderly people is practicing Physical activity (above baseline "normal" daily activity levels) at an intensity of moderate to moderately vigorous aerobic (endurance) activity (3.3 to 4.2 METS; 3-4 mph walk; >50%  $VO_{2max}$ ), with a total weekly volume of 150 - 180 min/wk (3

hours at moderate pace or 2.5 hours of a more vigorous walking, or other types of aerobic activities, with each physical activity session lasting at least 10 minutes). Aerobic exercise training programs, as the recommendations suggest, for older adults at this intensity and amount of exercise, have been effective in preventing functional limitations and potentially delaying movement disability in older age, but it is really hard to take it as life habit, as it should be. However, it is clear that this physical activity would translate into a >30% decrease in the relative risk of morbidity and mortality and loss of independence, and further benefit would accrue with greater physical activity and greater fitness gains (~60% reduction in risks). Additionally, in some recent studies it has been demonstrated that it is relevant to supplement aerobic exercise by including, twice per week, "resistance" exercises of major muscle groups to counter the age-related loss of muscle mass, and maintain the strength and power requirements needed in daily activities and to prevent falls <sup>(5)</sup>. Anyway, the combination between cardio fitness training and strength training is the best solution. Even if aerobic exercise remains the preferred exercise for elderly because it is safer and it conditions directly the cardiovascular component, while strength exercise is more dangerous, because it causes sudden changes in the system that are hard to be held by an inefficient heart but the improvement in muscle mass can also benefit the cardio circulatory component thanks to greater efficiency of the muscular pump function. Aging, indeed, is a complex process involving subtle changes in function of many systems, but the most frequent weakness regards the cardiovascular system. It is important, therefore, to determine the possible mechanisms which lead to the decline in the ability to exercise with age and, in particular, to determine whether these mechanisms are of cardiac origin. It is ascertained that cardiac output and stroke volume are lower in the older subjects and the maximal values are also lower than in the young, and looking at the overall circulation as reflected in calculated peripheral resistance, older subjects undergo lower degrees of vasodilatation than younger ones.<sup>(1,6)</sup> Moreover Cardiac Output ( $Q_c$  \_CO), that is a major determinant of systemic O<sub>2</sub> transport in humans is reduced during exercise with aging , and this reduction explains a significant portion of the age-related decline in maximal O<sub>2</sub> uptake ( $\dot{V}O_{2\text{ max}}$ ). In healthy older individuals at rest, CO is usually lower compared with younger control subjects <sup>(2)</sup>. Metabolic response in older subjects show a decline in maximal oxygen consumption by ≈10% per decade after 30 years of age; this decline is proportional to a decreased cardiac output reserve, peak heart rate, and peak stroke volume in older subjects, so the age-associated decline in maximal oxygen consumption can be attenuated by habitual aerobic exercise.<sup>(6)</sup>

All these declines in CO, VO<sub>2</sub> etc...with ageing can be slowed down by doing physical activity and: "Lifestyle changes are the hardest ones to make". So, no one is too old to reap the benefits of a

healthful lifestyle, it is found that doing things like exercising and not smoking at age 70 greatly raises one's chances of living to age 90, the men who lived to at least 90 enjoyed better physical function and mental well-being late in their lives than men who died at a younger age.

## **Diabetics**

Diabetes mellitus is a condition in which the level of glucose in the blood is too high because the body is unable to process it properly due to either a lack of, or insensitivity to, the hormone insulin. Glucose is an essential fuel, derived from food, transported in the blood and used by the body's cells. Without insulin, glucose cannot enter the cells, cannot be stored as glycogen and cannot be used as fuel. We therefore need insulin to survive. There are two types of diabetes mellitus – type 1 and type 2; we worked only with type 2.

Around 90% of diabetics have type 2 diabetes (also called non-insulin dependent diabetes mellitus or adult-onset diabetes). Although its exact causes are uncertain, it is linked to obesity (around 80% of type 2 diabetics are obese) and genetics (the identical twin of a type 2 diabetic has up to a 90% chance of developing the disease). Type 2 diabetes results from the following changes: the pancreas produces less insulin in response to glucose in the blood; cells in the muscles, liver and fat become less sensitive to the insulin that is produced, so less glucose is taken out of the bloodstream into the cells; the liver produces more glucose than normal at rest. Type 2 diabetes normally affects those over the age of 40, although, with increasing levels of obesity in society, the diagnosis is increasingly being made earlier. Treatment may require dietary control tablets and/or insulin. Diabetes, especially if poorly managed, can lead to numerous complications. The short-term complications include the following, all of which can kill if left untreated: Hypoglycemia – low blood glucose due to inadequate intake of food, excessive physical activity and / or overdose of diabetic drugs such as insulin; Diabetic ketoacidosis (DKA) – mainly affects type 1 diabetics; it requires urgent treatment to prevent coma and death; Hyperosmolar non-ketotic acidosis (HONK) – only affects type 2 diabetics. HONK requires emergency hospital treatment with intravenous fluid and insulin. The long-term complications of diabetes mellitus include an increased risk of heart attack, stroke and damage to the blood vessels that supply the arms and legs, kidney failure, visual problems due to diabetic retinopathy, nerve damage leading to weakness, loss of sensation and (in combination with damage to blood vessels) diabetic foot ulcers. Foot ulcers are of particular concern to athletes; nerve damage can mean that an ill-fitting shoe or piece of grit in the shoe can damage the skin and start a foot ulcer without the athlete feeling anything. Diabetic athletes should therefore regularly check their feet for signs of damage and their shoes for stones etc. Of particular

relevance to athletes is the fact that diabetes can also increase the risk of a number of musculoskeletal conditions.

Individuals with diabetes are frequently deconditioned and live a sedentary lifestyle<sup>(7, 8, and 9)</sup>. Diabetic patients are often advised to exercise because exercise can reduce the likelihood of the complications of diabetes. The aim of diabetes treatment is to control closely blood glucose levels in order to prevent the short-term and long-term complications of the disease. Blood glucose should ideally be kept between 5 and 7 mmol per liter although a level of less than 10 is fine in the two hours following a meal. The management of diabetes is based on diet and exercise plus or minus drugs, depending on type and severity. Perhaps the most important point about the treatment of diabetes is that everyone is different. Some type 2 diabetics need no more than a good diet to achieve control of their diabetes.

Exercise reduces the risk of developing type 2 diabetes and is generally of benefit to both types of diabetes. However, exercise can worsen or cause some of the short- and long-term complications of diabetes, but with care these risks can be minimized. Type 2 diabetics can reverse some of the changes that result in the disease by performing regular exercise. The immediate effect of exercise on blood glucose depends on the intensity of the exercise – high intensity anaerobic exercise tends to increase blood glucose levels whilst long duration aerobic exercise decreases levels.

The possibility to study also this kind of population permits to compare healthy with pathology patients and to explain the global physiological adjustments to the exercise, as HR, VO<sub>2</sub>, FBF (femoral blood flow) FBF etc that accompany the variation of glucose and the endocrine parameters.

For many years, physical activity has been considered —along with diet and medication— fundamental in the treatment of diabetes, and based on a number of large randomized controlled trials, physical activity and exercise have recently been recommended to prevent and treat diabetes according to ADA ACSM and other national guidelines. Moreover, considering the potential adverse effects attributed to some drugs, the clinical importance of physical activity, as well as that of therapeutic education is even increasing. However, the terms “physical activity” and “exercise” denote two different concepts. “Physical activity” refers to any bodily movement produced by skeletal muscles that results in an expenditure of energy (expressed in kilocalories) and includes a broad range of occupational, leisure and daily activities. “Exercise” refers to planned or structured physical activity. It involves repetitive bodily movements performed to improve or maintain one or more of the components of physical fitness: aerobic capacity (or endurance capacity), muscular strength, muscular endurance, flexibility and body composition<sup>(10)</sup>. Both are essential for a healthy life style, but the most part of adults don't practice any kind of activity except what is necessary

during daily life. The modest amounts of exercise and the absence of weight loss positively affect markers of glucose and fat metabolism in previously sedentary adults and it predisposes to the onset of diabetes <sup>(11)</sup>. Standing up and moving around more can, by themselves, lower metabolic risk and health benefits result from concurrently reducing total time engaged in sedentary pursuits and interspersing frequent, short bouts of standing and physical activity between periods of sedentary activity, even in physically active adults <sup>(12,13)</sup>. Making small changes in daily activity levels, such as taking a 5-min walking break every hour, also likely benefits weight management. An individual will theoretically expend an additional 24, 59, or 132 kcal during an 8-h workday by walking around at a normal, self-selected pace for 1, 2, or 5 min every hour, respectively, compared with sitting for that whole time, is a potential way to lose weight and prevent weight gain, and it may assist in preventing the onset of type 2 diabetes. <sup>(14)</sup>

Untrained people with type 2 diabetes have been shown to have a reduced  $\text{VO}_2$  max compared with non diabetic people, even in the absence of cardiovascular disease. In addition, it has been reported that  $\text{VO}_2$  kinetics are impaired, also, in women with type 2 diabetes, and it appears that the exercise effort expenditure by people with diabetes may be greater for a given workload (even at very low workloads) than for non diabetic subjects. Exercise activity can reduce the onset but also the symptoms and slow the evolutions of type 2 diabetes to worse levels. Individuals who are currently sedentary, unfit, or overweight can benefit metabolically from simply taking breaks from sitting. Since avoidance of sedentary behavior appears to have a large impact on glycemic management, all individuals with type 2 diabetes should be encouraged to minimally engage in greater daily movement to better manage their diabetes and body weight. In addition, engaging in physical activity of any intensity (including low-intensity ones) likely positively impacts insulin action and blood glucose control acutely. Moreover, as long as total caloric expenditure during exercise is matched (i.e., total exercise dose), daily exercise may even be done every other day with the same glycemic results, although at least 150 min of weekly physical activity is recommended. Both aerobic and resistance training are important for individuals with diabetes, and ideally a program that combines the two types of training should be undertaken to achieve maximal glycemic control and other benefits. Once individuals have successfully implemented more daily movement into their lifestyle, they will be more likely to participate in structured forms of physical activity to gain additional benefits. In a recent study, individuals with impaired glucose tolerance, or type 2 diabetes, engaged in a single session of either 30 min of moderate aerobic exercise or 45 min of moderate resistance training <sup>(15)</sup>. A single bout of either exercise substantially reduced the prevalence of hyperglycemia (blood glucose levels >10 mmol/L) for the following 24 h using continuous glucose monitoring. It also appears that total exercise need not be completed in a single

session to be effective since in elderly men with type 2 diabetes, moderate- to high-intensity training performed more frequently (done as three, 10-min sessions daily) resulted in more beneficial effects on glycemic control than doing a single, 30-min session, even though cardio respiratory fitness increased similarly. Recently, low-volume, high-intensity training (HIT) was shown to rapidly improve glucose control and induce adaptations in skeletal muscle that are linked to improved metabolic health in adults with type 2 diabetes. In that study, participants undertook 2 weeks of thrice weekly exercise that consisted in ten 60 s sessions, separated by 1 min rest, at 90% of maximal heart rate. Training reduced blood glucose by 13% over the 24-h period following training, as well as postprandial glucose spikes for several days afterwards. However, given the intensity of such training, each individual's fitness level and cardiovascular risk factors should be carefully considered before HIT is prescribed. Conversely, physical activity does not need to be intense to be beneficial. Adults with type 2 diabetes who performed an iso-energetic bout of endurance-type exercise for 60 min at a low intensity or 30 min at a high intensity reduced their prevalence of hyperglycemia by 50 and 19%, respectively, for 24 h afterwards. Therefore, a single bout of low-intensity work may actually be more effective at lowering the prevalence of hyperglycemia throughout the subsequent 24-h period than high-intensity work. Resistance training has been shown to improve musculoskeletal health, enhance the ability to perform activities of daily living, and lower the risk of injury (including from accidental falls) and descent into frailty. In fact properly designed resistance programs may improve cardiovascular function, glucose tolerance, strength, and body composition, allowing older adults to remain more independent and self-sufficient as they age. Resistance training has additional metabolic benefits. It can improve glycemic control, likely even more so than aerobic training. Much of the observed enhancement in insulin action with resistance exercise may be related to greater muscle mass, which can result from a variety of different training intensities. In a recent meta-analysis, aerobic, resistance, and combined exercise training were found to be associated with HbA1c reductions of 0.67% following 12 or more weeks of training. Structured exercise exceeding 150 min/week, however, was associated with greater glycemic benefit (0.89% lower HbA1c) than 150 min or less (0.36% reduction), although any type of training caused greater declines in glycemic levels than physical activity advice alone.<sup>(16)</sup>

## **EXERCISES**

We considered 3 different exercises: aerobic, isometric and isotonic; they were chosen because they represent the most common exercise executions that everyone finds in any kind of gym; in this way at the end of the project we will give guidelines for the execution and physiologic adjustments that must become relevant during the training planning and performance.

### **Aerobic exercise**

Aerobic exercise (also known as cardio) is a physical exercise of relatively low intensity that depends primarily on the aerobic energy-generating process. Aerobic literally means "living in air", and refers to the use of oxygen to adequately meet energy demands during exercise via aerobic metabolism. Generally, light-to-moderate intensity activities that are sufficiently supported by aerobic metabolism and can be performed for extended periods of time represent examples of this kind of exercise. In our study this exercise is represented by cycling.

The American College of Sports Medicine (ACSM) defines aerobic exercise as "any activity that uses large muscle groups, can be maintained continuously, and is rhythmic in nature." It is also defined as an exercise that increases the need for oxygen. Aerobic exercise is used interchangeably with the terms: cardiovascular exercise, cardio-respiratory exercise and cardio. Some examples of aerobic exercise include: walking, jogging, running, dancing, rollerblading, bicycling, swimming, aerobics classes (both land and water), rowing, stair climbing, etc.

Aerobic exercise strengthens heart and lungs (which make up the cardiovascular system). During exercise, muscles demand more oxygen-rich blood and give off more carbon dioxide and other waste products. As a result, your heart has to beat faster to keep up. Following a consistent aerobic exercise plan, heart grows stronger so it can meet the muscles' demands without as much effort. Everyone, regardless of their weight, age, or gender, can benefit from aerobic exercise.

Regular aerobic exercise, performed most days of the week, also helps reduce the risk of illness and premature death. Regular aerobic exercise improves health in the following ways:

- Reduces body fat and improves weight control
- Reduces resting blood pressure (systolic and diastolic)
- Increases HDL (good) cholesterol
- Decreases total cholesterol
- Improves glucose tolerance and reduces insulin resistance
- Decreases clinical symptoms of anxiety, tension and depression

- Increases maximal oxygen consumption (VO<sub>2</sub> max)
- Improves heart and lung function
- Increases blood supply to the muscles
- Enhances the muscles' ability to use oxygen
- Lowers resting heart rate
- Increased threshold for muscle fatigue (lactic acid accumulation)

When considering the guidelines for aerobic exercise, it is important to keep the FITT principles in mind (Frequency, Intensity, Time and Type).

Frequency: Number of aerobic exercise sessions per week

Start with a minimum of 3 days per week with no more than 2 days off between sessions. Gradually work your way up to 5 or 6 days per week. Frequency is especially important when it comes to weight loss since more cardio sessions will help you burn more calories. Give yourself at least 1 to 2 days off from aerobic exercise each week.

Intensity: How hard you should exercise during each session

Aerobic exercise should take place at a “moderate” intensity level (not too easy, not too hard). This intensity is ideal for the general health benefits that come with exercise, and for weight loss. Exercise intensity is most often measured using heart rate. The recommended heart rate range is 60%-85% of your maximum heart rate. This range is called the target heart rate (THR) zone. Other methods for measuring intensity exist, including the "Talk Test" or Rate of Perceived Exertion, which also work well.

Time: How long each exercise session should last

Start with a minimum of 20 minutes per session. Gradually work up to about 60 minutes over time. The further you go over 20 minutes, the more calories you'll burn and the more endurance you will build. Of course, you might not start an exercise program with a lot of endurance, but you'll slowly build up. Time can be cumulative. You don't have to do 60 minutes all at once. You can do several 10-minute mini-workouts each day and add them up for pretty much the same benefits.

Type:

Any activity can count as cardio/aerobic exercise as long as it meets the 3 requirements above (frequency of 3-5 days a week, moderate intensity, and last at least 20 minutes per session).

There are various types of training methods, depending on personal preference. Use each of the methods periodically to add variety to your workouts.

- Continuous training is the most common method of aerobic exercise. It involves sustaining one exercise intensity for several minutes (20-60 or more for long-distance training) at a time.
- Interval training involves alternating between higher and lower intensity intervals throughout one workout.
- Circuit training uses a series of exercise stations (which could also include strength training stations), with relatively brief rest intervals between each station. The purpose is to keep the heart rate elevated near the aerobic level for a variety of exercises. Cross-training basically means participating in a variety of different forms of aerobic exercise, either within each session (for example, biking for 15 minutes and then running for 15 minutes) or day-to-day (for example, running 2 days a week, cycling 2 days a week, and swimming 1 day a week). It's a good idea to cross-train to prevent plateaus and overuse injuries and boost your overall fitness level.

VO<sub>2</sub> max, or maximal oxygen uptake, is one factor that can determine an athlete's capacity to perform sustained exercise and is linked to aerobic exercise. VO<sub>2</sub> max refers to the maximum amount of oxygen that an individual can utilize during intense or maximal exercise. It is measured as liters per minute or "milliliters of oxygen used in one minute per kilogram of body weight." This measurement is generally considered the best marker of an athlete's cardiovascular fitness and aerobic endurance. Theoretically, the more oxygen you can use during high level exercise, the more ATP (energy) you can produce. This is often the case with elite endurance athletes who typically have very high VO<sub>2</sub> max values. VO<sub>2</sub> max should not be confused with the lactate threshold (LT) or anaerobic threshold (AT), which refers to the point, during exhaustive all-out exercise, at which lactate builds up in the muscles. With proper training, athletes are often able to substantially increase their AT and to exercise for longer time at a higher intensity. Measuring VO<sub>2</sub> max accurately requires an all-out effort (usually on a treadmill or bicycle) performed under a strict protocol in a sports performance lab. These protocols involve specific increases in the speed and

intensity of the exercise and collection and measurement of the volume and oxygen concentration of inhaled and exhaled air. This determines how much oxygen the athlete is using.

As exercise intensity increases so does oxygen consumption. However, a point is reached where exercise intensity can continue to increase without the associated rise in oxygen consumption.

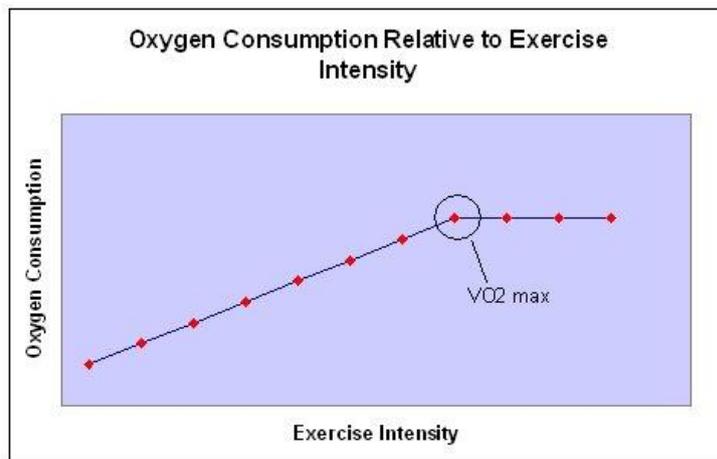


Figure 1: Typical trend of oxygen consumption during incremental exercise

The point at which oxygen consumption plateaus (Fig. 1) defines the  $VO_2$  max or an individual's maximal aerobic capacity. It is generally considered the best indicator of cardio respiratory endurance and aerobic fitness. However, as we'll discuss in a moment, it is more useful as an indicator of a person's aerobic potential or upper limit than as a predictor of success in endurance events.

$VO_2$  max varies greatly between individuals and even between elite athletes that compete in the same sport. The table below lists normative data for  $VO_2$  max in various population groups:

Maximal Oxygen Uptake (ml/kg/min) in Various Population Groups			
Non Athletes	Age	Males	Females
	10-19	47-56	38-46
	20-29	43-52	33-42
	30-39	39-48	30-38
	40-49	36-44	26-35
	50-59	34-41	24-33
	60-69	31-38	22-30
	70-79	28-35	20-27
<b>Athletes</b>			
Baseball/softball	18-32	48-56	52-57
Basketball	18-30	40-60	43-60
Bicycling	18-26	62-74	47-57
Canoeing	22-28	55-67	48-52
Football	20-36	42-60	
Gymnastics	18-22	52-58	36-50
Ice Hockey	10-30	50-63	
Jockey	20-40	50-60	
Orienteering	20-60	47-53	46-60
Racquetball	20-35	55-62	50-60
Rowing	20-35	60-72	58-65
Skiing, alpine	18-30	57-68	50-55
Skiing, nordic	20-28	65-94	60-75
Ski jumping	18-24	58-63	
Soccer	22-28	54-64	50-60
Speed skating	18-24	56-73	44-55
Swimming	10-25	50-70	40-60
Track & field, discus	22-30	42-55	
Track & field, running	18-39	60-85	50-75
	40-75	40-60	35-60
Track & field, shot put	22-30	40-46	
Volleyball	18-22		40-56
Weightlifting	20-30	38-52	
Wrestling	20-30	52-65	

Taken from Wilmore and Costill (2005) (3)

Table 1: Maximal Oxygen Uptake in Various Population Groups

Genetics plays a major role in a person  $VO_2$  max<sup>(17)</sup> and heredity can account for up to 25-50% of the variance seen between individuals. The highest ever recorded  $VO_2$  max is 94 ml/kg/min in men and 77 ml/kg/min in women. Both were cross-country skiers<sup>(18)</sup>. In previously sedentary people, training at 75% of aerobic power, for 30 minutes, 3 times a week over 6 months increases  $VO_2$  max an average of 15-20%. However, this is an average and there are large individual variations with increases ranging from 4% to 93%<sup>(19)</sup>. Crucially, once a plateau in  $VO_2$  max has been reached further improvements in performance are still seen with training. This is because the athlete is able to perform at a higher percentage of his  $VO_2$  max for prolonged periods<sup>(20)</sup>. Two major reasons for this are improvements in anaerobic threshold and running economy. Resistance training and intense 'burst-type' anaerobic training have little effect on  $VO_2$  max. Any improvements that do occur are usually smaller in subjects who had a higher level of fitness<sup>(21)</sup>. Resistance training alone does not increase  $VO_2$  max<sup>(22, 23, 24)</sup> even when short rest intervals are used between sets and exercises<sup>(25)</sup>.

Considerable training is required to reach the upper limit for  $\text{VO}_2$  max. However, much less is required to maintain it. In fact peak aerobic power can be maintained even when training is decreased by two thirds <sup>(26)</sup>. Runners and swimmers have reduced training volume by 60% for a period of 15-21 days prior to competition (a technique known as tapering) with no loss in  $\text{VO}_2$  max. In elite athletes,  $\text{VO}_2$  max is not a good predictor of performance. The winner of a marathon race for example, cannot be predicted from his maximal oxygen uptake. Perhaps more significant than  $\text{VO}_2$  max is the speed at which an athlete can run, bike or swim at  $\text{VO}_2$  max. Two athletes may have the same level of aerobic power but one may reach his  $\text{VO}_2$  max at a running speed of 20 km/hr and the other at 22 km/hr.

While a high  $\text{VO}_2$  max may be a prerequisite for performance in endurance events at the highest level, other markers such as lactate threshold are more predictive of performance. Again, the speed at lactate threshold is more significant than the actual value itself.

### **Resistance Exercise: Isometric and Dynamic**

Isometric exercise, or isometrics, is a type of strength training in which the joint angle and muscle length do not change during contraction (compared to concentric or eccentric contractions, called dynamic/isotonic movements). Isometrics are done in static positions, rather than being dynamic through a range of motion. Isometric exercise is a form of exercise involving the static contraction of a muscle without any visible movement in the angle of the joint. This is reflected in the name; the term "isometric" combines from Greek the prefixed "iso" (same) with "metric" (distance), meaning that in these exercises the length of the muscle and the angle of the joint do not change, though contraction strength may be varied. In our study it is represented by a leg press steady contraction.

Dynamic exercise is an alternation of isotonic and isometric contractions. In an isotonic contraction, tension remains unchanged and the muscle's length changes. Lifting an object at a constant speed is an example of isotonic contraction. There are two types of isotonic contractions: (1) concentric and (2) eccentric. In a concentric contraction, the muscle tension rises to meet the resistance. This type is typical of most exercises. The external force on the muscle is less than the force the muscle is generating - a shortening contraction. The effect is not visible during the classic biceps curl, which is in fact auxotonic because the resistance (the weight being lifted) does not remain the same through the exercise. Tension is highest at a parallel to the floor level, and eases off above and below this point. Therefore tension changes as well as muscle length. In eccentric contractions, the muscle lengthens due to the resistance being greater than the force the muscle is producing. There are two main features to note regarding eccentric contractions. First, the absolute tensions achieved

can be very high relative to the muscle's maximum tetanic tension generating capacity (you can set down a much heavier object than you can lift). Second, the absolute tension is relatively independent of lengthening velocity. This suggests that skeletal muscles are very resistant to lengthening, thereby allowing very high levels of tension to develop as can occur in isometric exercise.

The adaptation changes and health implications of resistance exercise are variable to each individual. For long-lasting changes, there needs to be a systematic administration of a sufficient stimulus, followed by an adaptation of the individual, and then the introduction of a new, progressively greater stimulus. Whether training for sports performance or health enhancement, much of the success of the program will be attributable to the effectiveness of the exercise prescription in manipulating the progression of the resistance stimulus, the variation in the program design and the individualization of the program <sup>(27)</sup>.

One important resistance training effect is the increase in size of muscle that is referred to as hypertrophy. The 'pump' one feels from a single exercise bout is referred to as transient hypertrophy. This short term effect is attributable to fluid accumulation, from blood plasma, in the intracellular and interstitial spaces of the muscle. In contrast, chronic hypertrophy refers to the increase in muscle size associated with long-term resistance training. Increases in the cross-sectional area of muscle fibers range from 20% to 45% in most training studies <sup>(28)</sup>. Muscle fiber hypertrophy has been shown to require more than 16 workouts to produce significant effects <sup>(29)</sup>. In addition, fast-twitch (glycolytic) muscle fiber has the potential to show greater increases in size as compared to slow-twitch (oxidative) muscle fiber <sup>(30)</sup>.

The increases in muscular strength during the initial periods of a resistance training program are not associated with changes in cross-sectional area of the muscle <sup>(31)</sup>. Changes in strength evidenced in the first few weeks of resistance training are rather associated with neural adaptations <sup>(32)</sup>, which encompass the development of more efficient neural pathways along the route to the muscle. The motor unit (motor nerve fiber and the muscle fibers it innervates) recruitment is central to the early (2 to 8 weeks) gains in strength. Collectively, the learned recruitment of additional motor units, which may respond in a synchronous (the coincident timing of impulses from 2 or more motor units) fashion, the increased activation of synergistic muscles, and the inhibition of neural protective mechanisms <sup>(27,31,32)</sup>, all contribute to enhance the muscle's ability to generate more force. It is possible that two adjacent muscle fibers, with different motor nerves, could result in one fiber being activated to generate force while the other moves passively. Long-term changes in strength

are more likely attributable to hypertrophy of the muscle fibers or muscle group<sup>(33)</sup>. The range of increase of strength is quite variable to the individual and may range from 7% to 45%. Velocity of execution best characterizes the probability that the greatest increases in strength occur at or near the same velocity exercise to be performed<sup>(34)</sup>. Therefore, slow-speed training will result in greater gains at slow movement speeds, while fast-speed training will realize the improvements in strength at faster movement speeds. Activities that stimulate bone growth need to include progressive overload, variation of load, and specificity of loading<sup>(34)</sup>. Specificity of loading refers to exercises that directly place a load on a certain region of the skeleton. With osteoporosis, the sites of fractures that are most devastating are in the axial skeleton (the spine and hip). Conroy et al. recommended that more intense loading of the spine and hip be done during early adulthood when the body is more capable of taking on an increased load and developing its peak bone mass. Progressive overload is necessary so the bone and associated connective tissue are not asked to exceed the critical level that would place them at risk. Resistance training programs can, also, increase fat-free mass and decrease the percentage of body fat. One of the outstanding benefits of resistance exercise, as it relates to weight loss, is the positive impact of increasing energy expenditure during the exercise session and somewhat during recovery, and on maintaining or increasing fat-free body mass while encouraging the loss of fat body weight<sup>(35)</sup>. It is more likely that body composition is affected and controlled by resistance training programs using the larger muscle groups and greater total volume<sup>(36)</sup>. Volume in resistance training is equal to the total workload, which is directly proportional to the energy expenditure of the work bout. Total volume is determined by the total number of repetitions (repetitions x sets) performed times the weight of the load (total repetitions x weight). An impressive finding to be highlighted with resistance training is that the energy expenditure following the higher total volume workouts appears to be elevated, compared to other forms of exercise, and thus, further contributes to weight loss objectives. Moreover cardiovascular system changes with resistance training, indeed Heart rate is acutely elevated immediately following a work bout and affected by the resistance, the number of repetitions and the muscle mass involved in the contraction (small vs. large mass exercises)<sup>(37)</sup>. Interestingly, in terms of chronic adaptations, there appears to be a reduction in heart rate from resistance training, which is considered beneficial. Long term adaptations observed in the research, from no change up to a 11% decrease in heart rate, may be explained by the differences in intensity, volume, rest between sets, use of small vs. large muscle mass, duration of study and fitness level of the subjects. Approximately 1 in 4 adults have high blood pressure. More than 90% of these cases are identified as primary hypertension, which increases the risk of heart failure, kidney disease, stroke, and myocardial infarction<sup>(38)</sup>. During a resistance exercise bout, systolic and diastolic blood pressures

may show dramatic increases, which suggest that caution should be taken in persons with cardiovascular disease, or known risk factors. The extent of the increase in blood pressure is dependent on the time the contraction is held, the intensity of the contraction, and the amount of muscle mass involved in the contraction. More dynamic forms of resistance training, such as circuit training, that involve moderate resistance and high repetitions with short rests are associated with reductions in blood pressure. Studies have shown decreases in diastolic blood pressure<sup>(39)</sup>, no change in blood pressure<sup>(40)</sup> and decreases in systolic blood pressure<sup>(41)</sup>. The effects of resistance training on blood pressure are varied largely because of differences in study design, which suggests that more research is necessary to clearly understand the role of resistance training in blood pressure management. Other Studies of strength-trained athletes have shown that there is an increase in left ventricular wall thickness, absolute left ventricular wall mass, and septum wall thickness with resistance training, as contrasted to increases in volume of the left ventricular chamber seen with aerobic-trained individuals. The strength training program, usually, consisted of two sets (90 second rests between sets) of exercise, using loads that could be lifted 12 - 15 times (per set) for 11 different exercises. Exercises include squats, leg extensions, leg curls, decline presses, pullovers, arm cross-overs, overhead presses, lateral raises, rows, hip and back exercises, and modified sit-ups. It is evident from the high number of adaptations that occur with resistance training that there are several health-related benefits.

## **PARAMETERS**

We decided to evaluate cardiovascular, metabolic and muscular adaptations to exercise. To quantify and evaluate the heart impact to different exercises, to study VO<sub>2</sub> kinetics and other ventilatory adaptations and corresponding muscular utilizations should give a complete picture of the mechanisms underlying the response to physical activity.

During each session data collection was uninterrupted throughout the tests for all parameters.

### **Cardiovascular**

Cardiovascular adaptations were collected by Portapres\*, TNO in terms of HR Heart Rate, SV Stroke Volume, CO Cardiac Output, BP Blood Pressure and TPR Total Peripherals Resistance. These variables can describe in detail what happens at the central level, at heart level, and explain the mechanisms behind the cardiac functionality and efficacy<sup>(42,43,44)</sup>.

Heart rate has been found to be significantly correlated to blood pressure<sup>(45)</sup>. HR showed significant changes in the response to activity throughout the day. Peaks in HR reactivity coincided with the peaks in BP reactivity<sup>(46)</sup>. The linear increase during exercise for HR, CO and SV, attests to a slow

persistent increase in the oxygen deficit. The CO increase observed during the first 2 min of exercise can equally be explained by a parallel increase of its components HR and SV, reaching respectively 73, 83 and 87% of their end values. Faster circulatory adjustments and therefore better oxygen delivery could have accounted for a reduced oxygen deficit after training, thus contributing to increase the time to fatigue<sup>(47)</sup>.

## **Metabolic**

Metabolic parameters were documented by K4\*, QUARK b<sup>2\*</sup>, in terms of VO<sub>2</sub> Oxygen consumption, VCO<sub>2</sub> Carbon dioxide production, VE expiratory volume, VT tidal volume, P<sub>ET</sub>O<sub>2</sub> end tidal Oxygen pressure, P<sub>ET</sub>CO<sub>2</sub> end tidal Carbon dioxide pressure, R respiratory quotient. With these parameters it is possible to have a clear explanation about ventilatory response to the exercise and the description of the different strategies utilized in order to support different exercises.

Maximal oxygen uptake ( $\dot{V}O_{2max}$ ) is one of the most ubiquitous measurements in all of exercise science research, it is used in clinical science as a measure of exercise performance<sup>(48,49,50,51)</sup>.

VO<sub>2 max</sub> has been defined as:

"The highest rate of oxygen consumption attainable during maximal or exhaustive exercise"

VO<sub>2 max</sub> decreases with age. The average rate of decline is generally accepted to be about 1% per year or 10% per decade after the age of 25. One large cross sectional study found the average decrease was 0.46 ml/kg/min per year in men (1.2%) and 0.54 ml/kg/min in women (1.7%)<sup>(52,53)</sup>.

However, this deterioration is not necessarily due to the aging process. In some cases the decrease may be purely a reflection of increased body weight with no change in absolute values for ventilation of oxygen. Recall that VO<sub>2 max</sub> is usually expressed relative to body weight. If this increases, as tends to happen with age, and aerobic fitness stays the same, then VO<sub>2 max</sub> measured in ml/kg/min will decrease.

Usually, the decline in age-related VO<sub>2 max</sub> can be accounted for by a reduction in maximum heart rate, maximal stroke volume and maximal a-vO<sub>2</sub> difference i.e. the difference between oxygen concentration arterial blood and Venous blood. Vigorous training at a younger age does not seem to prevent the fall in VO<sub>2 max</sub> if training is ceased altogether. Elite athletes have been shown to decline by 43% from ages 23 to 50 (from 70 ml/kg/min to 40 ml/kg/min) when they stop training after their careers are over<sup>(54)</sup>. In some cases, the relative decline is greater than for the average population - as much as 15% per decade or 1.5% per year<sup>(55,56,57)</sup>. However in comparison, master athletes who continue to keep fit only show a decrease of 5-6% per decade or 0.5-0.6% per year.

When they maintain the same relative intensity of training, a decrease of only 3.6% over 25 years has been reported and most of the decrease was attributable to a small increase in bodyweight. It seems that training can slow the rate of decline in  $\text{VO}_2$  max but becomes less effective after the age of about 50.

The 'classical' view of maximal oxygen uptake  $\text{VO}_{2\text{max}}$  is that maximal rates of oxygen utilization (and sustainable rates of oxidative ATP production) in skeletal muscle are limited under most circumstances by the ability of the heart to deliver oxygen <sup>(58)</sup>

## **Muscular**

Near-infrared spectroscopy (NIRS) is a non-invasive technique that has been extensively used to infer on the physiological mechanisms that regulate muscle  $\text{O}_2$  delivery and utilization, during metabolic transitions, in exercising humans. The NIRS deoxygenated hemoglobin (HHb) signal directly depends on the ratio between the muscular  $\text{O}_2$  utilization rate and the capillary  $\text{O}_2$  delivery in the region explored by the probe, providing a non-invasive estimate of the changes in  $\text{O}_2$  extraction occurring inside the muscles. <sup>(59,60,61)</sup> Muscular values were: HhbDeOxy Deoxygenated Hemoglobin, HhbOxy Oxygenated hemoglobin, total Hemoglobin, % saturation (NIRS, ISS). NIRS data document the oxygen extraction before, during and post exercise and it gives an indication of oxygen utilization at muscular level; while blood flow measurements at femoral level quantify and clarify blood flow distribution. The use of NIRS for the study of oxidative metabolism in skeletal muscle has several advantages and many limitations. One of the problems, represented by the lack of correlation, after a few minutes of constant-load exercise, between NIRS oxygenation indexes and the simultaneously determined deep vein Hb saturation it is solved from deoxyHb parameter, that represents <sup>(62,63)</sup> the muscle oxygenation index

In addition to muscular saturation it also possible to analyze blood flow (FBF) by Echo Doppler (Therason P50); this is utilized in sport science to evaluate blood flow distribution during exercise and recovery.

The muscle tension and time for relaxation can have a profound effect on blood flow into exercising limbs in humans. The muscle blood flow response follows the progressive increase of  $\text{VO}_2$  during exercise, but during recovery it is dependent on the type and the duration of the exercise. Immediately after intense static contractions blood flow to the exercised muscles increases markedly. A mismatch between the time course of changes in blood flow and oxygen uptake suggests that the blood flow is not directly regulated by the need of oxygen in the exercised muscles. <sup>(64)</sup> Retrograde blood flow due to muscle contraction is a function of muscle tension and appears to be independent of contraction frequency.

## Integration

The integration between all these adjustments can describe the interaction between systems and clarify where, what, how the training affects our organism, to help exercise prescriptions.

I report some examples of studies that compare and correlate some parameters :

“During incremental exercise, stroke volume plateaus at 40% of  $VO_{2MAX}$  , but a recent research has documented that stroke volume progressively increases to  $VO_{2MAX}$  in both trained and untrained subjects. The stroke volume response to incremental exercise to  $VO_{2MAX}$  may be influenced by training status, age, and sex.”<sup>(65)</sup>

“The systemic aerobic capacity (maximal cardiac output and  $VO_{2max}$ ) was positively correlated with peripheral vascular reserve, as measured by peak blood flow and conducting capacity of the contracting knee extensor muscles, in men but not women. This relationship was most pronounced in older men, regardless of how peripheral vasodilator capacity was expressed or normalized. The disparate balance between maximal cardiac output and peripheral vascular reserve suggest different cardiovascular limitations to aerobic capacity in men and women particularly with aging”<sup>(66)</sup>

“Computer simulations revealed that sigmoid increases in deoxy-(Hb Mb) reflect a nonlinear relationship between microvascular  $Q'm$  and  $V'O_{2max}$  during incremental ramp exercise. The mechanistic implications of our findings are that, in most healthy subjects,  $Q'm$  increased at a faster rate than  $V'O_2$  early in the exercise test and slowed progressively as maximal work rate was approached”<sup>(67)</sup> .

**Our research.** Given the general benefits of various physical training programs on different populations that we have summarized above, it must be emphasized that any training-based research requires longitudinal studies, suffering for the need of long lasting observations and repeated measurement, which may prove to be particularly demanding when dealing with special populations, such as cardiovascular and diabetes patients as well as the general older age population. To circumvent such inconveniences, we focused on the acute effects of exercise that still deserve attention in the light of a wide comparison among different exercise modalities and populations. Knowledge of the acute effects sets the basis to differentiate among individualized training projects.



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## CAP 2 : STUDY 1

**“Cardiovascular, metabolic and muscular responses during incremental cycle ergometer test: gender, age and pathology-related differences”**





## Incremental test

The evaluation of human physiological limit through Incremental Exercise Testing (IET) has become an important clinical tool to evaluate exercise capacity and predict outcomes in patients with or without disease. It allows assessment of the integrative exercise responses involving the pulmonary, cardiovascular and skeletal muscle systems. IET is increasingly being used in a wide spectrum of clinical applications for evaluation of undiagnosed exercise intolerance and for objective determination of functional capacity and impairment.

The body has an upper limit for O<sub>2</sub> utilization at a particular state of fitness, age, sex and pathology.<sup>(1, 2, 3, 4, 5)</sup> This is determined by the maximal cardiac output (cardiovascular parameters), the arterial O<sub>2</sub> content (metabolic parameters), the fractional distribution of the cardiac output to the exercising muscle and the ability of the muscle to extract O<sub>2</sub> (muscular response). The rate of oxygen delivery to working muscles, the oxygen-carrying capacity of the blood, and the amount of oxygen extracted from the blood and utilized by working muscles are all key determinants in maximal oxygen consumption (VO<sub>2max</sub>). The dynamic responses of O<sub>2</sub> uptake (VO<sub>2</sub>) to a range of constant power output levels are related to exercise intensity<sup>(6)</sup>. However an age-associated decline in VO<sub>2max</sub> has been demonstrated in humans, even after accounting for changes in whole-body and appendicle fat-free muscle mass. Moreover decreases in cardiac output play an important role in the age-related decrease in whole-body oxidative capacity<sup>(7)</sup> and it may depend, also, on the role of the muscles themselves (muscle atrophy)<sup>(8)</sup>. In addition CO is usually lower in elderly compared with younger control subjects<sup>(9, 10)</sup>.

Persons with type II diabetes mellitus (D2) are reported, even in the absence of a clinical cardiovascular disease, to have a reduced maximal oxygen consumption compared with non diabetic subjects. In addition the rate of increase in oxygen consumption during graded treadmill exercise is attenuated in DM<sup>(11)</sup>. The reduced VO<sub>2max</sub> in DM may not simply be due to early termination of graded exercise, or deconditioning, but to a qualitative difference in the rate of rise in VO<sub>2</sub> with graded exercise. However, observations made during incremental exercise do not represent steady-state phenomena and may be influenced by a variety of factors, including the rate of progression in workload and the ability of the cardiovascular system to respond to the increased work demand<sup>(12,13)</sup>.

## Parameters

Concluding, the most relevant parameter studied by IET is  $\text{VO}_{2\text{max}}$ , which represents the metabolic determinant of endurance performance as a true parametric measure of cardio respiratory capacity for an individual at a given degree of fitness and oxygen availability. High  $\text{VO}_{2\text{max}}$ , is, also, the primary distinguishing characteristic of elite endurance athletes that allows them to run fast over prolonged periods of time. The  $\text{VO}_{2\text{max}}$  response to exercise is linear until maximal  $\text{VO}_2$  is achieved. In many people, a plateau is reached at near maximal exercise, beyond which the  $\text{VO}_2$  does not change further. Exercise training enables the person to achieve a greater maximal workload and a higher  $\text{VO}_{2\text{max}}$ , because several important changes occur when a healthy person goes from rest to maximal exercise before and after exercise training<sup>(14)</sup>.

The other important aspect, during ramp exercise, are cardiovascular adjustments. Blood Pressure and HR follow a progressive increase during IET, but peculiar kinetics of systemic cardiovascular and metabolic responses to changes in work rate lead to a nonlinear relationship between cardiac output (CO) and pulmonary  $\text{O}_2$  uptake ( $\text{VO}_2$ ). Consequently, arterial venous  $\text{O}_2$  difference [(a-v) $\text{O}_2$ ] or fractional  $\text{O}_2$  extraction displays a hyperbolic profile when plotted as a function of  $\dot{V}\text{O}_2$  (or work rate)<sup>(15)</sup>. Moreover, after training, the resting heart rate is lower at each stage of sub-maximal exercise, but the maximal heart rate does not change. This approximates “220 bpm – age”. The stroke volume response is curvilinear, increasing early in exercise with little change thereafter. The training effect increases the resting stroke volume and the stroke volume at each workload<sup>(16)</sup>. However Athletes stop exercising at  $\dot{V}\text{O}_{2\text{max}}$  because of severe functional alterations at the local muscle level due to what is ultimately a limitation in convective oxygen transport, which activates muscle afferents leading to cessation of central motor drive and voluntary effort<sup>(17)</sup>.

At muscular level, another important parameter is given by an indirect measurement by NIRS, the DeOxy-Hb, which reflects the temporal profile of fractional  $\text{O}_2$  extraction (the ratio of  $\text{O}_2$  delivery and uptake) in the microvascular compartment investigated (predominantly capillaries), moreover the microvascular compartment contributing to the NIRS signal does not change with exercise and exercise intensities, and changes from baseline to exercise reflect the response of muscle fractional  $\text{O}_2$  extraction<sup>(18)</sup>. A progressively increasing work rate exercise test is the best way to study the limits of the organism, and to collect an integrated physiological response.

## **Test**

The incremental test, furthermore, has several advantages: the test starts out at a relatively low work rate, so that it does not require the application of great muscle force or a sudden, large cardio respiratory stress; the  $VO_{2max}$  or peak  $VO_2$  can be established in an exercise test in which the period of increasing work rate lasts only 8 to 12 minutes, and the subject is stressed for only a few minutes at relatively high work rates. It is important that to obtain the best data for interpreting the measured responses to a progressively increasing work rate exercise test, the work rate increments should be uniform in magnitude and duration.

## **Aim**

The literature on cardiovascular responses to cardiopulmonary exercise test does not unanimously clarify the role of stroke volume changes in the enhancement of cardiac output <sup>(19,20,21)</sup>.

The aim of the present project was to characterize the cardiovascular response, in terms of Heart Rate (HR), Stroke Volume (SV) and Cardiac Output (CO), during cycle-ergometer incremental tests, in young and aged subjects of both sexes with and without pathology.

Moreover to compare also the metabolic and the muscular responses in order to have a characterization of each system contributions, and to clarify their integration to support exhaustive effort.

## METHODS

### Groups

We recruited sedentary young, elderly and diabetic subjects, both male and female.

D2M/F: sedentary (International Physical Activity Questionnaire <1000 MET min\*week), diet and/or oral hypoglycaemic agents, diabetes diagnosis at least 1 year before (15.1±6.9y D2M 11.1±4.9y D2F) and, HbA1c 7.1±0.5 % D2M and 6.4±2.2 D2F, HDL 53.1±10.1 mg/dL D2M and 47.5±17.4 mg/dL D2F, Total Cholesterol 142.8±20.9 mg/dL D2M and 140.8±48.5 mg/dL D2F, non-smokers, no evidence of chronic complications.

HEM/F: sedentary, non-smokers, no evidence of chronic complications or presence of other pathologies

HYM/F: sedentary, non-smokers, no evidence of chronic complications or presence of other pathologies

GROUP	HYF	HEF	D2F	HYM	HEM	D2M
N°	12	12	4	13	13	9
Age.yr	23.6±2.4	67.1±7.1	57.25±5.9	22.6±1.3	67.3±2.7	60.3±6.4
Weight.kg	55.1±5.7	58.2±5.0	65.2±1.0	68.6±8.7	83.7±8.5	82.1±11.5
Height.cm	1.64±0.1	1.57±0.1	1.59±0.0	1.75±0.1	1.70±0.0	1.73±0.0
B.M.I.	20.6±2.1	23.4±2.3	25.7±1.4	22.2±2.6	28.8±3.0	27.1±3.4
load.watt	155.8±16	104±15	110±18	258.3±41	188.1±25	152.5±19

Table2: Groups Anthropometric Characteristics

HYF Healthy Young Female; D2F Diabetes 2 Female; HEF Healthy Elderly Female; HYM Healthy Young Male; D2M Diabetes 2 Male; HEM Healthy Elderly Male.

The inclusions criteria were: no smokers, or at least 10 years without smoking, healthy status, and sedentary, i.e. performing just some daily life activity and some recreational hobby with low energy cost. (walking, cooking...etc). The exclusion criteria were: presence of some joint injury, hormonal alterations (thyroid etc) and frank obesity.

## **Protocol**

IET on cycle ergo-meter started with a load of 40 W for 3 min followed by 10 or 20 W increments each minute, for females and males, respectively, up to voluntary exhaustion. After achieving stable baseline conditions (Hr 60-80 bpm; VO<sub>2</sub> 200-350 ml/min), the test begins with 3 minutes of pedaling with no load (warming up), followed by a starting load of 50 watts (for young and elderly healthy subjects) or 30 watts (for pathological subjects), increased every minute by 20 or 10 watt up to voluntary exhaustion. The pedaling rhythm is between 65-70 rpm and the subject is continually monitored by an expert operator to secure a good quality of execution and data acquisition. In addition, a physician is always present to guarantee a medical support if necessary and to monitor the trend of life parameters. The end load is considered the last workload sustained for one minute. The trial ends because of different causes: muscular exhaustion, high production of CO<sub>2</sub> and hyperventilation, or because the subject exceeds cardiovascular limit parameters (blood pressure higher than 220/110, HR higher than maximal calculated value). Sometimes, However, the test is stopped in order to protect the structural integrity of the subject because the parameters evidence some dangerous conditions.

## **Instruments**

Every subject is equipped, for all test and part of recovery, with a cardiovascular monitoring instrument (Portapres, TNO), that collects data about Blood Pressure (SAP, Systolic Arterial Pressure. DAP Diastolic Arterial Pressure. Mean Arterial Pressure), HR (Heart Rate), SV (Stroke Volume), CO (Cardiac Output), TPR (Total Peripheral Resistance) a NIRS device on vastus lateralis muscle (ISS, Oxiplex) for muscular oxygen extraction (DeOxy Hb, deoxygenated hemoglobin), and a gas exchange analyzer (QuarkB<sup>2</sup> COSMED, IT ) which reports VO<sub>2</sub> uptake, CO<sub>2</sub> production, Tidal Volume (VT) etc. Moreover at the beginning and at the end of the exercise we collected a single drop of blood from the finger/ear to test LA<sup>+</sup> (lactate blood concentration, by Accutrend) and Hb (Hemoglobin blood concentration), the concentrations are evaluated to consider the lactate accumulation after an exhaustive exercise and possible changes in hemoglobin concentration.

## Statistics

Since the time course of exercises was not identical among the subjects, data are presented as mean  $\pm$  SD at 4 points: rest, 40%, 80% and at maximum workload ( $V'O_2$  max). Two Way Repeated Measures ANOVA (One Factor Repetition) was used to detect significant differences ( $P < 0.05$ ).

The significance of differences are reported as follows: AGE ( $\text{\AE}$ ), SEX ( $\text{\$}$ ), presence of Pathology ( $\text{\textcircled{d}}$ )

## Results

The workload was always higher in male than in female, except for D2M who performed at lower loads than HYF.

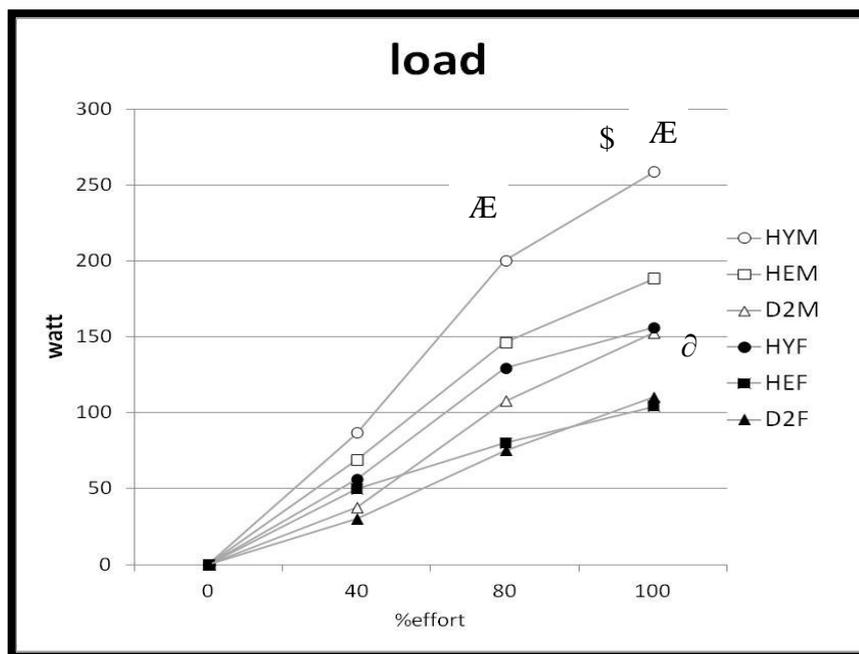


Figure 2: Workload During Incremental Test

## Metabolic

The Oxygen uptake increases relation to the workload that is reported as a percentage (%) of maximum load, in this way all graphs describe 4 conditions: baseline, 40%, 80%, and 100% of the maximal effort.  $VO_2$  response follows the literature. It increases for all groups in relation to workload increase, but the amount of the increase is different per sex and age (figure 3).

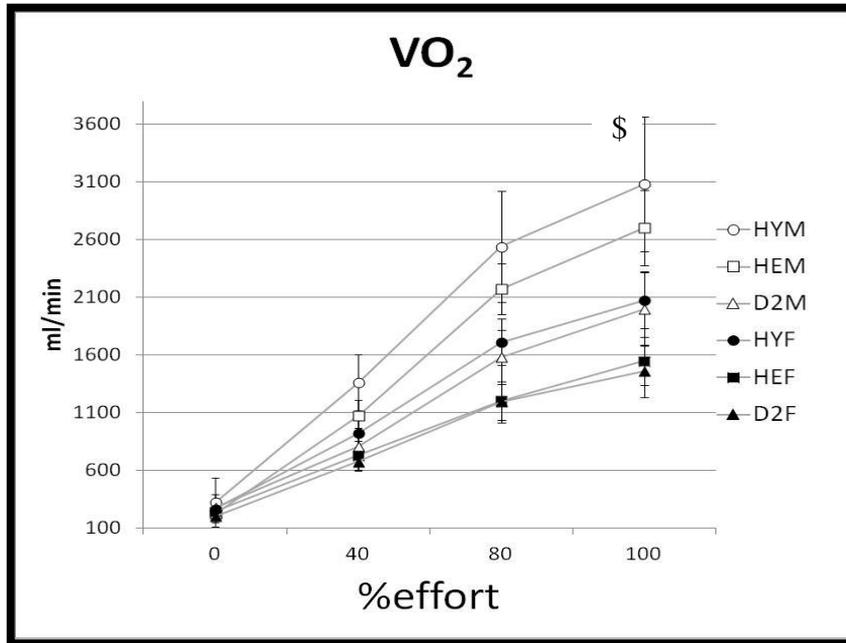


Figure 3:  $VO_2$ , Oxygen Uptake During Incremental Test

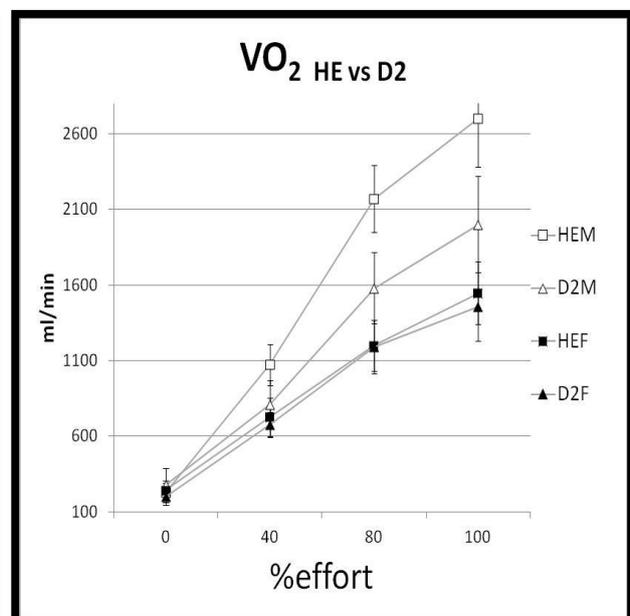
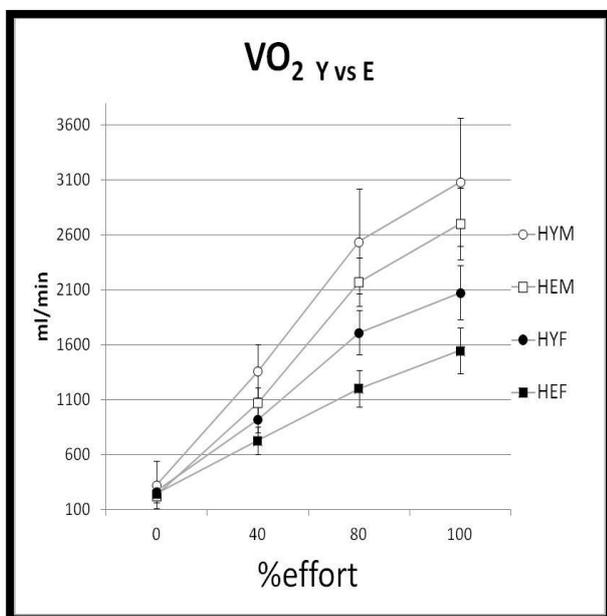


Figure 4;5: (4) Oxygen Consumption, Comparison Between Young And Elderly Subjects; (5) Oxygen Consumption, Comparison Between Elderly And Diabetics

In Fig 4 and 5 we reported the same data. grouped per age: it is evident that elderly people display lower values than young subjects, but this relation does not hold in the comparison with Diabetics subjects, who are impaired at metabolic level, and seem to be unable to increase the oxygen consumption to high levels.

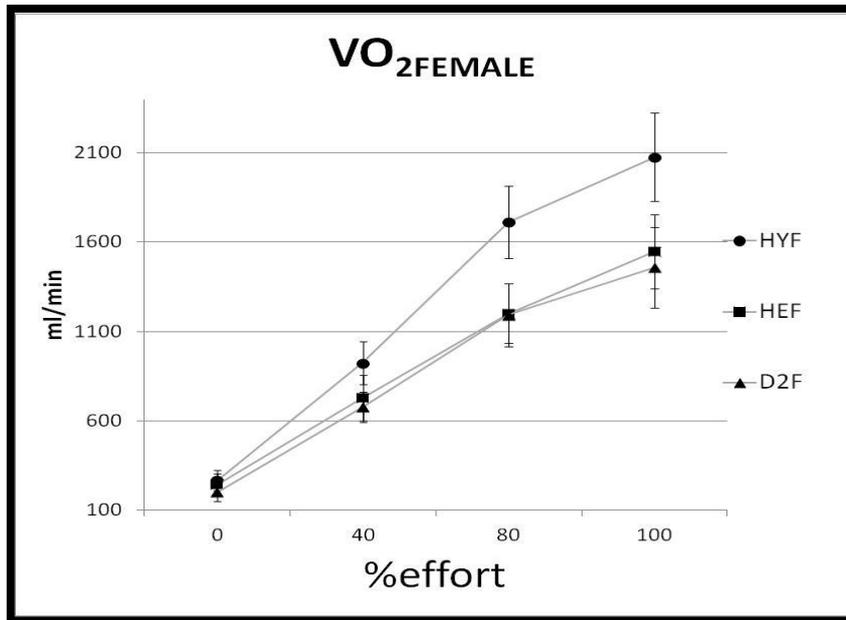


Figure 6: Oxygen Consumption, Comparison Among Female Subjects

If the age effect clearly reduces the oxygen consumption both in males and females, the effect of diabetes is more marked in males, whose trend is lower than for HEM, while female diabetics behaved like HEF.

HYM show the highest values among all groups, and HYF have higher value between Females groups.

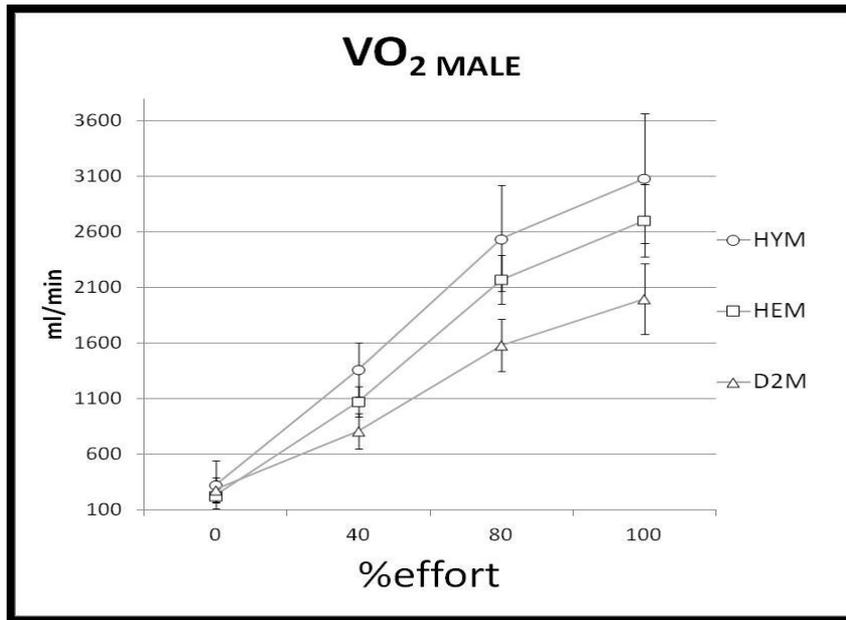


Figure 7: Oxygen Consumption, Comparison Among Male Subjects

VO <sub>2</sub> (ml/min)						
EFFORT	HYM	HEM	D2M	HYF	HEF	D2F
<b>BASELINE</b>	323.5±215.1	228.0±63.4	279.7±109.0	266.1±54.7	243.4±59.6	201.8±54.7
<b>40%</b>	1361.9±242.9	1074.5±135.8	808.9±158.2	923.5±120.8	728.7±127.2	676.8±84.0
<b>80%</b>	2541.4±47.4	2173.0±234.9	1580.8±231.7	1713.8±201.15	1200.6±168.5	1192.7±177.5
<b>100%</b>	3081.8±584.3	2704.6±326.2	1999.6±317.8	2077.7±248.1	1548.1±209.7	1459.3±226.7

Table 3: VO<sub>2</sub> at baseline, 40% -80% and (100%) of maximal effort

The anaerobic contribution to support the exhaustive effort is represented by CO<sub>2</sub> production, which shows a similar rather linear trend for all groups except HYM. The slope of the relation VCO<sub>2</sub>/relative workload changes at the highest loads in HYM.

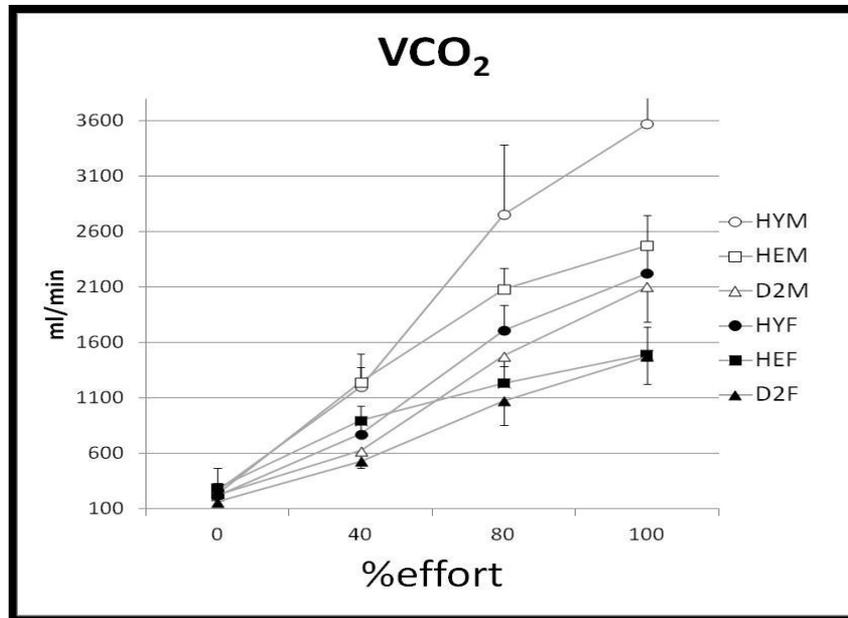


Figure 8: Carbon Dioxide Productions During Incremental Test

VCO <sub>2</sub>						
EFFORT	HYM	HEM	D2M	HYF	HEF	D2F
<b>BASE</b>	267,9±200,6	238,7±95,7	224,9±82,2	219,9±49,7	287,0±46,8	165,2±41,6
<b>40%</b>	1205,8±290,8	1247,9±127,5	627,5±126,4	778,8±135,7	900,3±128,5	533,4±62,6
<b>80%</b>	2760,7±624,19	2085,6±188,2	1481,4±209,7	1711,4±225,0	1237,2±153,1	1075,1±215,2
<b>100%</b>	3574,8±867,5	2479,6±273,4	2107,8±319,7	2228,6±253,9	1498,5±244,2	1476,1±249,5

Table 4: VCO<sub>2</sub> at baseline, 40% - 80% and (100%) of maximal effort

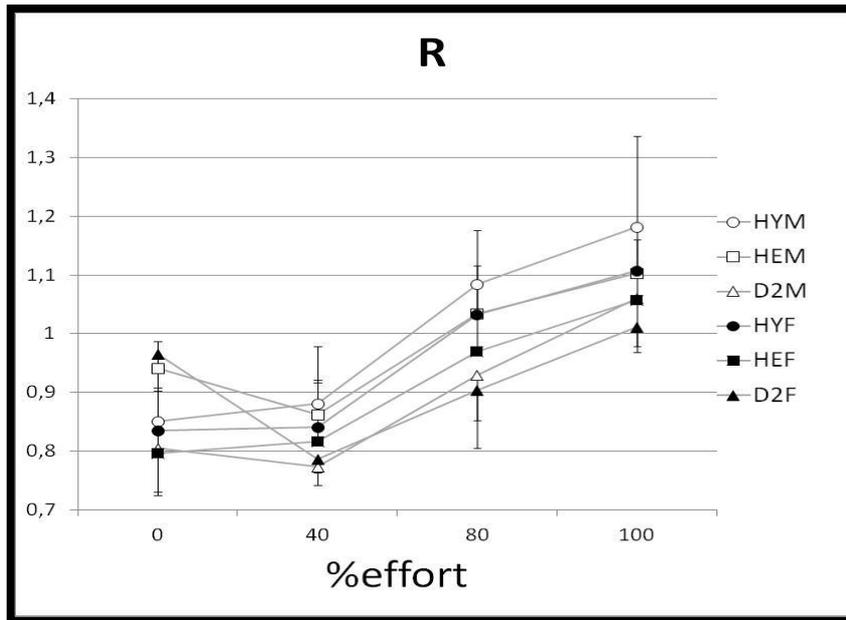


Figure 9: Respiratory Quotient During Incremental Test

The respiratory quotient (R) trends set all groups over 1 at maximal workload, but only HYM raises more than 1.1. Here HYF and HEM look very similar, and D2M/F get the lower values.

R						
EFFORT	HYM	HEM	D2M	HYF	HEF	D2F
<b>BASELINE</b>	0,85±0,13	0,94±0,18	0,80±0,08	0,83±0,07	0,79±0,08	0,96±0,2
<b>40%</b>	0,88±0,09	0,86±0,06	0,77±0,03	0,84±0,08	0,81±0,07	0,78±0,02
<b>80%</b>	1,08±0,09	1,03±0,05	0,92±0,07	1,03±0,08	0,96±0,06	0,90±0,09
<b>100%</b>	1,18±0,15	1,10±0,05	1,05±0,08	1,10±0,79	1,05±0,08	1,01±0,04

Table 5: R at baseline, 40% - 80% and (100%) of maximal effort

## Cardiovascular

The heart rate during IET reflects the well known dependence of maximal heart rate on age. It is noteworthy, however, that all diabetic subjects had a lower slope of the HR/relative workload line than non diabetic subjects.

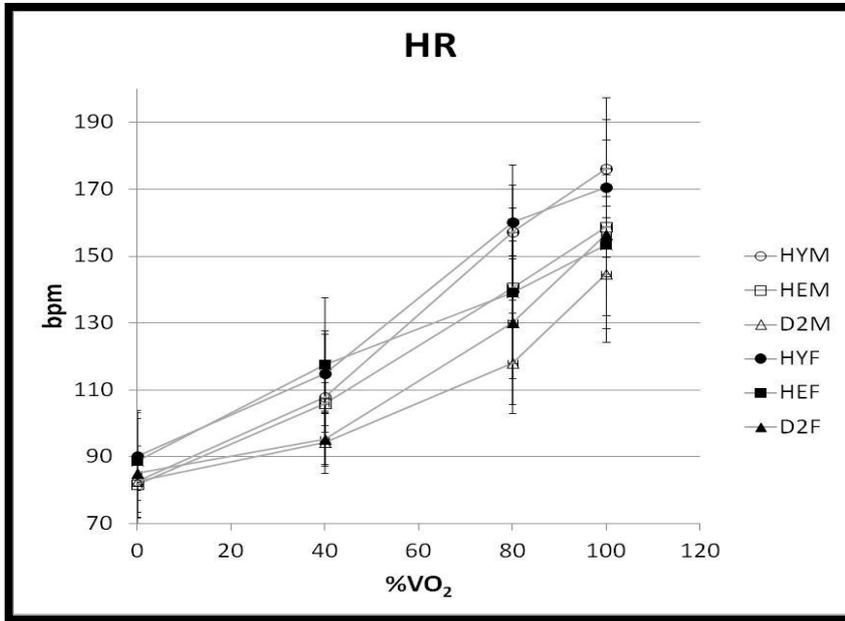


Figure 10: Heart Rate Response To The Incremental Test

In addition, maximal HR is lower in women than in men. In the diabetics HR increases less at submaximal workloads.

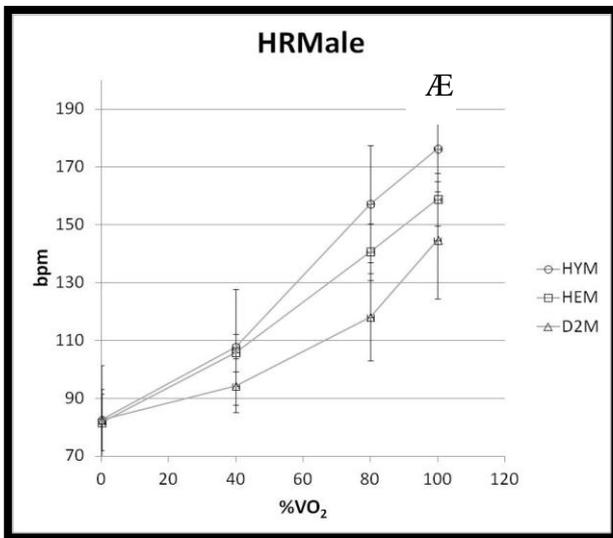


Figure 11: HR, Comparison Among Male

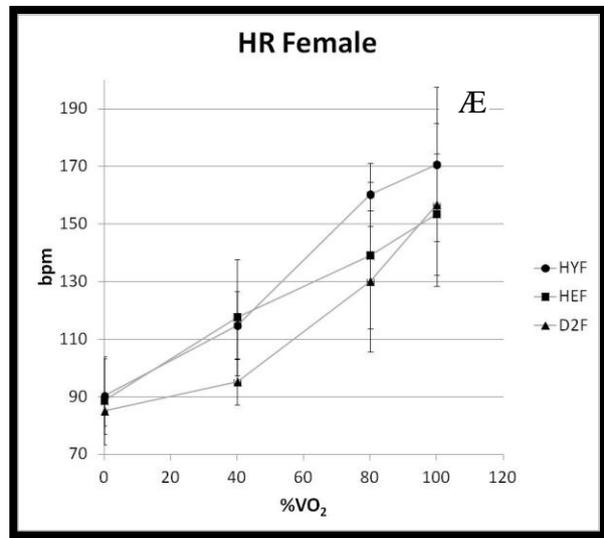
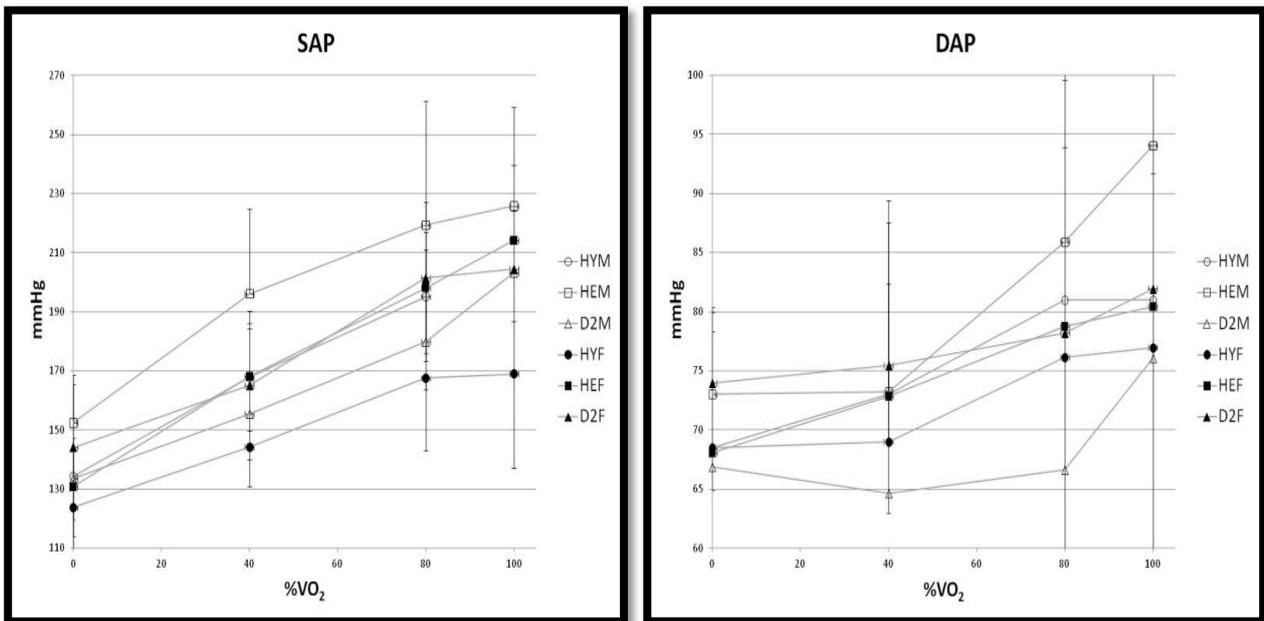


Figure 12: HR, Comparison Among Female

HR								
	HYM	HEM	D2M	HYF	HEF	D2F	Age. eff. ( P value)	Gen. eff. ( P value)
<b>BASE</b>	74.5±13	81.7 ± 9	82.6±10	89.1±14	88.7±15.	82.6.±5	ns	ns
<b>40%</b>	101.7±15	105.8±6	94.3±9	116.4±13	117.6±20	95.3±7	ns	< 0.027
<b>80%</b>	154.4±21	140.6±9	118.1±15	165.1±10	139.0±25	130.1±24	<0,05	ns
<b>100%</b>	179.6±15	158.8±9	144.7±20	177.6±7	153.3±21.	156.6±28	<0,05	ns

Table 6: VO2 at baseline, 40% - 80% and (100%) of maximal effort

The rise in systolic arterial pressure (SAP) is linearly related to workload in all subjects, with age and sex related differences in basal values: higher in elderly and lower in females.



Figures 13 – 14: Systolic and Diastolic Arterial Pressure During Incremental Test

While DAP response is similar in female groups and HEM, HYF and D2M follow different adaptations. HYF show a high increase at 80% and 100%. D2M display a slight fall until 80% and an large increase at peak exercise.

SV increases linearly as  $VO_2$  in all groups except in HEM. SV is lower in all females. like the other cardiovascular variables.

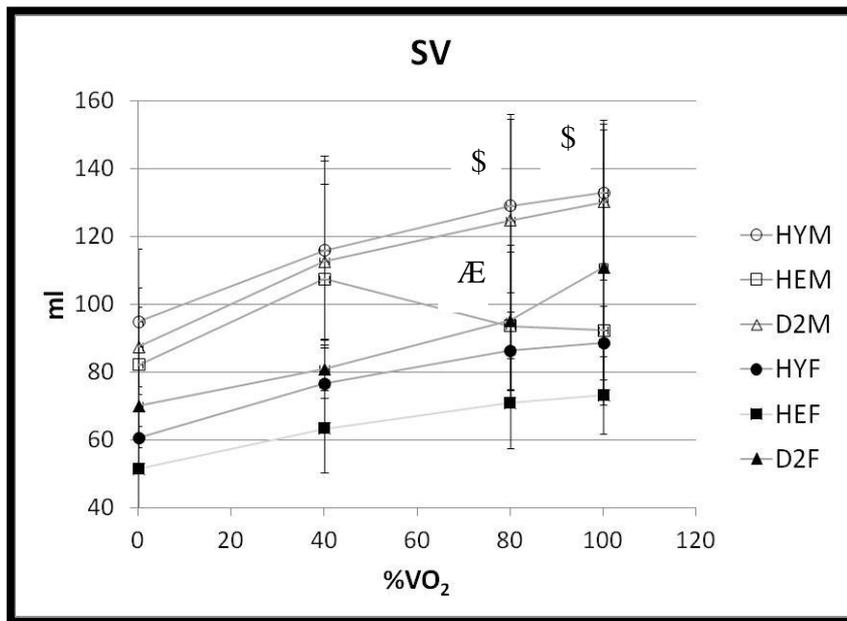


Figure 15: Stroke Volume during incremental test

In order to stress the differences among the groups, in the following graphs the same data are reported as a changes (delta) with respect to basal values. This representation shows quite clearly that the elderly healthy males are unable to keep their SV enhanced while the heart cycle shortens as the workload increases.

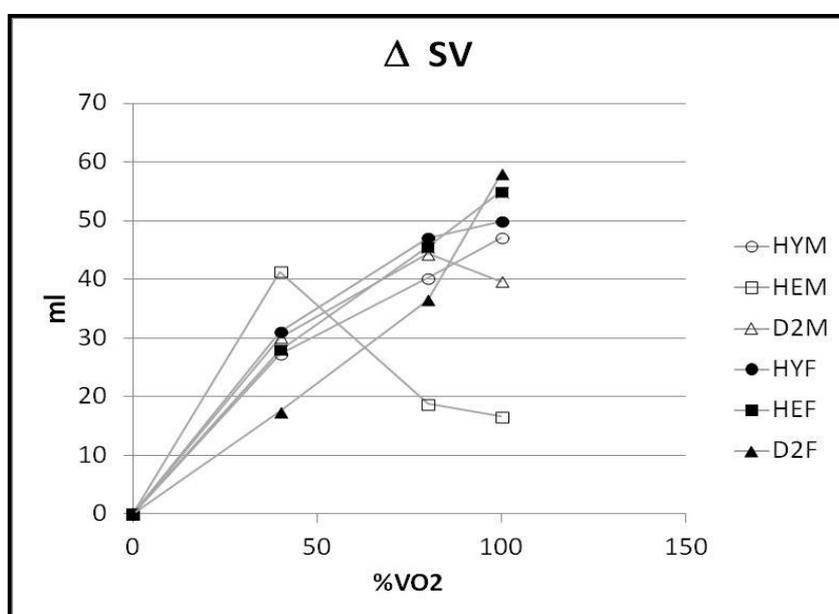


Figure 16: Delta SV; differences in absolute values

The adjustment strategies are different in HEM that decrease SV from 40% to the end of the test.

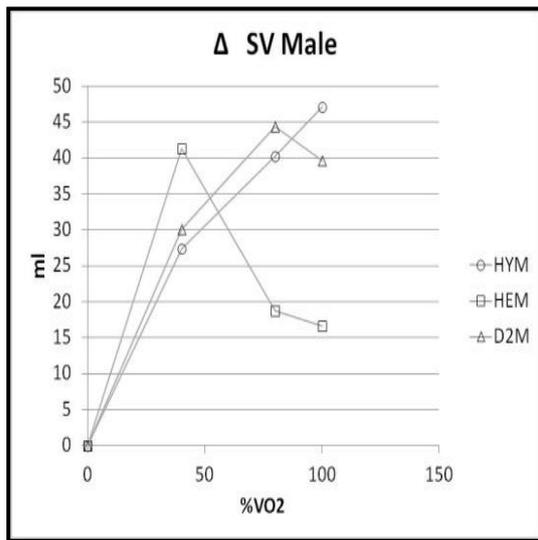


Figure 17: Delta SV, Comparison Among Male

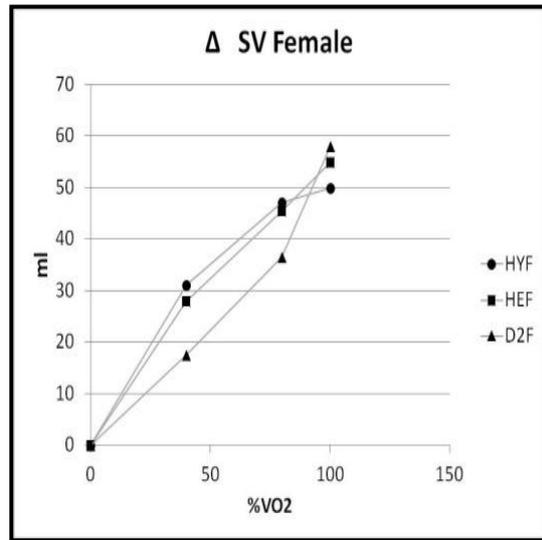


Figure 18: Delta SV, Comparison Among Female

SV								
	HYM	HEM	D2M	HYF	HEF	D2F	Age eff. ( P value)	Gen. eff. ( P value)
BASE	95.4±23.0	82.3±22.6	87.5±11.7	62.2±7.8	51.5±12.6	70.0±12.2	ns	ns
40%	127.2±24.3	107.5 ±35.0	112.7±22.7	72.3±11.8	63.4±13.0	81.0±6.4	n.s.	<0.001
80%	132.5±25.5	97.3±26.7	124.8±31.2	81.1±8.6	70.9±13.3	95.2±20.4	<0.05	<0.001
100%	135.9±13.9	99.1±14.0	130.3±22.8	85.1±8.9	73.3±11.4	111.0±40.5	<0.05	<0.001

Table 7: VO<sub>2</sub> at baseline, 40% - 80% and (100%) of maximal effort, HYM is significantly different from HEM/F in all steps, at peak also D2M, while HEM is significantly different from others males at 80% and at the peak conditions.

The changes in CO are mainly related to age since HEF and HEM display lower values, while HYM and HYF show the higher data. D2M and F, anyway, have greater response respect elderly

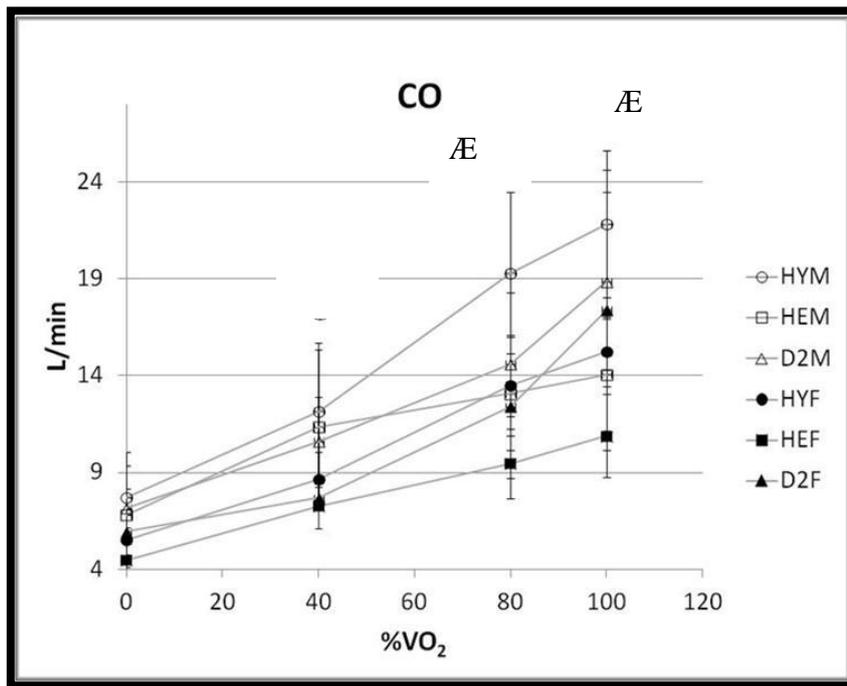


Figure 19: Cardiac Output Response During Incremental Test

If the same data are plotted in function of VO<sub>2</sub> ml/min (instead of %VO<sub>2max</sub>), the Diabetics response becomes evident. D2M and D2F increase more than the other groups.

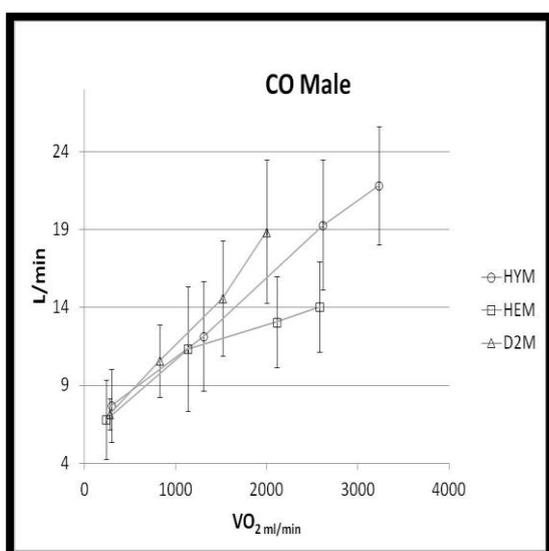


Figure 20: CO Comparison Among Male

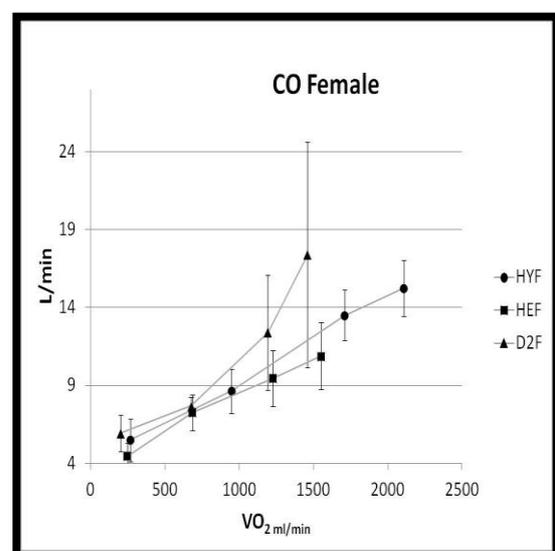


Figure 21: CO Comparison Among Female

CO

CO	HYM	HEM	D2M	HYF	HEF	D2F	Age eff. ( P value )	Gen. eff.ect ( P value)
BASE	6.8±0.8	6.8±2.5	7.1±1.0	5.5±1.2	4.4±0.8	5.9±1.1	ns	ns
40%	12.2±2.3	11.3±4.0	10.6±2.3	8.2±1.3	7.2±1.1	7.6±0.5	ns	ns
80%	18.8±2.7	13.0±2.9	14.6±3.7	12.9±1.6	9.4±1.7	12.3±3.7	<0.001	ns
100%	21.8±1.6	14.0±2.9	18.8±4.6	14.5±1.4	10.8±2.	17.4±7	<0.001	<0.001

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Table8: Cardiac output at baseline, 40% -80% end (100%) of maximal effort

The last cardiovascular parameter that considered was TPR. All groups display similar progressively decreasing patterns, except HEM, who level off after 40% of effort.

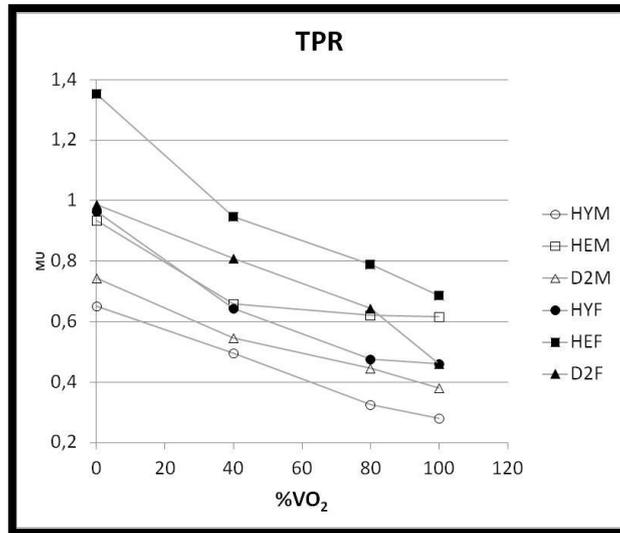


Figure 22: Total Peripheral Resistance During Incremental Test

The following 2 plots report the same data but represented per sex, it is evident that the response follow an Age effect. Elderly display the smaller response; diabetics show the average measurements and young the major fall of peripheral resistance.

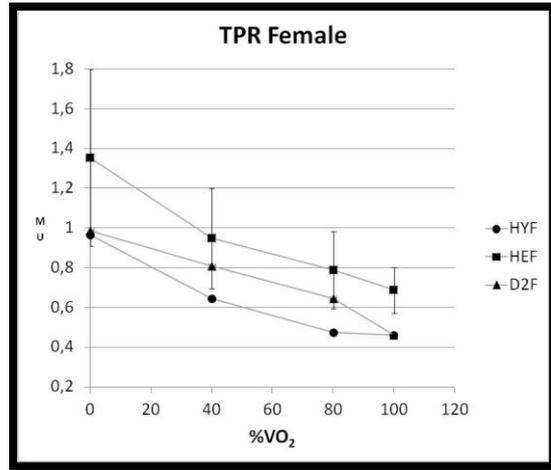
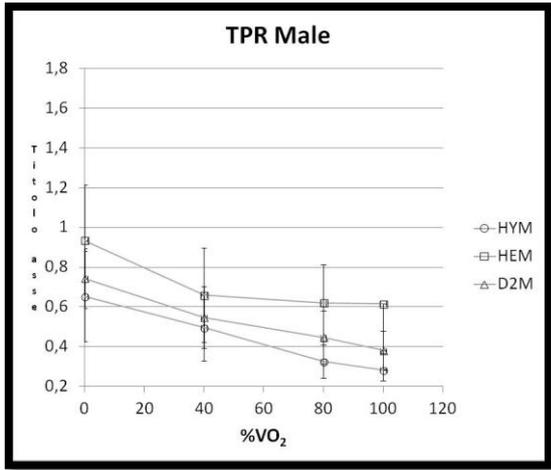


Figure 23-24 Total Peripheral Resistance During Incremental Test, comparison per sex

## Muscular

Muscular adaptations are described from DeOxy Hemoglobin which is reported as a good index of oxygen extractions at muscular level. During incremental test all groups increase their Oxygen extractions that conforms to the increase of Oxygen uptake at metabolic level. The male's groups also for this parameter, display higher measures. D2M and D2F show greater response than Young. HEM and HEF display lowest extraction that can represent an age-effect response.

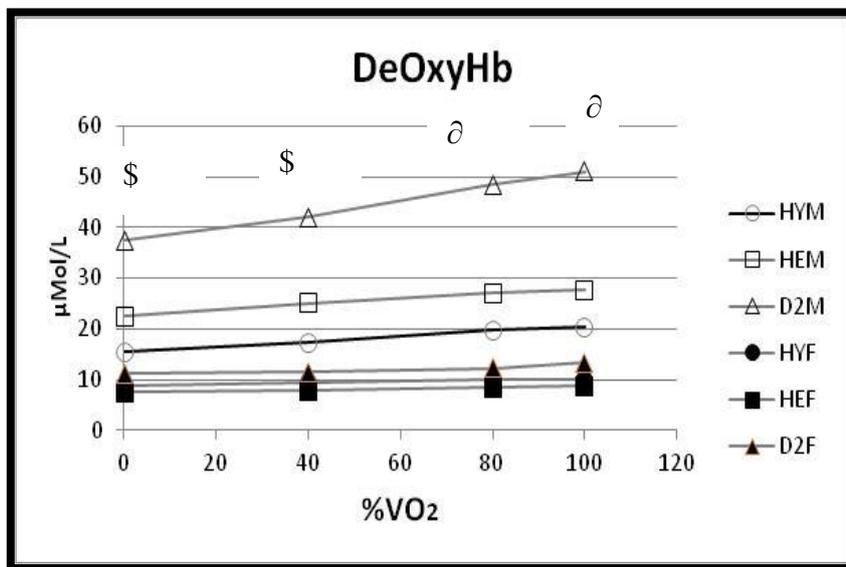


Figure 25: Delta Oxygen Saturation At Vastus Lateral Muscle Level

## Blood lactate

The blood lactate concentration showed values higher than 4 mmol/l that represent the change from aerobic to anaerobic metabolisms. All young subjects have highest values even because they performed highest workloads.

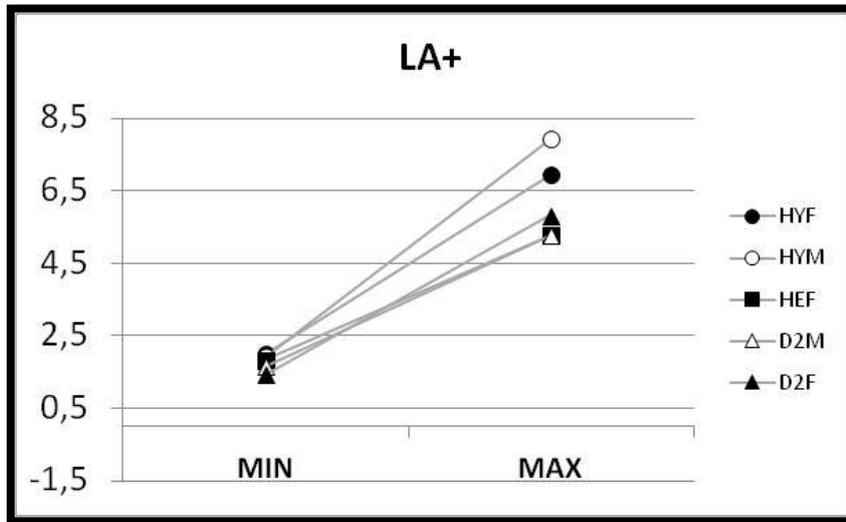


Figure 26: Blood Lactate during incremental test

LA <sup>+</sup>								
	HYM	HEM	HYF	HEF	D2M	D2F	Age eff. ( P value )	Gen. eff. ( P value )
BASE	1,9±0,4	NE	2±0,6	1,8±0,4	1,6±0,2	1,4±0,2	ns	ns
PEAK	7,9±2,2	NE	6,9±1,5	5,2±1,8	5,2±0,8	5,8±0,8	ns	<0.001

Table 9: Blood Lactate during incremental test

## Discussion

This study evaluates the overall physiological response to Incremental test, with a particular attention to the cardiovascular component, that seems to be critical in the adaptations to the exercise, and presents some peculiarity per Sex and Age <sup>(24, 25, 26)</sup>.

The baseline findings for sedentary young and old subjects have previously been described but the novelty of the present study consist in focusing widely integrated mechanisms.

The major finding regards SV adjustment: most of our results are similar to those found in the literature, which however often fail to pool together metabolic, muscular and cardiac responses <sup>(27)</sup>.

Some results reproduce previous data, such as HR, that decreases with age <sup>(28, 29)</sup>. Cristou reported, also, that age-related differences in HR at rest (15 beats/min) and during strenuous sub maximal cycle ergometry exercise (13 beats/min) were similar in small groups of healthy young and middle-aged men. This is in agreement with our results, HYM have 21 beats/min more than HEM and HYF 24 beats/min more than HEM, D2M and D2F follow the elderly groups probably per Age effect. The gender difference is significant at the beginning of exercise by 40% of  $VO_{2max}$ : female groups have lower HR response.

$VO_2$ , as well as load, increases progressively until the end of the exercise test, as is well known <sup>(1, 2, 3, 4, 30)</sup>, moreover it follows the same adjustments of HR per gender and sex.  $VO_{2max}$  is an important determinant of endurance performance <sup>(17)</sup>, and the pathology-related effect consists in an impairment of aerobic capacity in D2M, who have an oxygen uptake lower than HYF, and of D2F who have the lowest  $VO_{2max}$ . These data indicate that the increase in micro vascular blood flow with exercise is abnormally slow in type 2 diabetes and suggest that the limitation of oxygen uptake during sub maximal load may be related to impaired control or misdistribution of muscle blood flow <sup>(31)</sup>. Thus, Diabetic subjects show a compensative strategy by the enhancement of oxygen extraction at muscular level at the peak of exercise with the largest increase (35% over the basal value, D2M). We can hypothesize that the mitochondrial deficit dampens the oxygen consumption in response to an inefficient cellular respiration that is compensated by an elevated availability of oxygen at muscular level that makes it possible to bear the effort <sup>(32)</sup>.

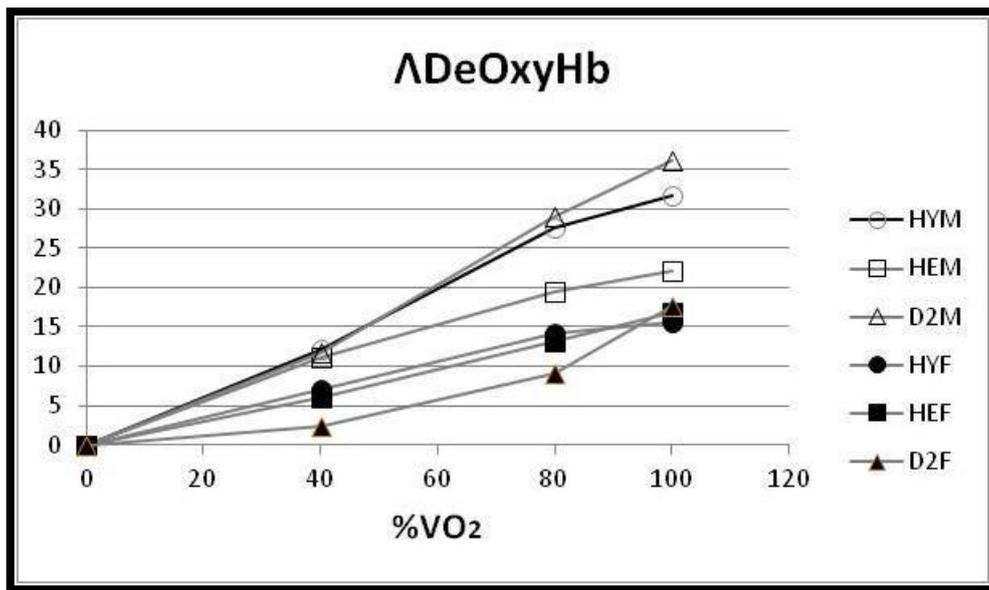


Figure 27: delta HHb over basal values

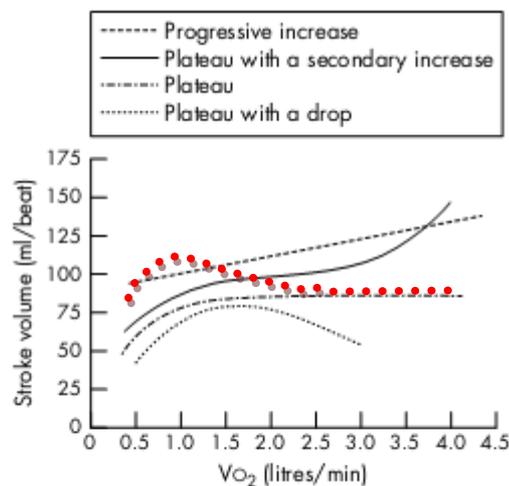
Impaired skeletal muscle oxygen delivery in response to exercise may thus contribute to the observed exercise deficit of D2. Moreover, several studies show reduced activity of oxidative enzymes in skeletal muscles of type 2 diabetics. The increase in HHb is a measure of the increase in the local muscle deoxygenated hemoglobin concentration, the overshoot HHb response observed in D2M provides evidence for an impaired increase of muscle blood flow relative to muscle Oxygen uptake after onset of exercise<sup>(33)</sup>.

This/our findings appear to support the concept that early increase in muscle blood flow may be attenuated in type 2 diabetes, and this abnormality may contribute to the slowed VO<sub>2</sub> kinetics and exercise deficit observed in type 2 diabetes.

The effects of Age on hemodynamic responses to maximal cycling exercise are generally consistent with previously published data for non-aerobically trained men and women. Martin reported that the age-related increase in blood pressure during exercise is greater in women than in men<sup>(34)</sup>. Hart et al. reported that the exercise hypertension during IET is lower in elderly subjects, probably in relation to lower workloads, furthermore it appears that arterial pressure regulation is fundamentally different between the sexes; this may be due to influences of female reproductive hormones on cardiovascular function<sup>(35)</sup>. In our study BP is different per gender, men show higher values than women, maybe due to higher workload, but there is also an age effect, the young attain lower BP, (SAP<sub>max</sub>: HEM 225; HEF 215; HYM 195; HYF 150) even if they perform at higher power; anyway the differences are not significant, because at baseline elderly subjects show a slightly hypertensive value, so the increase in BP is comparable among all groups. Diabetic subjects

are different from all the others; their curves are located just in the middle among the others, without consistent difference per gender (Fig 13).

However our most consistent result regards the SV response. In this study the HEM SV response is peculiar, while in all other groups SV increases progressively with the enhancement of workload. In a classical publication Vella classified 4 different types of SV adaptation during exercise (here reported in Fig 28), and the D2M/F HE/HYF HYM follow the commonest response reported, the progressive increase line (black dotted line). HEM appear different (red dotted line)<sup>(36)</sup>.



**Figure 1** The four types of stroke volume response with increasing exercise intensity.

Figure 28: Vella Reference graph

This finding describes a peculiar adaptation of elderly male, which is repeated in TPR pattern, which is not related to age or gender. The strong decrease in SV of HEM at 80% could be caused by relatively compromised vasodilator function, which does not keep proportional to the effort, since TPR fails to decrease as in the other groups. In HEM TPR after the initial fall (from 0.9 MU to 0.6 MU) keeps the same value until the end of exercise. Seals reported that, in healthy sedentary adults, aging is associated with increased stiffness (reduced compliance) of large elastic arteries<sup>(37)</sup>, which could be an explanation of this peculiar adaptation, which in our study is true only with men.

Hossack et al. results describe that Stroke Volume and Cardiac Output at maximal exercise were lower in women than in men, thus, a Sex difference in stroke volume ( $p < 0.001$ ) was responsible for virtually all of the effect of sex on maximal cardiac output<sup>(38)</sup>. Moreover younger men had higher values for  $VO_{2max}$  and maximal cardiac output than younger women<sup>(39, 40)</sup>. Both results are consistent with our research. SV is significantly different among groups at all workloads only for

gender effect, while at higher workload CO is significantly different per Sex and Age among groups, because CO is down-regulated by HR (different per Age) and SV (different per Sex)<sup>(41,42)</sup>.

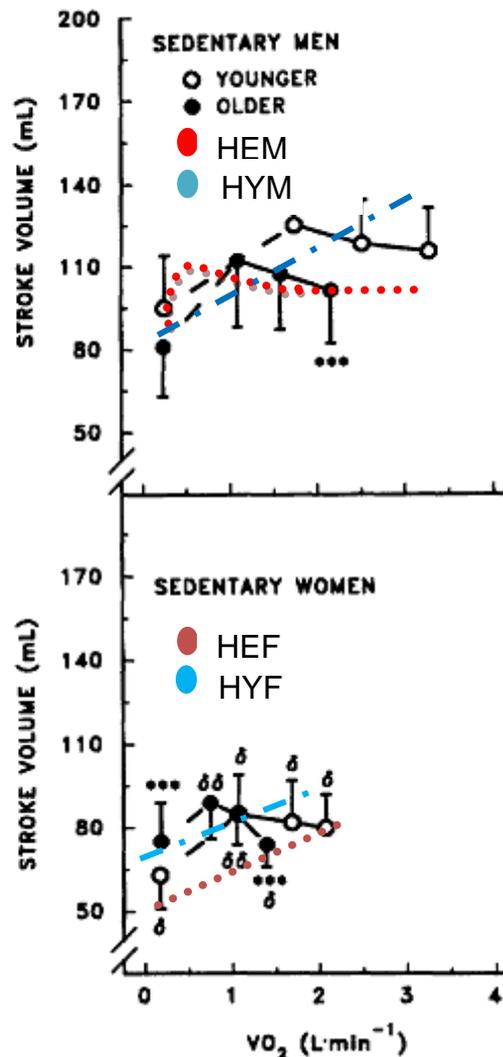


Figure 29 Ogawa et al<sup>(9)</sup>; HEM/F and HYM/F trends added

Furthermore, males and females use two different strategies to enhance CO during the effort: Females progressively and continuously deploy the pumping reserve function of their heart, Males after a similar initial rise in SV to 40%, follow 2 different patterns, that do not change the CO result but indicate that HEM are unable to further enhance their SV.

The skeletal muscle oxidative capacity is lower in older than in younger sedentary subjects<sup>(39, 40)</sup>, but diabetics subjects, even if closer in age to our elderly subjects, show an oxygen extraction similar to that of young groups. It may be proposed that the difficulty encountered by the diabetics in utilizing carbohydrate substrates for cellular metabolism is partially compensated by a sustained enrichment of mitochondrial oxidative enzymes in order to improve fatty acid utilization.





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**CAP 3. STUDY 2:**

**“Gender, age and Pathology-related factors in acute cardiovascular adjustments to dynamic resistance and isometric exercise”**





## LEG PRESS DYNAMIC TEST

### Hypothesis

We tested the hypothesis that cardiovascular adaptations to dynamic exercise are different per sex and gender, and in presence of pathology.

### Background

An integrated view of the physiological responses to physical exercise is seldom offered by the available literature, since hemodynamic, metabolic and muscle variables are generally studied in different subjects, by a variety of methods and tools. In this study Cardiovascular changes are matched to metabolic and muscle-related adjustments during resistance exercise, in order to collect the performance characteristics and strategies of the different population (young and elderly men, etc). The resistive exercise is by definition the exercise that augments muscle mass, but is also important in sports and rehabilitation because it produces a lot of beneficial effects, such as muscle hypertrophy, better coordination, injury prevention, increment of nervous system connection with the muscles, aerobic capacity, microcirculatory adaptations etc <sup>(1,2,3,4)</sup>. In contrast to aerobic exercise, which involves low resistance and high number of repetitions, resistance exercise includes high-resistance and low number of repetitions. It is however known that this kind of exercise is not devoid of training effects on the overall aerobic power. Furthermore Harridge et al. suggested that the age related decline in aerobic capacity can be explained in part by decreased muscle mass <sup>(5)</sup>. This is associated with increased risk of cardiovascular disease, stroke, hypertension, and mortality <sup>(6, 7, 8, 9)</sup>. During exercise numerous physiological interactions occur and the most significant interplay is between the cardio respiratory system and skeletal muscle, which determines both O<sub>2</sub> supply and demands <sup>(11)</sup>. Moreover it is well documented that both muscle mass and strength, decline with age. This decline is associated with an increased risk of falls, hip fractures and a loss of bone mineral density. Consequently, these changes may predispose elderly individuals to osteoporosis, atherosclerosis, and diabetes as well as to functional limitations in activities of daily living <sup>(11)</sup>. It was also reported that 50% of the decline in VO<sub>2max</sub> with aging was accounted for by the decline in muscle mass and increase in fat mass; thus, the remaining 50% was related to a decline in oxygen delivery and / or oxygen extraction <sup>(12, 13)</sup>. In addition resistive exercise induced neural adaptations resulting in increased weight-lifting capacity <sup>(14, 15, 16)</sup>. However the majority of data suggest that the relative strength gains are similar between young and old individuals <sup>(17)</sup>, but older individuals did not hypertrophy as much as younger individuals. Jubrias demonstrated a significant improvement in oxidative metabolism after acute exercise and attributed these changes to the low initial habitual physical activity level of older that have reduced abilities to perform daily

living activities. Furthermore, resistance exercise training can improve function in healthy and hospitalized individuals; for this reason it is crucial to study what happens during the performance of resistance exercise, such as on the leg press machine<sup>(18)</sup> that was used for our experiments. These training induced strength gains are attributed to adaptations occurring in a number of components of the motor system. Although hypertrophy is reported as one of the major factors contributing to strength gains with training, the increase in muscle size does not solely account for the increase in strength. This indicates that other factors, such as increased activation capacity of agonist muscles, reduced activation of antagonist muscles, and changes in tendon stiffness, might play a role in the strength gains observed with training in older age<sup>(19)</sup>. Resistive exercise, thus, can improve the global fitness of individuals: that is why we considered really important to clarify the physiological implications, and characterized every component. In our study we used bilateral leg press exercise, that is a multi joint (hip, knee and ankle) exercise, one of the most common resistance training type of exercise used to enhance performance in sports and in knee rehabilitation<sup>(20)</sup>. Moreover regarding leg press exercise, greatly increased blood pressure during high intensity static exercises has been found. However, there have not been many studies dealing with cardio respiratory responses to leg press exercise. Although during strength exercise blood flow and oxygen uptake increase rapidly<sup>(21)</sup>, a mismatch between the time course of changes in blood flow and oxygen uptake suggests that blood flow is not directly regulated by the need of oxygen in the exercised muscles. The hyperemic response may be linked to locally released factors, such as ions and metabolites<sup>(22, 23)</sup>. However the signal by which blood flow is elevated remains unknown, and the cardiovascular effects of resistance exercise, matched with metabolic and peripheral O<sub>2</sub> utilization data, are still poorly understood<sup>(24)</sup>.

In additions Resistance Exercise plays an important role in the prevention and control of insulin resistance, prediabetes, type 2 diabetes, and diabetes-related health complications. Both aerobic and resistance training improve insulin action, at least acutely, and can assist with the management of lipids, Blood Pressure, Cardiovascular risk and mortality, but exercise must be undertaken regularly to have continued benefits and likely include regular training of varying types. Persons with type 2 diabetes should undertake moderate to vigorous resistance training at least 2–3 days/week<sup>(25, 26, 27, 28)</sup>. Reduced exercise capacity in diabetics has been attributed to limitations in cardiac function and microvascular dysfunction leading to impaired oxygen supply and nutritive perfusion to exercising muscles.<sup>(29)</sup> Furthermore Strength training has been shown to be of great value in preventing and managing diseases and promoting health. It increases muscle force, lose fat, under regulate blood pressure, etc. There are a lot of data about resistive exercise, but it is still important to clarify the contributions of central and peripheral adjustments in response to leg press exercise in order to

quantify and interpret the whole adaptation to this kind of stimuli and adapt training strategy per gender, age or presence of pathology.

## Aim

The aim of the present project is to characterize hemodynamic acute responses during leg press exercise, matched with metabolic and peripheral data, in different subjects: Healthy elderly (HEM/F) and Healthy Young Subjects (HYM/F), Diabetes mellitus type 2 Patients (D2M/F), male and female. The present project characterizes cardiovascular responses: pressure values (SYS DIA MAP systolic/diastolic), heart rate (HR), stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR); metabolic parameters: oxygen consumption ( $\text{VO}_2$ ), carbon dioxide production ( $\text{VCO}_2$ ), ventilation (VE), respiratory quotient (R); and muscle responses: oxygen extraction (DeOxyHb), Femoral Blood Flow (FBF).

## Methods

D2M/F: sedentary (International Physical Activity Questionnaire  $<1000$  MET min\*week), diet and/or oral hypoglycaemic agents, diabetes diagnosis at least 1 year before ( $15.1 \pm 6.9$ y D2M  $11.1 \pm 4.9$ y D2F) and, HbA1c  $7.1 \pm 0.5$  % D2M and  $6.4 \pm 2.2$  D2F, HDL  $53.1 \pm 10.1$  mg/dL D2M and  $47.5 \pm 17.4$  mg/dL D2F, Total Cholesterol  $142.8 \pm 20.9$  mg/dL D2M and  $140.8 \pm 48.5$  mg/dL D2F, non-smokers, no evidence of chronic complications.

HEM/F: sedentary, non-smokers, no evidence of chronic complications or presence of other pathologies

HYM/F: sedentary, non-smokers, no evidence of chronic complications or presence of other pathologies

GROUP	N°	AGE	WEIGHT	HEIGHT	B.M.I	1RM
<b>HYF</b>	12	$23,66 \pm 2,49$	$55,916 \pm 5,7$	$1,64 \pm 0,1$	$20,60 \pm 2,1$	$232,1 \pm 43,1$
<b>D2F</b>	4	$57,25 \pm 5,9$	$65,25 \pm 1,0$	$1,5925 \pm 0,0$	$25,7 \pm 1,4$	$205 \pm 5,7$
<b>HEF</b>	12	$67,1 \pm 7,1$	$58,2 \pm 5,0$	$1,57 \pm 0,1$	$23,47 \pm 2,3$	$158,5 \pm 23,4$
<b>HYM</b>	13	$22,6 \pm 1,3$	$68,6 \pm 8,7$	$1,75 \pm 0,1$	$22,27 \pm 2,6$	$273,8 \pm 36,8$
<b>D2M</b>	9	$60,3 \pm 6,4$	$82,1 \pm 11,5$	$1,73 \pm 0,0$	$27,19 \pm 3,4$	$263,3 \pm 48,0$
<b>HEM</b>	13	$67,3 \pm 2,7$	$83,75 \pm 8,5$	$1,705 \pm 0,0$	$28,84 \pm 3,0$	$251,2 \pm 65,8$

Table 10: Anthropometric data of groups, and maximal weight lifted on leg press (1RM)

## Protocol and equipment

On receiving each subject, the experimenter held a brief interview to record personal data and a health schedule with medical information and performed anthropometric measurements. He explained the functioning and use of the leg press machine and the experimental protocol, and obtained written consent. After a 15 min warm up by pedaling on a cycle ergometer with light load, the subjects sat on the leg press machine (Horizontal Leg Press Technogym, Italy) while the experimenter accurately checked for correct starting positioning: full leaning of the column on the backrest, feet pressing on the vertical board spaced at the hip level, 90° knee angle, right hand on the handgrip (the left hand was left free for arterial pressure measurement, as explained below).

The individual theoretical maximal load for 1 repetition (1RM) on the leg press was determined according to Brzycki formula<sup>(30, 31, 32, and 33)</sup>. The subject repeatedly pushed against a load initially set on the basis of his body weight. The load was increased in following series, after complete recovery from previous work fatigue, until the maximal repetition number did not exceeded 12; a resting pause by 3 min was allowed between series. The last load and repetition number were entered the formula:

$$1\text{-RM} = \text{weight lifted} * (1.0278 - (0.0278 * \text{repetition number}))^{-1}$$

70% 1RM was then selected as the individual load for the experiments that were started at least 30 min later<sup>(34, 35)</sup>. Each subject performed three series of dynamic resistance exercise at 70% of previously determined 1RM, separated by 10 min resting: two series with 12 repetitions and the third series with repetitions to voluntary exhaustion in order to estimate the individual maximal performance on the specific exercise. Each cycle of leg extension/flexion lasted about 5 seconds, as suggested by the operator by counting in a loud voice up to 2 and 3 for the concentric and the eccentric phase respectively; however, the overall duration of each series was not strictly constant. In order to minimize the confounding effects of Valsalva's maneuver during the efforts<sup>(36)</sup>, and the irregular expulsive maneuvers caused by simultaneous contraction of diaphragm and abdominal muscles<sup>(36)</sup> the subjects were also invited to avoid breath holding and to breathe regularly, which was eased by the vocal pace offered by the operator.



Figure 28: The pictures report the protocol setup.

The subjects were connected to a metabolimeter (K4 b<sup>2</sup> Cosmed, Italy). The middle finger of the left hand was wrapped with an appropriate size cuff of the apparatus for finger pressure measurement (Portapres TNO, Nederland). The left arm lay comfortably on the subject's waist. Arterial pressure was controlled by standard sphygmomanometry to check the finger pressure values, and if discrepancies > 10 mmHg were found the finger cuff was repositioned or substituted until satisfactory measurements were obtained.

The NIRS (ISS, Oxyplex) probe was positioned at the level of the lateral quadriceps, and was wrapped up with opaque tissue, in order to avoid interference by ambient light.

On the other leg we used an echo vascular Doppler to analyze femoral artery flow velocity.

The following variables were recorded and further analyzed offline:

- respiratory/metabolic (breath-by-breath): oxygen consumption ( $V'O_2$ ), carbon dioxide production ( $V'CO_2$ ), and respiratory quotient (R);
- cardiovascular (cycle-by-cycle): systolic (SP) and diastolic (DP) arterial pressure, heart rate (HR); by pressure contour method (Modelflow algorithm, TNO, Nederland) cardiac output (CO), stroke volume (SV) and total peripheral resistance (TPR).
- Oxygen muscular extractions, With Hhb DeOxy (deoxygenate Hemoglobin);
- FBF (Femoral Blood Flow), coupling diameter and blood velocity data of the vessel.( Echo Doppler P 50)

## Statistics

Since the time course of exercises was not identical among the subjects, data are presented as mean  $\pm$  SD at different points: baseline, 10 sec of exercise, peak, 20 sec post exercise, and 60 sec post exercise. Two Way Repeated Measures ANOVA (One Factor Repetition) was used to detect significant differences ( $P < 0.05$ ). Bonferroni correction was performed when group statistics indicated significant differences. SigmaPlot® (Systat USA) software was used.

The significance of differences is reported as: AGE ( $\text{Æ}$ ), SEX ( $\text{\$}$ ), presence of Pathology ( $\text{\hat{d}}$ ).

## RESULTS

### Cardiovascular

All cardiovascular parameters will be described as an average of the group at 5 different conditions: basal status (BASE); 10 seconds of exercise (10EXE); exercise peak (PEAK); 20 seconds of recovery (20REC) and after a minute post exercise (60 REC).

In the figures, white symbols represent male groups and black symbols female groups; the circles are young persons, squares are elderly people and triangles are diabetes 2 subjects.

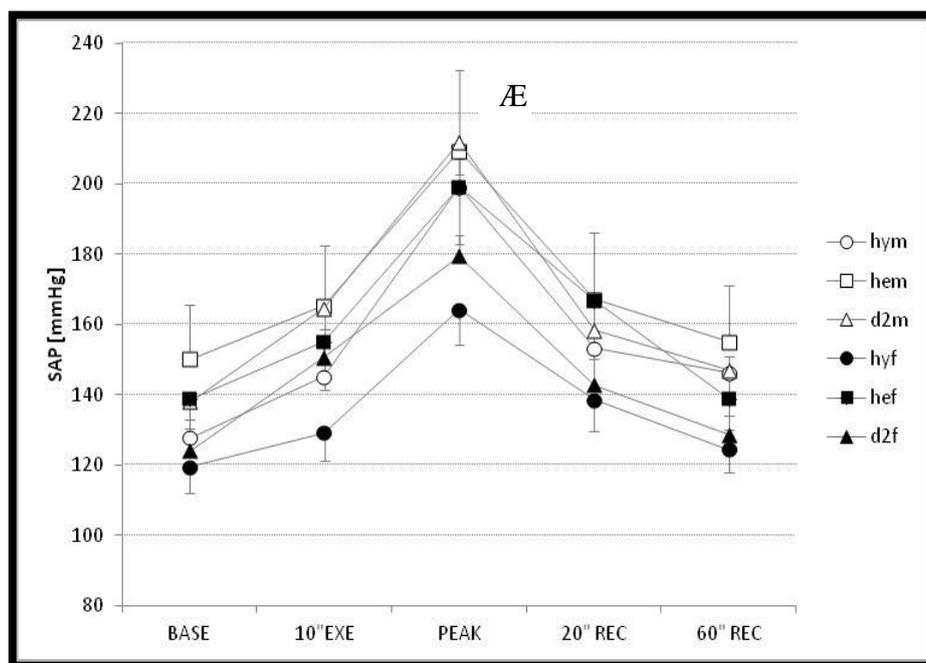


Figure 30: SAP during leg press exercise

BP, SAP and DAP, show that all subjects followed the known trend. With the protraction of the effort, all pressure values increase progressively until the peak, and rapidly fall down to reach the basal value after cessation of the efforts.

Elderly have higher values at baseline, but the relative increase to peak is similar to the other groups. In general, it is also evident that males attain higher relative pressure than females, and at the peak conditions both D2M/F and HEM/F display higher values than young subjects.

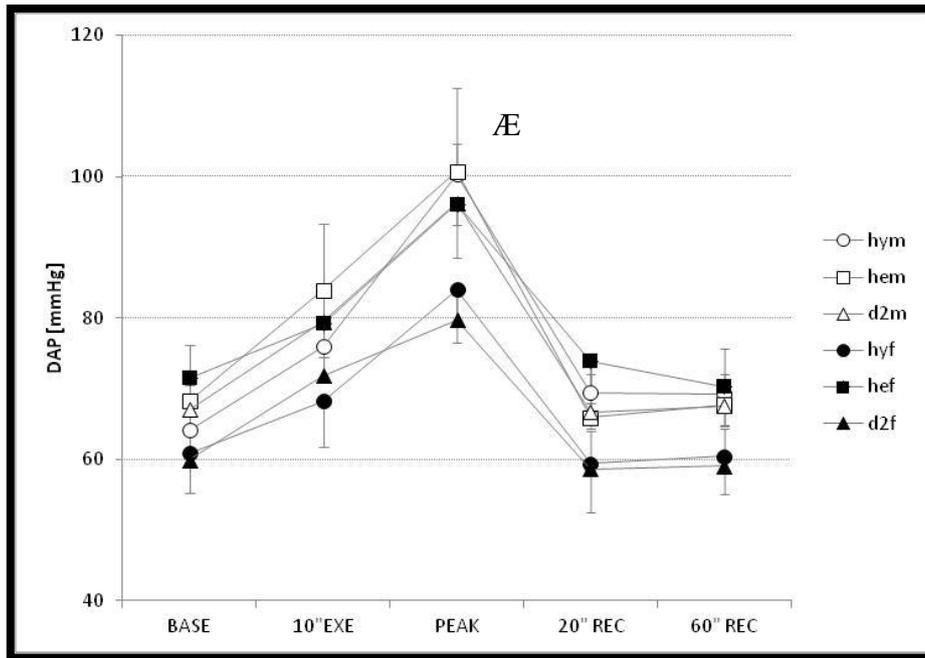


Figure 31: DAP during leg press exercise

The only evident difference between DAP and SAP, is that DAP decreases rapidly (20'') to get the basal level while SAP takes 60'' in all groups

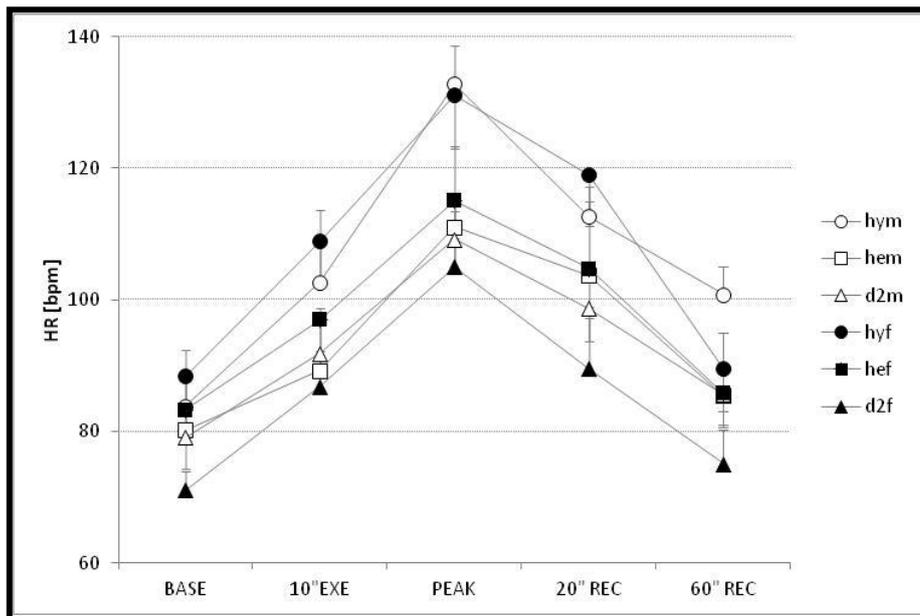


Figure 32: HR during leg press exercise

HR during leg press exercise increases rapidly until the peak. It is quite clear that young groups respond to the resistive exercise with higher heart rate. There is no difference per sex, but a significant difference per age at peak level.

HR					
	BASE	10"EXE	PEAK	20" REC	60" REC
HYF	88.42±18.1	108.96±19.3	131.14±25.7	118.94±24.6	89.52±20.2
HEF	83.29±11.3	97.02±12.9	115.12±15.1	104.69±15.2	85.81±13.2
D2F	71.06±5.0	86.82±4.1	104.99±14.6	89.46±13.2	75.06±9,1
HYM	83.84±28.0	102.67±36.4	132.8±19.5	112.67±14.6	100.77±14
HEM	80.16±27.3	89.21±29.9	111.08±38.5	103.64±35.5	85.37±30.6
D2M	79.04±14.0	91.83±11.13	109.19±13.3	98.63±15.1	85.65±13.9

Table 11: HR during and after leg press exercise

The other important parameter analyzed is Stroke Volume (SV) whose changes in this kind of exercise are peculiar and different among the populations studied.

The pattern of HYM/ HYF is similar, SV increases in parallel to HR and BP until peak and further increases at twenty seconds (20") post exercise. and sub sequentially slowly decreases towards basal values.

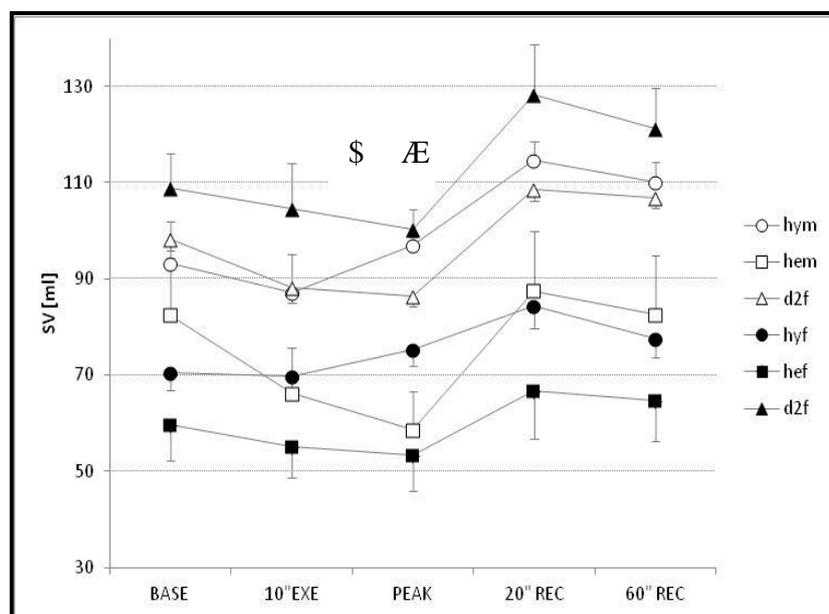


Figure 33: SV during leg press exercise

The tendency that has been evidenced previously in the post exercise phase is common to all populations. Therefore, it seems to represent a peculiar adaptation to this kind of stimulus. It must be noted, however, that D2M/F HEM/F adjust SV differently than the young groups: the pattern shows an evident decrease in SV during exercise until peak, which is exactly the opposite to the adaptations of the young.

SV					
	BASE	10"EXE	PEAK	20" REC	60" REC
HYF	70.54±11.74	69.71±10.63	75.297±10.98	84.26±14.73	77.52±11.83
HEF	59.56±19.25	55.05±16.86	53.27±19.73	66.74±26.31	64.76±22.57
D2F	108.74±12.63	104.59±16.51	100.34±7.26	128.33±17.99	121.30±14.47
HYM	93.27±28.4	87.17±26.40	97.00±5.73	114.70±12.68	110.13±13.87
HEM	82.48±37.38	66.17±29.77	58.63±24.98	87.52±39.27	82.52±37.38
D2M	98.33±7.3	88.07±8.92	86.33±6.38	108.55±7.13	106.78±6.26

Table 12: SV during and after leg press exercise

Cardiac output was generally characterized by a progressive increase during the effort and up to 20" post exercise, with obvious quantitative differences among the groups, but the increase did follow some peculiar patterns. HYF and HYM peaked at peak exercise and held the same level; diabetics (M and F) and HEF peaked at 20"; HEM failed to increase CO during the effort but displayed a large increase at 20".

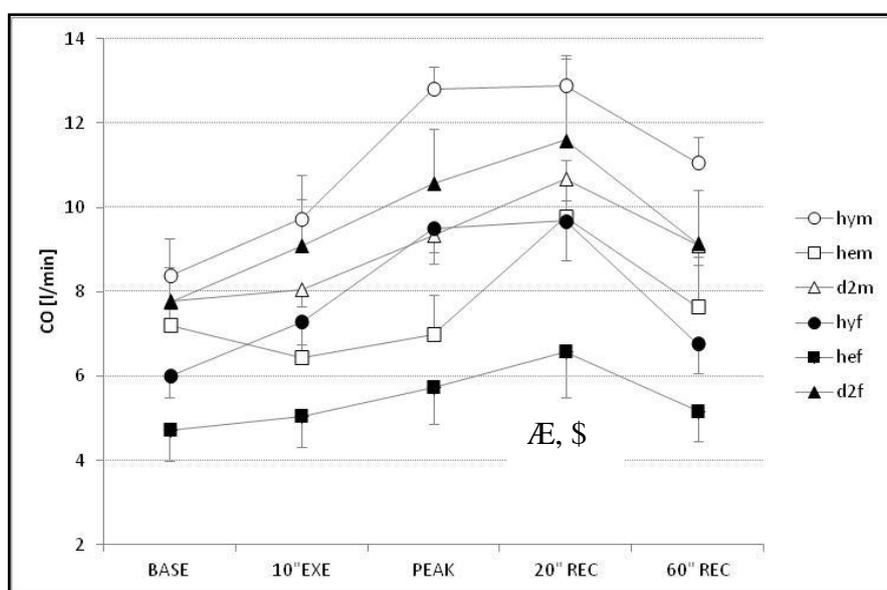


Figure 34: CO during leg press exercise

CO					
	BASE	10"EXE	PEAK	20" REC	60" REC
HYF	6±1.63	7.28±1.70	9.5±2.60	9.67±2.92	6.76±2.24
HEF	4.71±1.9	5.05±1.95	5.72±2.30	6.58±2.91	5.17±1.88
D2F	7.74±1.44	9.1±1.88	10.56±2.21	11.59±3.4	9.14±2.1
HYM	8.38±2.90	9.73±3.44	12.8±1.78	12.89±2.3	11.06±2.02
HEM	7.2±3.45	6.43±3.03	6.99±2.93	9.76±4.27	7.63±3.77
D2M	7.77±1.64	8.05±1.16	9.34±1.21	10.67±1.56	9.10±1.38

Table 13: CO during and after leg press exercise

The last cardiovascular parameter to be considered is Total Peripheral Resistance (TPR). If at 20'' recovery all groups show a decrease in TPR, preceding events are different: in particular TPR increased throughout the effort in the aged population while it was substantially unchanged in the others. As may be expected, absolute values of total peripheral resistance are age-related.

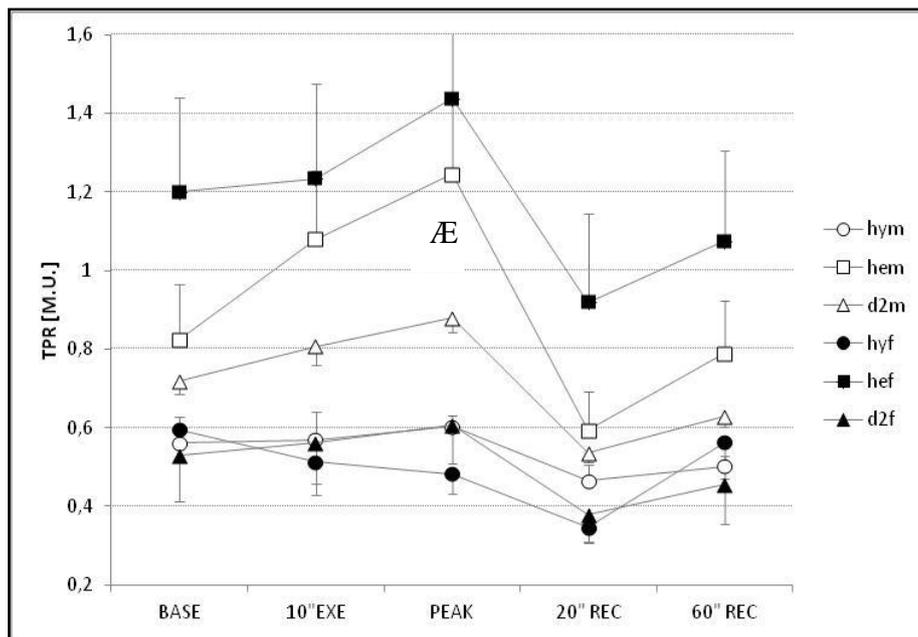


Figure 35: TPR during leg press exercise

## Metabolic

The oxygen uptake during resistive exercise has been already documented, but the post exercise oxygen consumption after a strength exercise deserves further attention.

VO<sub>2</sub> shows a progressive increase during the effort, similar in all groups, and a peculiar response after the end of the series on the leg press. During recovery the oxygen consumption follows different trends among the groups, but in all cases it does not decrease sharply at the end of the exercise, as is usually seen in VO<sub>2</sub> kinetics of aerobic exercise, even if strenuous.

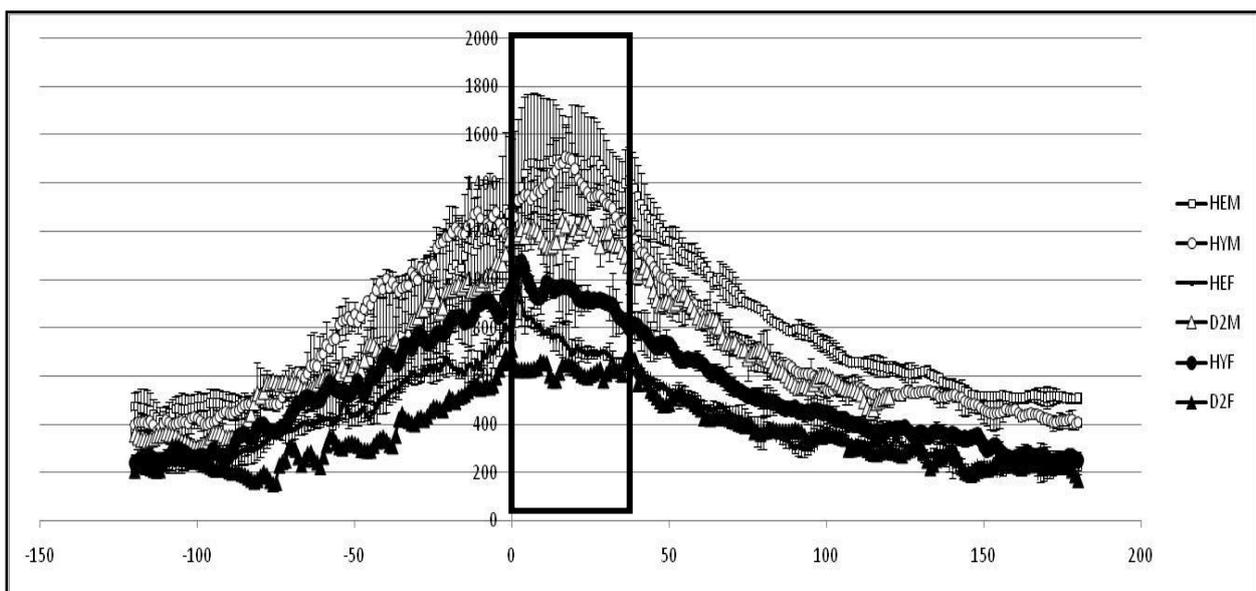


Figure 36: VO<sub>2</sub> during leg press exercise

The pattern of VO<sub>2</sub> changes during and after Leg Press exercise is not identical in each population: in the following 2 graphs that focus on Sex differences, it is clear how males and females adapt to the exercise.

Males have always higher value over the entire the test, but they increase VO<sub>2</sub> uptake during recovery more than the other groups: HEM and HYM maintain elevated oxygen consumption until 30 sec post exercise. D2M show a kind of steady state from the peak of exercise to 30 sec recovery. Females, HYF and HEF display a second peak of oxygen uptake at 10 sec recovery, differently from D2F that show an initial decrease with a second small steady state response until 40 sec. However only HYM and HEM display a significant increase in VO<sub>2</sub> consumption during recovery.

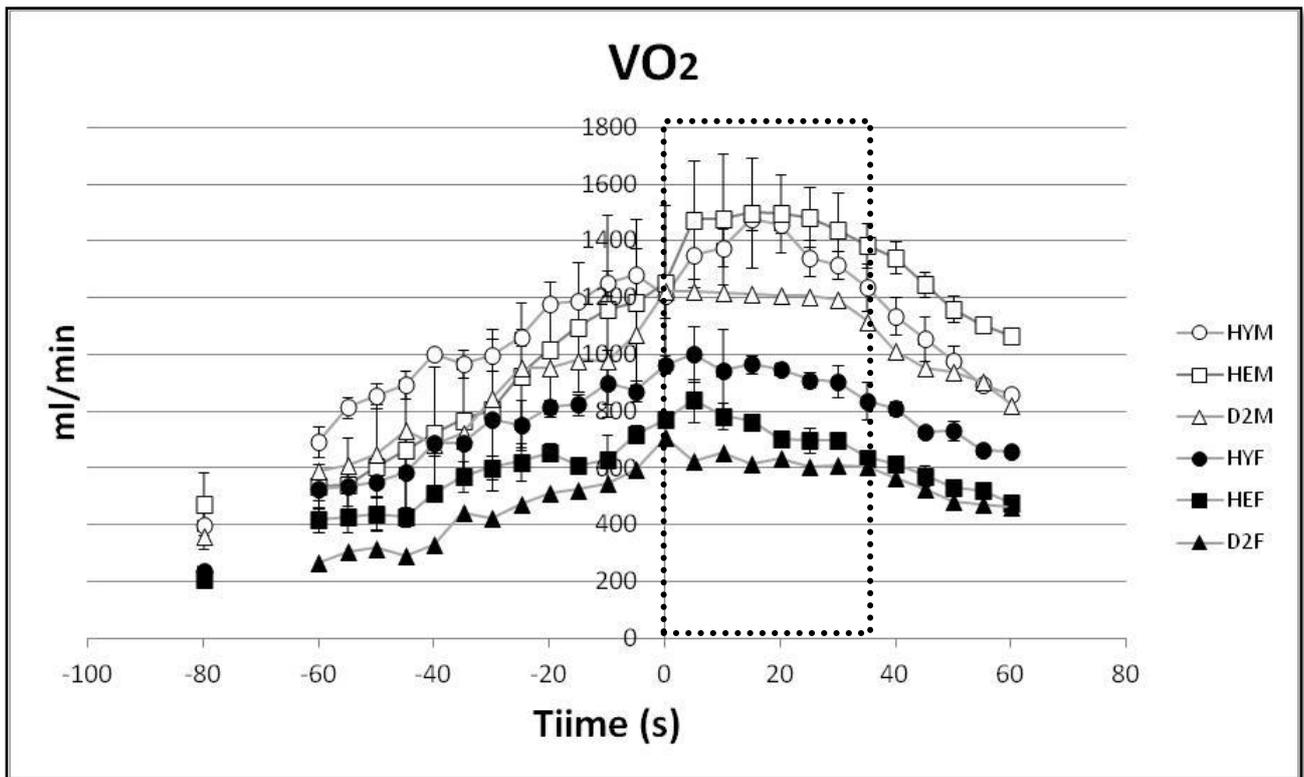


Figure 37: VO<sub>2</sub> during leg press exercise, every 5 sec

The Post VO<sub>2</sub> excess anyway, shows that the passive recovery is very slow for all groups, since all recovery trends take at least 40 sec to start a progressive decrease.

In the following figures the same data are reported, but in 5 standardized conditions: baseline, start of exercise (10 sec), peak of exercise, and 2 post exercise points (20 sec and 60 sec). In this way the differences are clearer, but at the same time in female groups VO<sub>2</sub> post exercise enhanced consumption disappears.

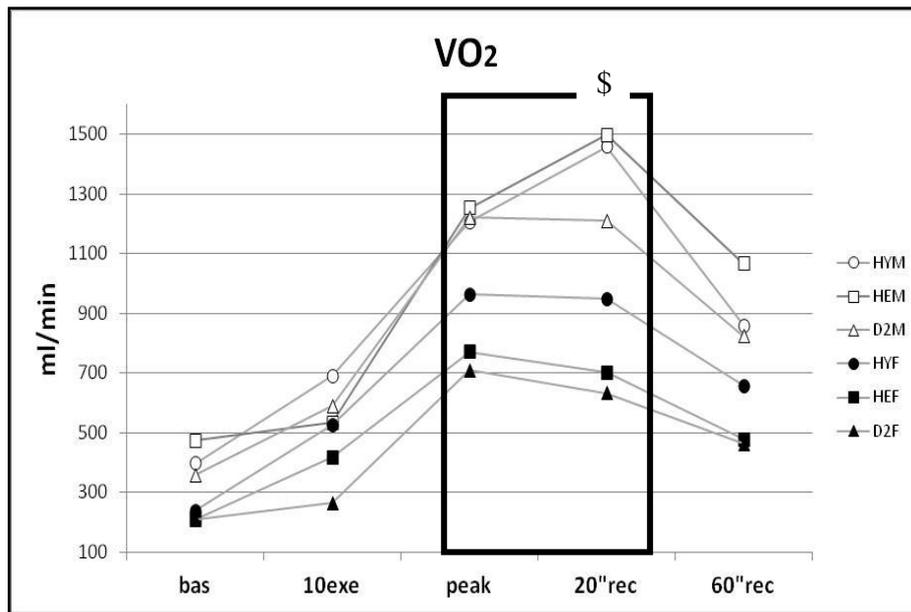


Figure 38: VO<sub>2</sub> during leg press exercise, 5 different time of exercise

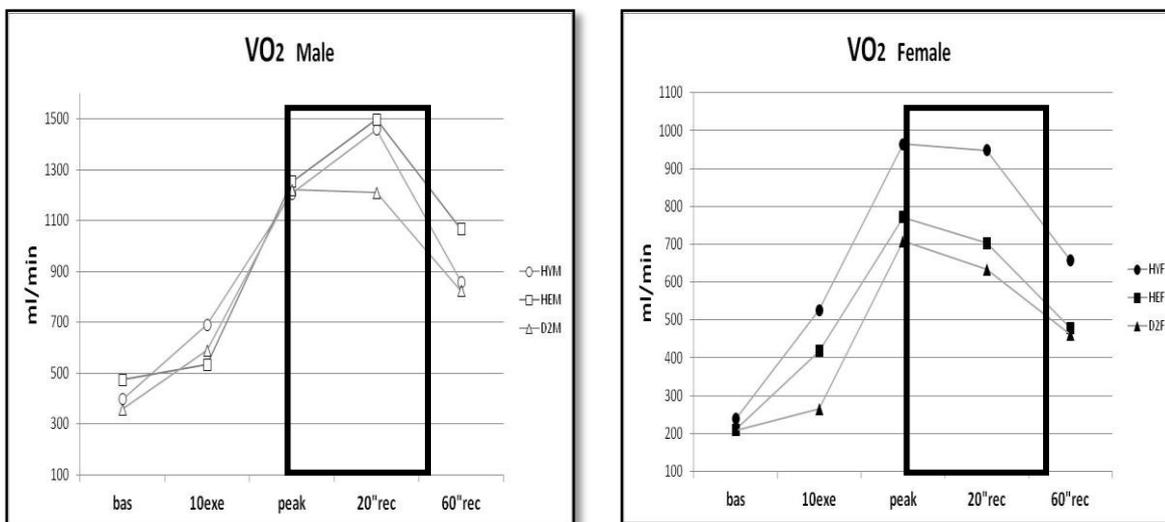


Figure 39; 40: VO<sub>2</sub> during leg press exercise, 5 different times of exercise, and per sex

In order to make clear the relative increase of Oxygen uptake at the end of exercise, in Fig 41 the same data are reported, but as a percentage of increase from the peak condition. It is evident that only HEM and HYM trends are clearly over the zero line to indicate a more marked post exercise hyperemia (PEH). However HYF group shows a point (5 sec post exercise) over the zero line, and also HEF have 2 points over zero. Moreover it is important to notice that the relative percent increase is quantitatively smaller in female.

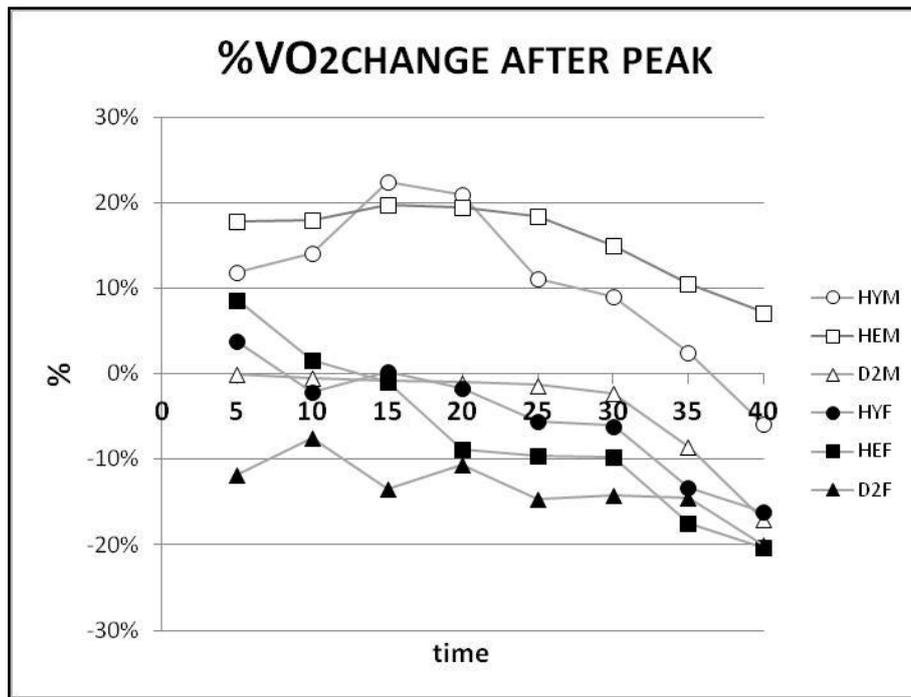


Figure 41: % VO<sub>2</sub> during recovery of leg press exercise

As is reported in table 14, POST EXERCISE consumption increases in: HEM until 40 sec from 20-18% to 7%; HYM until 35 from 22% to 3%; D2M until 10 sec and stand on 0% (steady state); HEF until 10 sec from 2% to 9%; HYF until 20 sec from 0% to 4%; D2F doesn't increase.

It is, also, interesting to consider the age-related differences. The PEH response is bigger in HEM than in HYM, as well as in HEF than in HYF.

Diabetics groups show completely different patterns during PEH phase: this might be due to a pathology related interaction peculiar to this post exercise phase, since during the exercise the trends are quite similar to the others groups, and follow the age and sex differences.

## Muscular

FBF (femoral blood flow) during leg press exercise is described in Figs 42 and 43, but HEM data are missing.

Immediately at the beginning of the exercise, FBF starts a progressive rise until the end of exercise, but the slope of the increase is quite different among groups, with highest values reached by HYM and D2M. At the end of the effort in the young subjects (and also in D2F) FBF kept increasing for further 10" and then declined, while in the other groups it immediately declined towards control levels that however were not attained within 90".

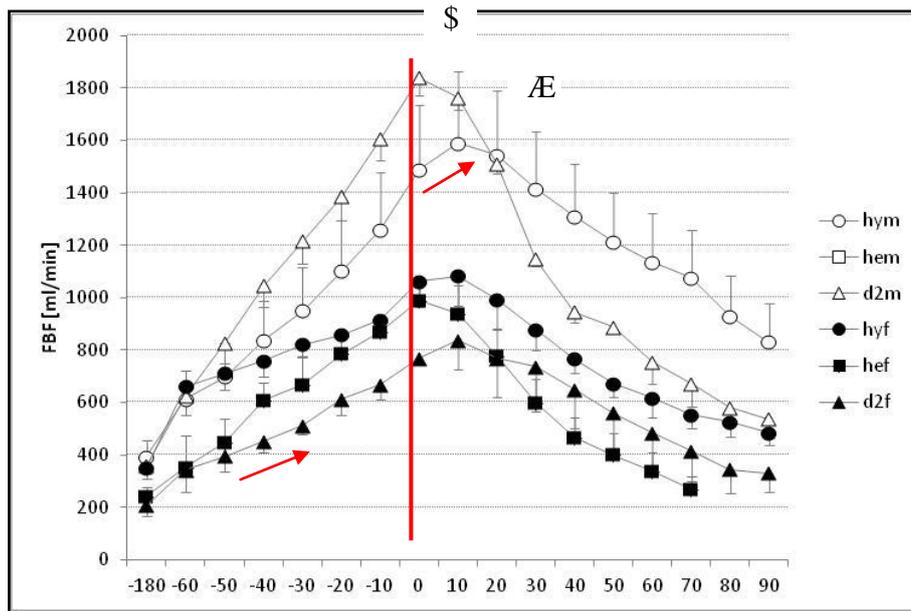


Figure 42: FBF of leg press exercise

The following table and figure report the percent changes in FBF. The relative increase during the exercise is rather similar among groups, with the notable exception of diabetics, whose FBF increases more.

	D2M	D2F	HEF	HYF	HYM
<b>baseline</b>	0	0	0	0	0
<b>-60</b>	74,37%	64,81%	45,66%	89,16%	56,00%
<b>-50</b>	131,32%	90,61%	85,43%	103,92%	77,73%
<b>-40</b>	191,98%	118,46%	152,54%	117,86%	113,51%
<b>-30</b>	239,42%	146,30%	176,49%	135,27%	142,03%
<b>-20</b>	286,87%	194,95%	225,02%	145,72%	180,84%
<b>-10</b>	348,30%	221,29%	260,16%	162,01%	221,08%
<b>peak</b>	<b>413,76%</b>	<b>270,58%</b>	<b>309,06%</b>	<b>203,74%</b>	<b>279,49%</b>

Table15: FBF during leg press exercise

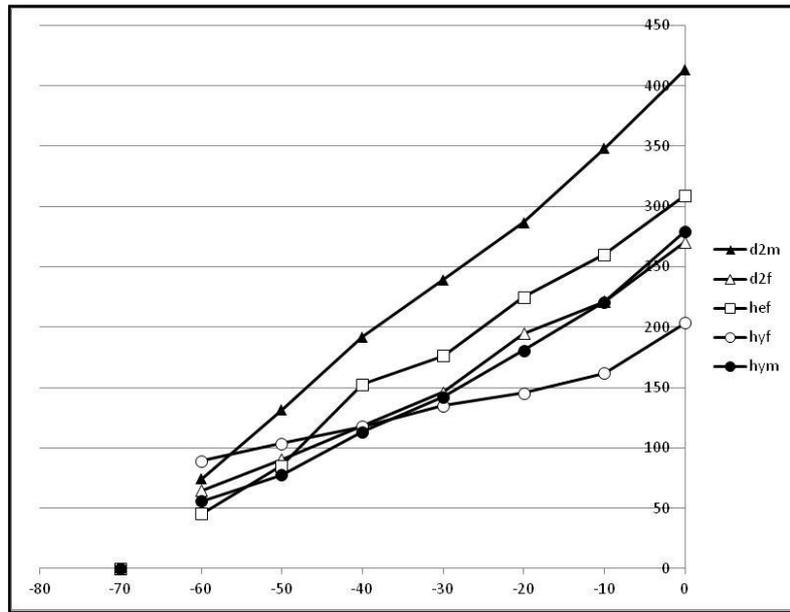


Figure 43: FBF during leg press exercise

The local oxygen extraction during and after leg press exercise was estimated on the basis of NIRS data, as reported in Fig. 44, showing changes in HHb. In all groups oxygen extraction increased during the exercise and progressively returned to control values thereafter. The trend was similar in all groups, but changes were much higher for diabetics when compared to same sex non diabetic subjects.

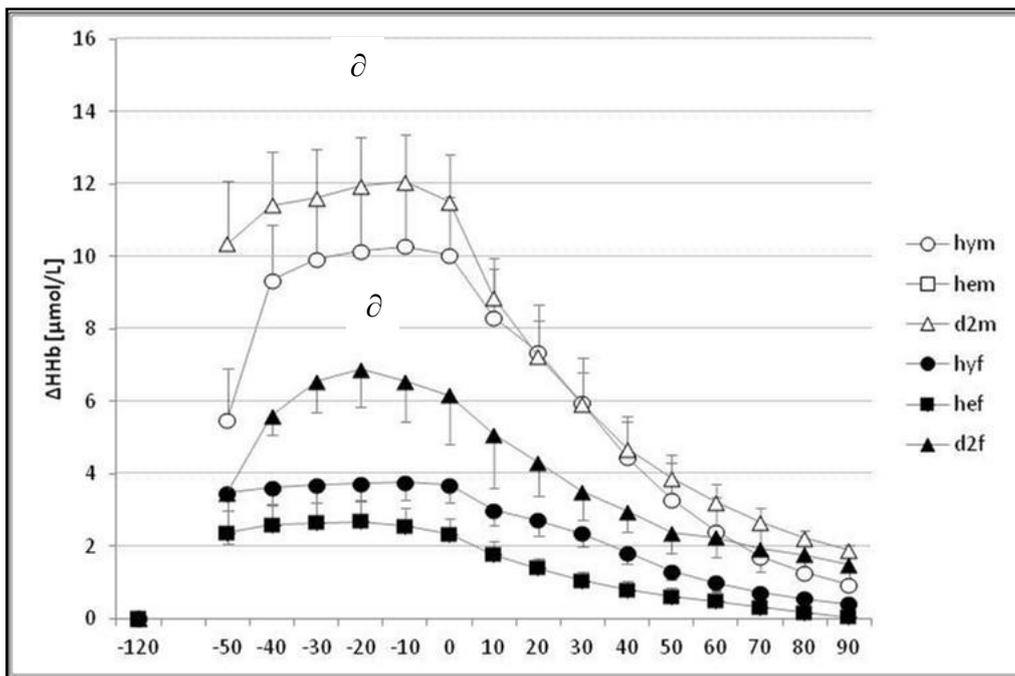


Figure 44: HHb during leg press exercise

## **Discussion**

The leg press machine is widely used in weight training sessions. This kind of exercise represents also a sequence of movements common to many ordinary behavior actions; for this reason it is often proposed to every kind of subjects <sup>(38)</sup>. Resistance exercise training and subsequent increases in muscle mass reduce multiple cardiovascular disease risk factors. The inclusion of Resistance exercise as part of an exercise program for promoting health and preventing disease has been endorsed by the American Heart Association, American College of Sports Medicine, and the American Diabetes Association as an integral part of an overall health and fitness program. Furthermore Cross-sectional studies have shown that muscular strength is inversely associated with all-cause mortality and the prevalence of metabolic syndrome independent of cardio respiratory fitness levels.

In this study we tried to clarify the acute response to a single bout of leg press exercise with a focus on overall response. The same methods were applied to every group in order to offer a complete description of each parameter in response to this exercise according to sex, age and pathology.

### **Cardiovascular response**

The hemodynamic response to large-muscle exercise was characterized by an increase in HR, following known literature data. Young groups reached higher HR than elderly and diabetics (who are anyway older than the young group), that display a reduced chronotropic capacity, but D2M and D2F show the lowest HR increase. In accordance with Halliwill J.R., who reported an increase of mean arterial pressure (MAP), during a single bout of dynamic exercise, in our study SAP and DAP look similar among the groups, both increasing until the end of the effort. HYM showed a larger increase of SAP in comparison with others, but this may possibly be related to the higher effort <sup>(39)</sup>. Women, independently of the age, always have lower pressure values, as reported for instance during graded single-intensity knee kicking <sup>(40, 41)</sup>, and fully confirmed by our data.

Cardiovascular acute adaptations in terms of SV and CO seem to be dependent on age. After an initial decrease (10" sec of exercise) HYM/F are able to increase the SV response during the entire exercise period, while HEM/F and D2M/F, display a drop until the end of exercise; at 20" sec recovery both HY and HE/D attain the same value (Fig 45).

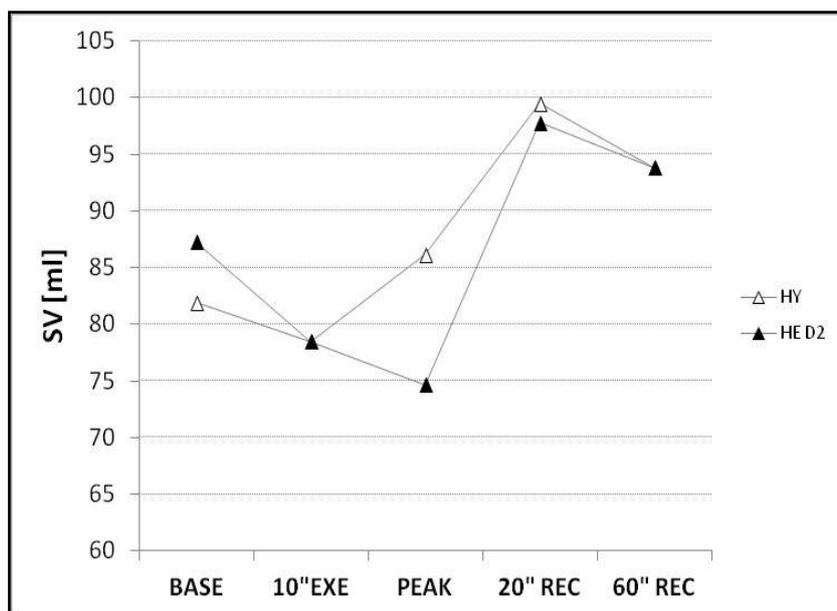


Figure 45: SV in absolute values, comparison between young and aged (D2M/F and HEF/M)

We suggest that in the older subjects the combined effects of reduced myocardial contractility and impaired vasodilatation in the contracting muscles combine to impair the ability of the heart to eject blood during a type of exercise that comprises relevant isometric phases. It is also possible that HEM and HEF helped their limb movements by contracting abdominal muscles in the concentric phase of the movements, thus raising intra abdominal pressure and decreasing venous return to the heart.

As a consequence of the peculiar pattern of SV changes, combined with more homogeneous changes in HR, CO practically does not change in the elderly group, while it rises in the young and exhibits an unexpected higher increase in the diabetics, especially female. A blunted response of CO in the elderly during strength exercise was reported by Ridout<sup>(62)</sup>.

In general, during dynamic strength exercise, TPR ought to fall, as stated by Lindle (1997), reporting “a profoundly reduced systemic vascular resistance during a single bout of dynamic exercise”<sup>(39)</sup>. This fall did not happen in our older subjects who, to the contrary, increased TPR until the end of the effort. One possibility is that they were unable to take advantage of the eccentric phase of their hind limb movements in the leg press machine, when most of the intramuscular pressure should be released thus allowing for muscular vasodilatation.

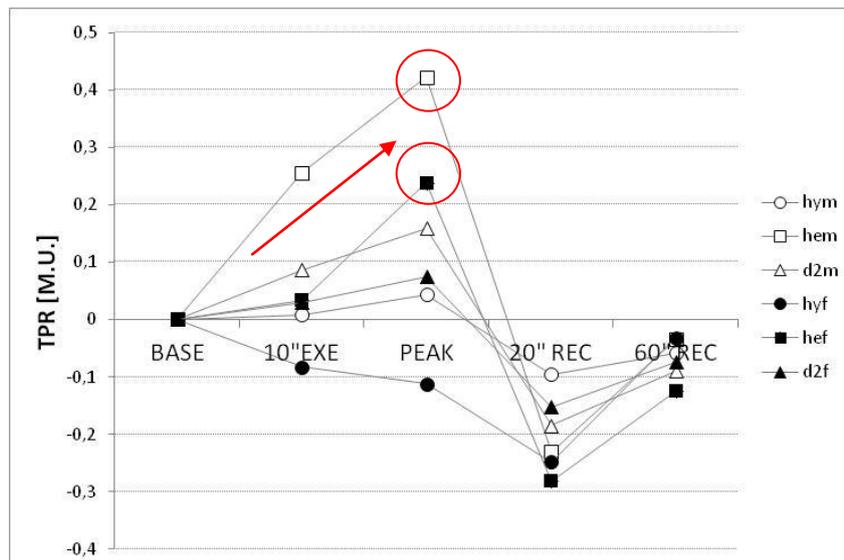


Figure 46: TPR delta on basal values

### Metabolic response

A single bout of dynamic exercise is reported to generate an elevated post exercise oxygen uptake ( $\dot{V}O_2$ )<sup>(2, 3, 16, 26, and 30)</sup>. This increase in post exercise  $\dot{V}O_2$  is commonly referred to as excess post exercise  $\dot{V}O_2$  and is described as the excess  $\dot{V}O_2$  above that required to support resting metabolic processes after exercise<sup>(39)</sup>. The difference between  $\dot{V}O_2$  after exercise and  $\dot{V}O_2$  at rest is known as the  $O_2$  debt. The  $O_2$  debt has traditionally been divided into alactacid and lactacid  $O_2$  debt<sup>(43)</sup>. The first term refers to restoration of phosphagen levels in the exercised muscles and reloading of myoglobin and hemoglobin with oxygen. The second term relates to resynthesis of glycogen from lactate in the exercised muscles<sup>(44, 45)</sup>.

It has been already reviewed that several factors are implicated in the generation of post exercise oxygen consumption, including, the metabolism of lactate and replenishment of creatine phosphate<sup>(46,47,48,49)</sup>, muscle glycogen resynthesis<sup>(50)</sup>, increased body temperature<sup>(51,52)</sup>, increased heart rate<sup>(53)</sup>, increased ventilatory rate<sup>(54)</sup>, increased circulating concentrations of catecholamines<sup>(55,56,57)</sup>, and replenishing the body resting oxygen levels. An integrated view, including gender and age differences, remains, however, incomplete<sup>(58)</sup>.

The excess of  $\dot{V}O_2$  consumption at the end of exercise is typical for males and only slight in women. The elevation of oxygen uptake reaches 20% of increase around 20 sec of leg press exercise peak in HYM and HEM; D2M keep the same value without any increase, while women enhanced  $\dot{V}O_2$  only at 10%; HEF (5 sec post exercise), 4% HYF (5 sec post exercise).

sec	HEM	HYM	D2M	HEF	HYF	D2F
0	0%	0%	0%	0%	0%	0%
5	18%	12%	0%	9%	4%	-12%
10	18%	14%	0%	2%	-2%	-8%
15	20%	22%	-1%	-1%	0%	-13%
20	20%	21%	-1%	-9%	-2%	-11%
25	18%	11%	-1%	-10%	-6%	-15%
30	15%	9%	-2%	-10%	-6%	-14%
35	10%	3%	-9%	-17%	-13%	-14%
40	7%	-6%	-17%	-20%	-16%	-20%
45	-1%	-13%	-22%	-26%	-24%	-26%

Table 16: percent post exercise excess oxygen consumption after leg press; highlighted numbers represent the percent of VO<sub>2</sub> increase during recovery

Bangsbo reported that the  $\dot{V}O_2$  of contracting muscles increases after only a few seconds of exercise and the time to reach 50 and 90% of peak oxygen extraction is 13 and 51 s, respectively. The limited oxygen utilization in the initial phase of intense exercise does not appear to be caused by insufficient oxygen availability, but it may rather be due to a non optimal distribution of blood flow in the exercising muscles and to a limited extraction of oxygen by the contracting muscle cells<sup>(45)</sup>. Moreover, it is possible that, in order to replace the initial oxygen debt, an excess consumptions at the end of a single dynamic bout takes place.

## Muscular response

### FBF (Femoral Blood Flow)

During intense dynamic exercise, human skeletal muscle blood flow rises markedly to meet the metabolic demand of active muscle tissue. Several methods have been utilized to estimate limb blood flow intermittently during or just after termination of exercise. In our study, measurements of blood velocity utilizing the noninvasive ultrasound Doppler that provide an alternative method for continuously estimating regional arterial inflow were performed. The method has been utilized previously to estimate leg blood flow at rest and during intermittent static contractions of the human quadriceps muscle.

During intense dynamical knee-extensor exercise blood flow to the exercising muscle has been observed to increase from about 10 ml/min to more than 300 ml/min<sup>(59)</sup>. Furthermore, under normal conditions, oxygen supply does not limit oxygen utilization during concentric exercise and

blood flow in the exercising thigh becomes adjusted in the first phase of exercise maybe as a consequence of reduced perfusion to non active tissues<sup>(60)</sup>. Moreover Lindle R reported that KE exercise (knee extension) revealed a consistently attenuated blood flow in old sedentary subjects when compared with young sedentary subjects of similar quadriceps muscle mass<sup>(11)</sup>.

In our study the FBF during a single bout on leg press machine displays a progressive increase in all groups, but with a marked sex-related effect. Women always show lower values than men. The results of the present study also show an age effect during the exercise execution, but during recovery this effect disappears in males: HYM and HEM are quite similar after effort, and D2M are somewhat lower. HEF and D2F show a lower FBF before and after exercise than HYF, and D2F display lowest values among females.

It is generally reported that immediately after resistive exercise a post contraction muscle hyperemia occurs, since blood flow to the exercised muscles increases further<sup>(61)</sup> (fig. 47).

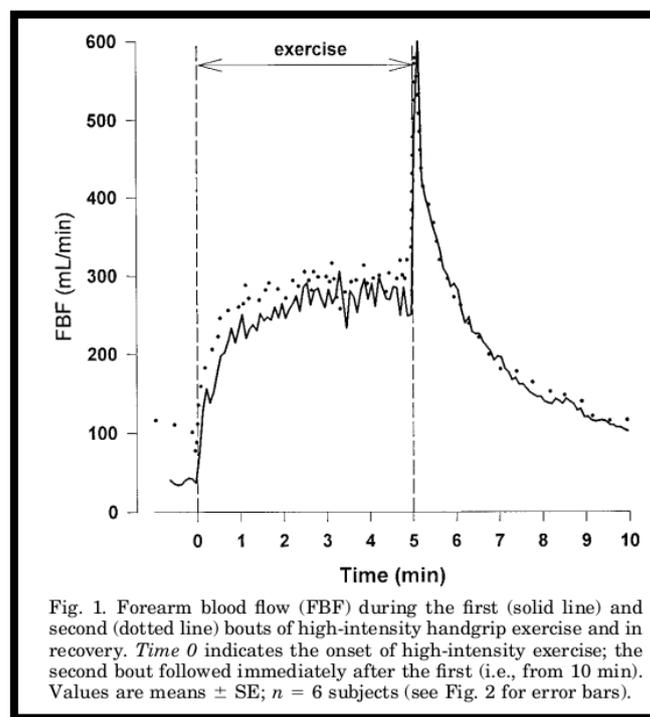


Figure 47: FBF during handgrip exercise, Hugson<sup>(61)</sup>;

The duration of post contraction muscle hyperemia is dependent on the type, intensity and duration of the previous exercise and also on the strength of the effort: higher muscle tension and slower relaxation can have a profound effect on blood flow into exercising limbs in humans<sup>(62)</sup>. There are several possibilities that have been discussed: 1) the increase in vascular conductance is quite marked, implying that there are further factors in addition to those existing during exercise that cause vasodilatation; 2) it is also possible that blood flow is mechanically hindered by muscle contraction during dynamical exercise and that release of this hindrance increases blood flow when exercise is terminated; 3) finally, the sympathetic nervous stimulation in the active muscles is reduced upon termination of exercise. During exercise, sympathetic activity appears to be elevated in most tissues and decreases rapidly after exercise. Taylor reported that “during dynamic exercise, vasoconstriction occurs in the non active limbs and the viscera, which contributes to an increase in arterial perfusion pressure and permits redistribution of blood flow to the contracting skeletal muscles”<sup>(63)</sup>. In addition other studies suggest that the arterial inflow to contracting muscle during dynamic exercise appears to be markedly affected by the transient variations in intramuscular pressure. The results of Redegran show a close relationship between the muscle contraction-relaxation phases and the variation in blood velocity, with mechanical hindrance to blood flow and a high intramuscular pressure during the contraction phase and with an unimpeded blood flow and low intramuscular pressure during the relaxation phase<sup>(64)</sup>. The present study reports an excess of FBF after exercise especially for two groups: D2M and HYM (HEM group not available). D2F display a sort of plateau for some seconds, while HEM and HYF do not show any post exercise hyperthermia.

Near Infrared Spectroscopy (NIRS) has been used to measure regional skeletal muscle deoxygenation by presenting a balance between oxygen delivery and demand in muscle tissue. NIRS is convenient since it is non-invasive and does not restrict ongoing activities at sports events. As seen also for the other types of exercise, NIRS data show a marked difference per sex among groups, but the most remarkable aspect regards the Diabetics groups, who exhibited the largest oxygen extraction at muscle level as compared with same sex young groups.

This suggests a greater potential for oxygen usage at muscle level.

To conclude, we compare Hugson (2001)  $VO_2$  and FBF results referring to hand grip exercise with the present findings. It is evident that the kind of exercise, especially because of the muscle mass involved, makes a large quantitative difference. It is clear, however, that FBF increases after the end of contractions in young male subjects, both after hand grip as well as in our results. The oxygen consumption response, on the contrary, behaves differently, because it decreases immediately after hand grip, but it keeps rising (HYM, HEM) or does not decline for the first 20" recovery in our experiments. Notably, the additional increase after the exercise characterizes the males, not the females, thus marking a possible sex related difference.

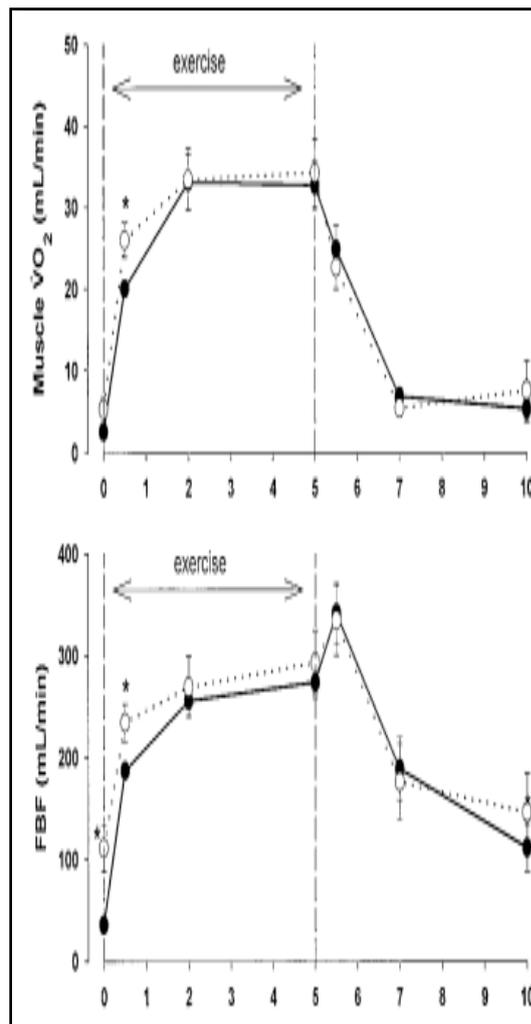
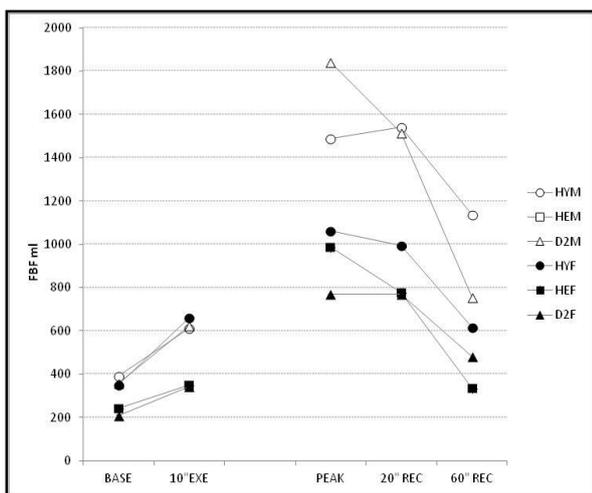
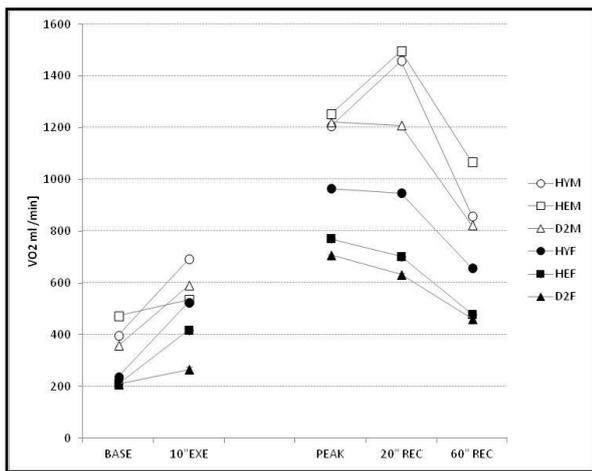


Figure 48; 49:  $VO_2$  (up) and FBF response (down) to leg press exercise (on the left); Hugson (2001)  $VO_2$  (up) and FBF response (down) to hand grip exercise (on the right).



## ISOMETRIC EXERCISE (IE)

### Protocol

The isometric exercise was performed with the same load used with resistance exercise, but each subject had to lift up the weight and maintain the squat contractions as long as he/she was able.

HEM group did not perform this test.

### Results

#### Cardiovascular

Overall cardiovascular adjustments during IE are similar to DE (Dynamic Exercise), except for SV and CO, as summarized in table 1 and in the following figures.

		HYM		HEM		D2M		HYF		HEF		D2F	
IE		EXE	REC										
SV		↓↓	↑	nv	nv	↓↓	↑	↓↓	↑	↓↓	↑	↓↓	↑
CO		↑↑	=	nv	nv	↑↑	↑↑	↑↑	=	↓	↑↑	↑	↑↑
DE		EXE	REC										
SV		↑↑	↑	↓↓↓	↑	↓↓	↑	↑↑	↑	↓↓	↑	↓↓	↑
CO		↑↑	↑=	↓	↑↑	↑↑↑	↑↑	↑↑	↑=	↓	↑↑	↑↑↑	↑↑

Table17: Qualitative comparison of stroke volume (SV) and cardiac output (CO) changes during isometric (IE) and dynamic (DE) exercise: ↑ increase ↓ decrease = no change, nv = not evaluated

SV falls in all groups during IE, while in DE it progressively increases in HYM and HYF groups. CO during IE increases in HYM/F and rises to a steady state during the beginning of recovery; in HEM/F and D2F it doesn't increase during the effort, but it largely increases thereafter.

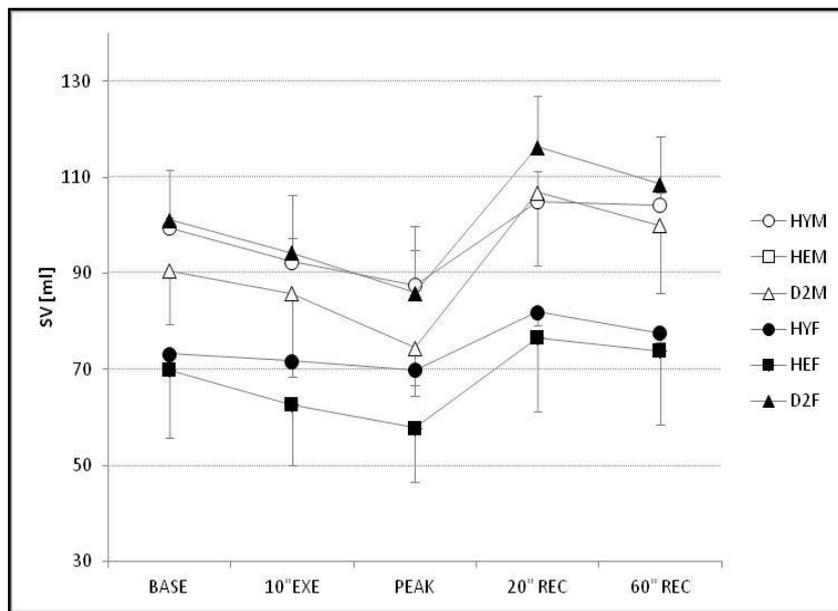
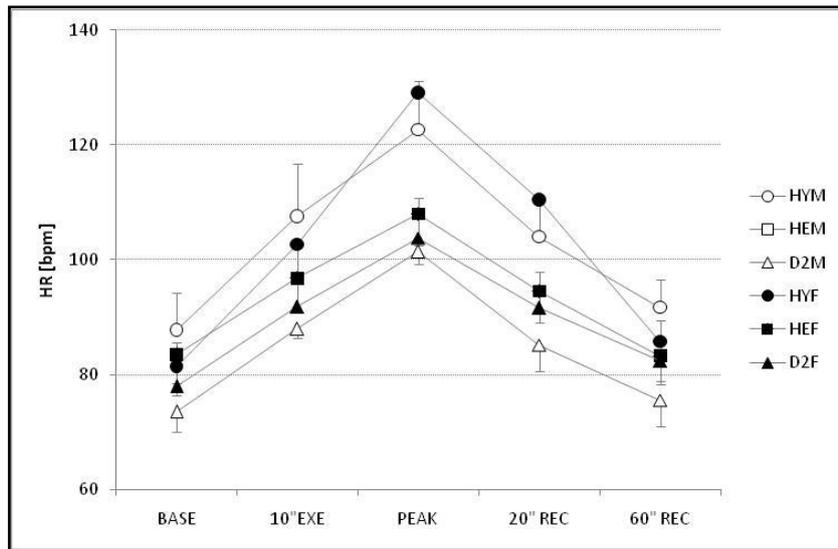


Figure 50a,50b: HR and SV response during and after isometric exercise

In the case of IE, at a difference with DE, in all groups SV follows the same trend, consisting in a progressive decrease lasting for the whole isometric contraction, with a more (diabetics) or less (young) accentuated rebound at recovery.

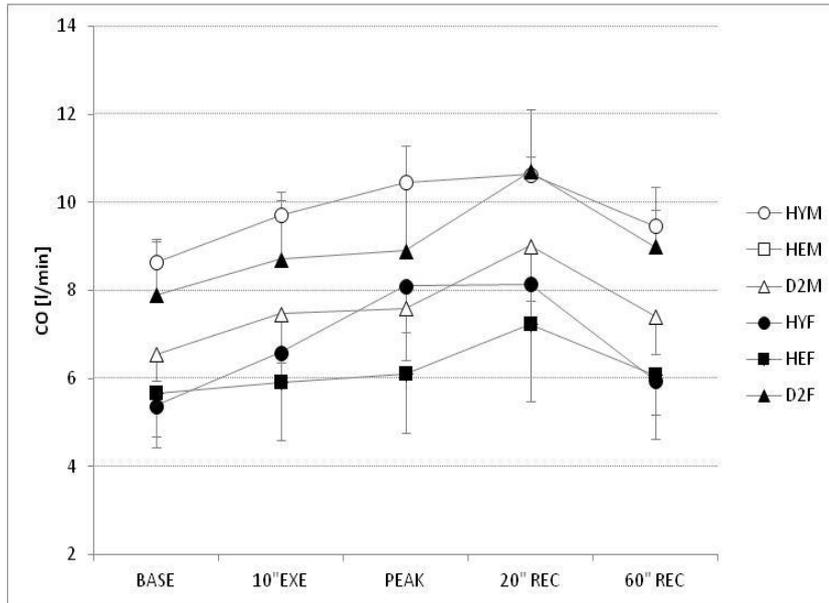


Figure 51: CO response during and after isometric exercise

Because of a relatively higher increase in HR, the young (HYM and HYF) were able to increase their CO during the contraction phase, with no further increase on relaxation. On the contrary in the other groups (HEM, D2F and D2M) CO increase slightly during the effort and peaks at 20 sec recovery.

## Metabolic

The increase in  $VO_2$  during IE was lower than during DE, and the pattern of the increase was similar for all groups. A clear further increase in  $VO_2$  after the effort was seen in HYM (and D2F), while HYF (and D2M) held a quasi constant  $VO_2$  for 30-40 s.

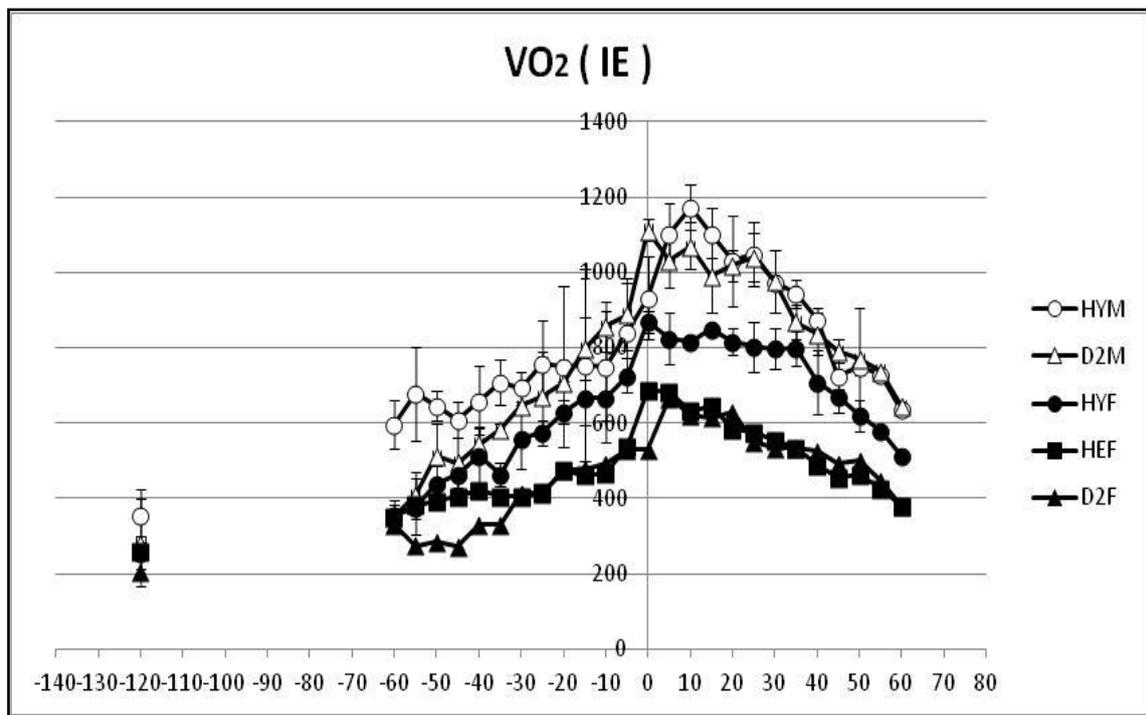


Figure 53:  $VO_2$  response during and after isometric exercise

On clustering the measurements at selected points for synthesis, as already done previously, the peculiar pattern of  $VO_2$  rebound on release of muscle contraction in HYM appears attenuated.

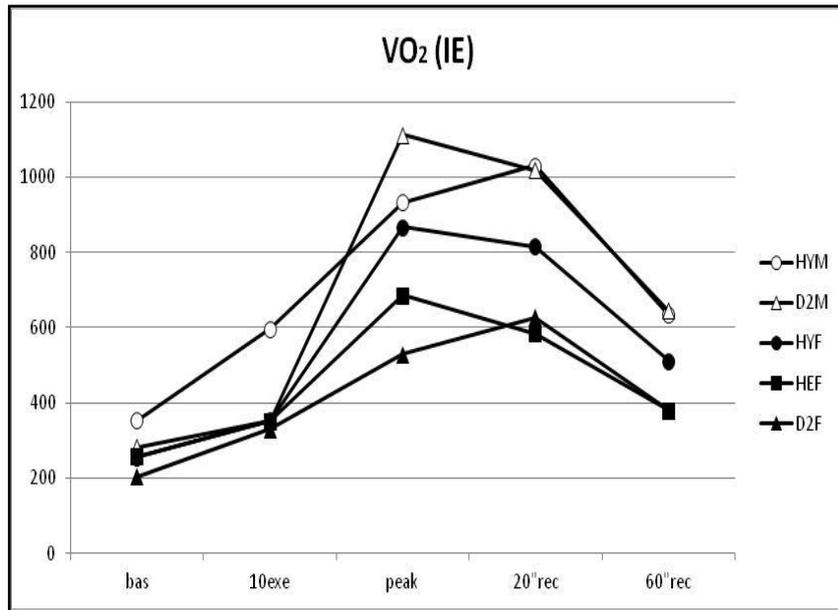


Figure 54: VO<sub>2</sub> in 5 conditions response during and after isometric exercise

### Muscular

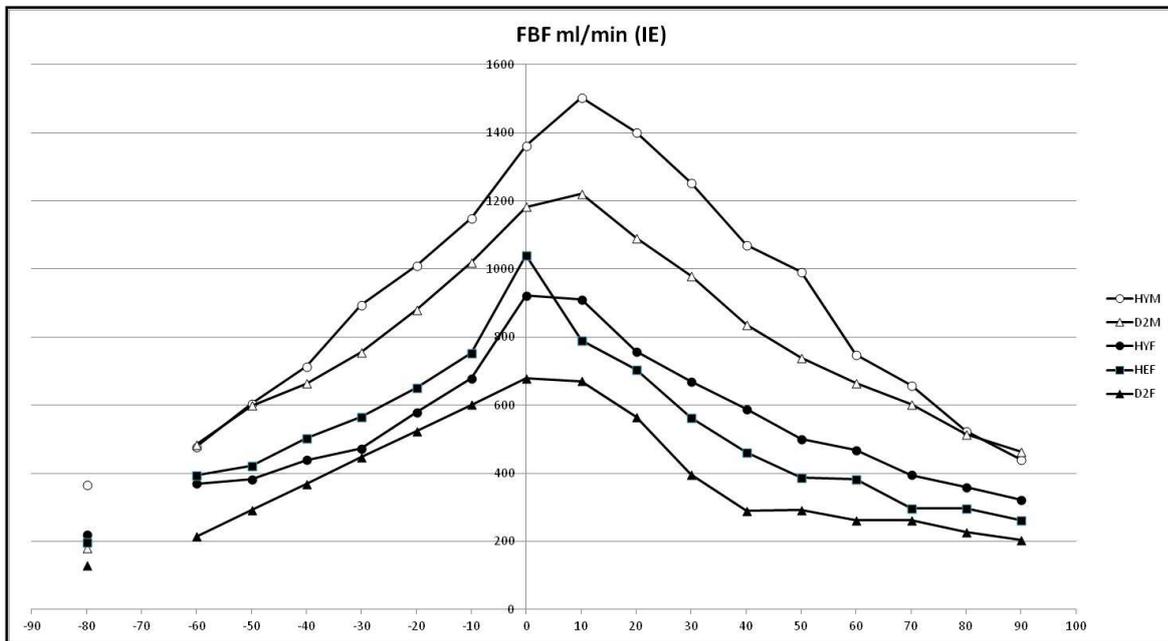


Figure 55: FBF response during and after isometric exercise

There is no quantitative difference between FBF during DE and IE, while the post exercise pattern is similarly differentiated among groups.

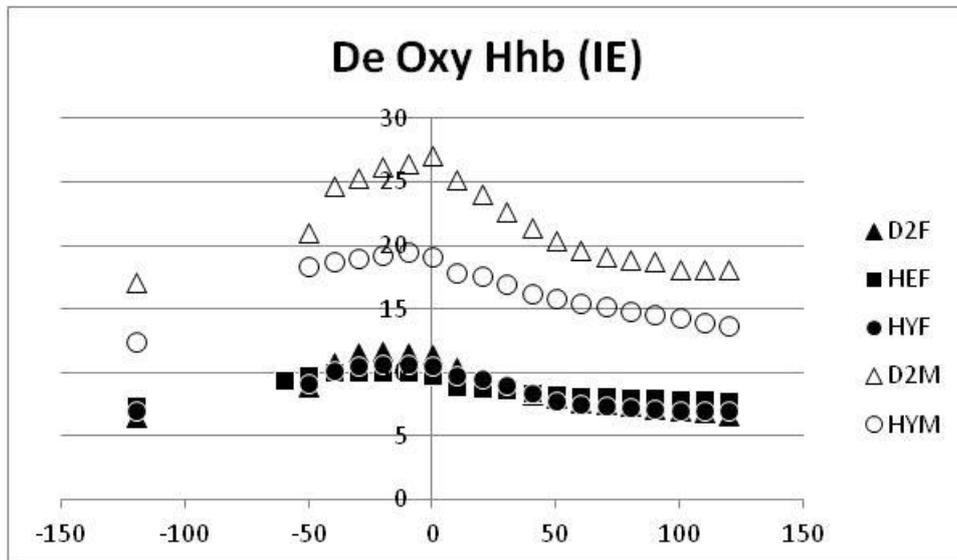


Figure 56: HHb response during and after isometric exercise

NIRS data confirm higher oxygen extractions at muscular levels in D2M group.

## Discussion

From a functional standpoint, maintaining successful independent living with increasing age requires the repeated use of both isometric and dynamic exercise<sup>(64)</sup>.

During isometric exercise there is well established progressive increase in heart rate, and blood pressure<sup>(65)</sup>. Some investigations suggest that older men and women fatigue more than young<sup>(66)</sup>. In our study results suggest a significant different adaptation to isometric exercise per sex and age generally and different adaptations of SV in young groups, respect to dynamic exercise.

HYM and HYF during Isometric contractions use the same strategy of all other groups, they decrease SV during the effort, while in dynamic exercise they adjust the response in the opposite way. This is probably caused by the typical characteristic of isometric contractions on leg press where all dorsal and abdominal muscles, in addition to leg muscles participate in the effort, thus hampering venous return and reducing SV. Thus, isometric contractions in all subjects resemble to dynamic exercise in HEM, further confirming that overall impairment of the ability of the heart to eject blood during a type of exercise that comprises relevant isometric phases plays a dominant role in this situation.





### References cap. 3

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## Cap 4: Study 3 SW “Square wave”: Constant Load Aerobic Exercise





## Introduction

Aerobic exercise is the most common activity in fitness world. Its role in reducing Cardiovascular risk factors, in enhancing fitness level, in maintaining mental health, etc... is undisputed. Some examples of aerobic exercise include: walking, jogging, running, dancing, rollerblading, bicycling, swimming, etc...<sup>(1,2)</sup> Regular aerobic exercise improves health in the following ways: it reduces body fat and improves weight control, it reduces resting blood pressure (systolic and diastolic), it increases HDL (good) cholesterol, it decreases total cholesterol, it improves glucose tolerance and reduces insulin. Endurance training decreases clinical symptoms of anxiety, tension and depression, increases maximal oxygen consumption ( $VO_{2max}$ ), improves heart and lung function, increases blood supply to the muscles and enhances your muscles' ability to use oxygen and it lowers resting heart rate; overall, it increases the threshold for muscle fatigue (lactic acid accumulation)<sup>(3,4)</sup>. Moreover Aerobic exercise can be performed at every age and conditions with reduced risks and high potential to grow up a sense of wellness. Its high applicability involves some physiological implications that are still investigated in different contest, methods and subjects. It is important to evaluate it in all subjects as an indication of the level of fitness in relation with cardiovascular parameter, muscular functionality and metabolic response, on one hand, and age, sex and pathology<sup>(5, 6)</sup> on the other hand. The American College of Sports Medicine (ACSM) defines aerobic exercise as "any activity that uses large muscle groups, can be maintained continuously, and is rhythmic in nature." It is a type of exercise that overloads the heart and lungs and causes them to work harder than at rest. Aerobic exercise, also, strengthens the heart and lungs (which make up the cardiovascular system). During exercise, muscles demand more oxygen-rich blood and give off more carbon dioxide and other waste products. As a result, heart has to beat faster to keep up. After a consistent aerobic exercise plan, heart grows stronger so it can meet the muscles' demands without as much effort. From aerobic exercise everyone can benefit regardless of their weight, age, or gender<sup>(7)</sup>. An increase in aerobic physical activity should be considered an important component of lifestyle modification for prevention and treatment of high blood pressure. High-intensity exercise led to increases in tension/anxiety and fatigue, whereas positive mood changes (vigor and exhilaration) were seen following low-intensity exercise only.

## Aerobic exercise in research

In research kinetics of aerobic exercise adaptations can be analyzed, that is the speed of each parameter in reaching new steady state values. Constant work rate tests (square wave) are suitable for studying cardiovascular, ventilator and gas exchange kinetics<sup>(8, 9)</sup>. Measurement of these variables, especially  $\dot{V}O_2$  by Quark (gas exchange analyzer), and Oxygen extractions (DeoxyHb) by NIRS (Near infrared spectroscopy), during transitions from rest to constant load exercise allows determination of the time constants ( $\tau$ ) or of the mean response time (MRT) characterizing the shift from baseline levels to new steady state values.  $\tau$ , MRT and the magnitude of change in  $\dot{V}O_2$  are well correlated with the fitness state<sup>(10, 11)</sup>.

Gas exchange kinetics can be described by 3 different phases: Phase I, (Cardiovascular phase) consists in an immediate increase in oxygen uptake at the beginning of the exercise. It is attributed to a sudden increase in pulmonary blood flow due to a rapid increase in heart rate and stroke volume (it lasts by 15 seconds); Phase II (cardiopulmonary phase) reflects the period of major increase in cellular respiration (until the third minute): if the exercise intensity is below VT (the ventilator threshold), a steady state in  $\dot{V}O_2$  is achieved by 3 minutes, while if the intensity is above VT, the steady state is not achieved before the subject fatigues; Phase III, (steady state) reflects the start of the steady state below VT; if the effort is above VT the increase in  $\dot{V}O_2$  is linearly correlated with the magnitude of the blood lactate accumulation<sup>(12,13,14,15)</sup>.

$O_2$  uptake kinetics<sup>(16)</sup>. During the transition to moderate-intensity exercise, pulmonary  $O_2$  uptake, reflecting muscle  $O_2$  utilization, increases exponentially towards a new steady state<sup>(17)</sup>. In healthy older adults, the adaptation of  $\dot{V}O_2$  (and presumably muscle  $O_2$  consumption) is slowed during the transition to exercise in comparison with young. There is evidence that muscle  $O_2$  delivery is attenuated in the older adult and may contribute to slower  $\dot{V}O_2$  kinetics<sup>(18)</sup> lower steady-state limb blood flow<sup>(19)</sup>, and indications of impaired local micro vascular flow in humans<sup>(20)</sup>.

Murias study showed that fitting phase II  $\dot{V}O_{2p}$  kinetics from the experimentally estimated phase I duration, or from 25 s to 45 s in the Older group and from 15 s to 45 s in the Young group resulted in no significant changes in  $\dot{V}O_2$ . It is also concluded that Older adults had a significantly longer phase I  $\dot{V}O_{2p}$  and a significantly longer phase II  $\dot{V}O_{2p}$  compared with their younger counterparts<sup>(21)</sup>.

Different strategies have been used in the literature to fit the exponential increase in the primary component of  $\dot{V}O_2$  during transitions from baseline to a given work rate in the moderate-intensity domain, but this item is still controversial. In any case, curve fitting algorithms must be applied to the recorded data in order to obtain a reliable description of the time course of changes in the

different variables from baseline to new steady state levels. The procedures are, however, strongly flawed by considerable noise in the data and by lack of time definition in breath-to-breath recordings. To reduce the impact of such inherent weaknesses, the square wave test is generally repeated two or three times, after adequate resting periods between successive trials, in seemingly identical conditions, and the records are superimposed to extend time resolution and reduce noise. In our laboratory we did follow the repetition criterion, but we were unable to proceed to curve fitting analysis, because of technical limitations.

To overcome the above limitations, we followed a different approach, consisting in calculating exercise-onset  $\text{VO}_2$  kinetics by geometrical integration of the curve joining baseline to steady state conditions and expressed as mean response time (MRT, calculated in seconds)<sup>(53)</sup>. The result of this calculation (MRT) correlates well with, and is not significantly different from, the time constant. Resting  $\text{VO}_2$  was calculated as the  $\text{VO}_2$  during the final minute before exercise. Steady-state  $\text{VO}_2$  was defined as the averaged value between the fifth and sixth minute of cycling. The difference between the rest  $\text{VO}_2$  and steady-state  $\text{VO}_2$  multiplied by exercise time (6 minutes) was defined as the expected amount of  $\text{VO}_2$  during the entire exercise bout<sup>(54)</sup>, and the ratio between the expected value and the real value (integrated curve) was calculated to obtain MRT.

## Dossier-CHF

### Diagnosis, symptoms and therapy

Initial diagnosis of heart failure in the elderly may be difficult because of non specific signs and symptoms that gradually occur. An anamnesis, which is the basis for the diagnosis of CHF, is often difficult, if not impossible, to obtain from some patients. One of the causes of failure to recognize CHF in the elderly is a non specific fatigue that is attributed to ageing, whereas limited clinical manifestations may result from decreased physical activity. Symptoms of CHF such as exceptional dispnea or fatigue may be associated with other conditions such as the respiratory system diseases, metabolic diseases, anemia as well as deteriorated tolerance for physical strain. In order to determine the best course of therapy, physicians often assess the stage of heart failure according to the New York Heart Association (NYHA) functional classification system. This system relates symptoms to everyday activities and the patient's quality of life.

<b>Class</b>	<b>Patient Symptoms</b>
Class I (Mild)	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).
Class II (Mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
Class III (Moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.
Class IV (Severe)	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

Table n. CHF classification by Heart Failure Society Of America, HFSA(2002)

An early stage of CHF may be manifested under “clinical masks” including insomnia, depression and frequent heart palpitation. Acute diseases (e.g. myocardial infarction, conditions with elevated temperature) or other chronic conditions such as anemia, hyper and hypothyroidism or atrial fibrillation may aggravate CHF or accelerate its appearance. In the diagnosis of CHF in the elderly, echocardiography plays an important role; according to the European Society of Cardiology (ESC) in 2005, it enables to determine the causes of heart failure and assessment of its type (systolic and/or diastolic). Unlike middle -aged people, in whom systolic heart dysfunction is a frequent cause of heart failure, in older subjects the clinical manifestations of heart failure often occur with the correct systolic function of the left ventricle. Heart failure with preserved left ventricular

systolic function is found in 40–80% of older people and occurs almost twice more often in women than men. Although prognosis in patients with CHF with preserved left ventricular function is slightly better than for people with CHF with disturbed systolic function, the mortality risk is 4 times higher than in subjects without CHF. The concentration of brain natriuretic peptide (BNP) or NT proBNP recognized bio chemical markers of heart failure (according to ESC), has a limited diagnostic value in older people with CHF. The mean level of these markers rises with age. In people >75 years of age without heart failure, fold high concentration of plasma BNP was found, which may be associated with decreased glomerular filtration rate, arterial hypertension and frequent atrial fibrillation. The typical pharmacological treatments provides: Diuretics,  $\beta$ -blockers,  $\beta$  Cardiac glycosides, Vasodilators. Non-pharmacological strategies recommend with CHF a reduction of salt intake and moderate exercise<sup>(32)</sup>. Despite significant therapeutic advances, CHF remains a leading cause of morbidity and mortality in developed and increasingly in developing countries, with a 5-year mortality rate of 50%, which rivals or exceeds that of many cancers<sup>(33)</sup>. In the United States the morbidity and mortality rates associated with CHF are extremely high. Eighty-five percent of men and 65% of women die within 6 years of CHF diagnosis, 5 and as many as 45% of hospitalized patients with CHF are readmitted within 90 days of hospital discharge. 6 Prognostic information for hospitalized patients with CHF with preserved systolic function versus systolic dysfunction is important to guide physicians' therapeutic management and to aid clinical decision making for hospitalized patients with CHF. Prognostic information also will help guide future research endeavors designed to improve survival and reduce hospitalization rates for patients with CHF with each type of systolic function. Whereas some studies have suggested that preserved systolic function in CHF is associated with lower mortality rates, 7-1° others have shown no survival difference between patients with preserved systolic function and those with systolic dysfunction. 1>~3 These discrepancies in prognosis for patients with CHF with preserved systolic function may result from study Congestive Heart Failure Systolic function, readmission rates, and survival among consecutively hospitalized patients with congestive heart failure<sup>(34)</sup>.

## **CHF and exercise**

Patients with chronic heart failure commonly present with symptoms of dyspnea and fatigue associated with decreased exercise tolerance. Small randomized trials of short duration evaluating the role of exercise training in chronic heart failure have shown improvements in quality of life and functional capacity. These improvements in functional capacity are associated with changes in

skeletal muscle structure, function, and blood flow and with decreases in resting neurohormonal activation. The exercise training study by Belardinelli and colleagues is one of the largest and longest studies of patients with chronic heart failure. Compliance and follow-up were excellent, most likely because the study was hospital-based and included younger patients with symptoms of mild to moderate chronic heart failure. Improvements in functional capacity and quality of life corroborated the results of other smaller studies. Although this study is the first to report decreased cardiac events in patients with chronic heart failure enrolled in an exercise training program, these results should be interpreted with caution because of the small sample size. The study is important because it shows the safety of exercise training in patients with chronic heart failure and provides evidence of an improvement in exercise performance in a hospital-based program. Larger studies to properly assess the effect of exercise training in chronic heart failure on mortality and morbidity are needed to confirm these promising results<sup>(35)</sup>. Therefore, exercise testing has become an important tool for the evaluation and monitoring of heart failure. Whereas the maximal aerobic capacity (peak  $\dot{V}\cdot\text{O}_2$ ) is a reliable indicator of the severity and prognosis of heart failure, sub maximal exercise parameters may be more closely related to the ability to perform daily activities. As such, oxygen ( $\text{O}_2$ ) uptake kinetics, describing the rate change of  $\text{O}_2$  uptake during onset or recovery of sub - maximal constant-load exercise ( $\text{O}_2$  onset and recovery kinetics, respectively), have been shown to be useful parameters for objectively evaluating the functional capacity of CHF patients. However, their evaluation in this population is not a routine part of daily clinical practice. Possible reasons for this include a lack of standardization of the assessment methodology and a limited number of studies evaluating the clinical use of  $\text{O}_2$  uptake kinetics in CHF patients. In addition, the pathophysiological mechanisms underlying the delay in  $\text{O}_2$  uptake kinetics in these patients are not completely understood<sup>(36)</sup>. Moreover One of the main determinants of reduced exercise capacity in these patients is systolic and/or diastolic left ventricular dysfunction, which causes an impaired hemodynamic response to exercise, that it is due to inability of the heart to maintain a sufficient cardiac output for adequate tissue oxygenation. Other pathophysiological mechanisms include an impaired muscle blood flow caused by increased vasoconstriction and/or an impaired local vasodilator capacity, muscle mitochondrial dysfunction, an exaggerated ventilatory response to exercise, and autonomic imbalance. Because resting indices of cardiac function and the level of perceived exercise intolerance correlate poorly with the exercise performance of these patients, exercise testing has become indispensable in the evaluation and monitoring of heart failure<sup>(37)</sup>.

### **Priming exercise** (prior exercise; Heavy warm-up (Hwu) exercise)

Priming exercise is a kind of warm up before the aerobic exercise session, it is also called prior exercise, heavy warm up exercise, because very often it consists in a high intensity warm up before a normal moderate aerobic exercise.

The  $\text{VO}_2$  kinetics at the onset of moderate, heavy or very heavy intensity exercise transitions, has been extensively investigated and the results obtained in these experiments have stirred a scientific debate between those in favor of a central limitation ( $\text{O}_2$  delivery) and those in support of a peripheral ( $\text{O}_2$  utilization) limitation of oxidative metabolism<sup>(38,39,40,41,42)</sup>. It is believed that Heavy warm-up (Hwu) can produce an acute improvement in oxygen delivery and muscle perfusion. Several studies have demonstrated an increase in the speed of adaptation of oxidative metabolism, during subsequent moderate intensity step transitions, in older but not in young adults<sup>(43)</sup>. Moreover the recovery period after high exercise priming reduces high intensity exercise tolerance, but does not change the maximal Power<sup>(44)</sup>, so the appropriate combination of prior exercise intensity and recovery duration enables an acceleration of  $\text{V}'\text{O}_2$  kinetics (overall  $\tau$ ) during subsequent severe-intensity exercise<sup>(45)</sup>. In older adults, at variance with young subjects, the effect of Hwu at the muscle level is a slower rate of  $\text{O}_2$  extraction. It is well documented that, in older adults as well as in young subjects, aerobic training results in faster  $\text{VO}_2$  kinetics and increased  $\text{VO}_{2\text{max}}$ <sup>(46)</sup>. Both high and intermediate intensity exercises exhibit a priming effect on  $\text{O}_2$  consumption kinetics. Intermediate intensity exercise can only increase the time to exhaustion of a subsequent high intensity exercise<sup>(47)</sup>.

## **Hypothesis**

It has been reported that in young athletes a bout of supramaximal exercise affects the time course of a subsequent exercise, provided this is also supramaximal, because of a “priming effect” whose mechanisms are still debated. It is hypothesized that in less fit subjects (e.g. elderly) the priming effect of a supramaximal exercise bout is effective also on a subsequent below (anaerobic) threshold exercise and that on still less fit subjects (e.g. CHF) even a moderate intensity exercise bout may exert a priming effect<sup>(55)</sup>.

## **Aim**

To verify whether MRT is reduced during a bout of constant load exercise preceded by an identical exercise (priming effect) in different populations, to gain insight about the mechanisms leading to the priming effect.

## **METHODS**

### **Protocol**

In a subsequent day, after the incremental test and the determination of  $V_T$  (ventilator threshold), the subjects performed sub maximal cycle ergometer tests (SW, square wave) in order to collect data useful for the study of kinetics.

After a full explanation, familiarization with the equipment and complete setting of the session test, the subjects were ready to start. We recorded baseline values for 3 min with the subjects sitting still on the cycle ergometer saddle, and further 3 minutes while the subjects pedaled without load, to record the effects of movement per se and to obtain adequate warm up; after that, the load was raised and kept constant for six minutes at a value corresponding to 80%  $VO_{2max}$ , at 60-70 rpm; after the subjects stopped pedaling, we kept collecting data during the recovery period, until reasonable recovery of basal conditions.

This exercise was repeated 3 times, separated by 10 minute of recovery. The exercise load was below  $V_T$ , to be sure that the exercise intensity represented a purely aerobic activity and steady state conditions were obtained within 3 minutes, while the cumulative load of the 3 repetitions was kept under the fatigue level. During all tests we monitored gas exchange data at the level of the mouth with a metabolimeter and cardiovascular parameters with a Portapres instrument. At the peripheral level, we studied the oxygen extraction by setting the probe of a NIRS equipment over the vastus lateralis of one leg. A physician was always present to guarantee the safety of the subject

and to check the pressure parameters. To complete the study, we also collected blood samples for lactate and hemoglobin concentration determinations, at rest and at the end of the third exercise.

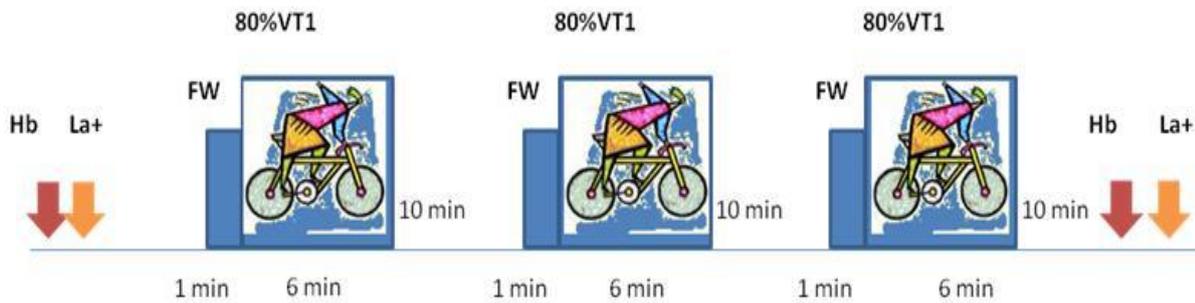


Table 18: Aerobic Test Flowchart

### Groups

We took advantage of the systematic repetition of SW exercise two or three times in all the subjects we have tested, in order to calculate the MRT of  $VO_2$  in search of a possible priming effect.

CHF: sedentary (International Physical Activity Questionnaire  $<1000$  MET min\*week), NYHA type II/III chronic heart failure, all subjects wearing an automatic implanted defibrillator for safety reasons, CHF diagnosis at least 1 year before.

D2M/F: sedentary (International Physical Activity Questionnaire  $<1000$  MET min\*week), diet and/or oral hypoglycaemic agents, diabetes diagnosis at least 1 year before ( $15.1\pm 6.9$ y D2M  $11.1\pm 4.9$ y D2F), HbA1c  $7.1\pm 0.5\%$  D2M and  $6.4\pm 2.2$  D2F, HDL  $53.1\pm 10.1$  mg/dL D2M and  $47.5\pm 17.4$  mg/dL D2F, Total Cholesterol  $142.8\pm 20.9$  mg/dL D2M and  $140.8\pm 48.5$  mg/dL D2F, non-smokers, no evidence of chronic complications.

HEM/F: sedentary, non-smokers, no evidence of chronic complications or presence of other pathologies

HYM/F: sedentary, non-smokers, no evidence of chronic complications or presence of other pathologies

GROUP	N°	Age	HEIGHT	WEIGHT	BMI	Load
		Years	cm	Kg	Kg/m <sup>2</sup>	Watt
CHFF	2	59.0±1.4	163.5±4.9	67.0±17	24.9±4.8	48.0±11
D2F	4	57.5±6.2	156.8±5.3	65.8±2.5	26.9±2.5	69.0±11
HYF	11	24.2±3.1	164.5±6.4	57.1±7.2	21.1±2.4	98.73±20
HEF	10	67.3±6.5	157.6±5.5	57.8±6.6	23.3±3.1	64.56±15
CHFM	27	66.3±5.8	172.3±7.3	77.4±11.8	26.03.3±	58.19±13
D2M	9	59.8±6.3	173.6±4.8	81.4±11.1	27.0±3.4	98.0±13
HYM	40	26.6±6	176.4±6	73.8±8.8	23.7±2.3	147.55±54
HEM	22	65.3±5.5	171.9±6.8	80.6±7.7	27.3±2.5	91.45±31

Table19: Groups Characteristics

## Computation Procedure

Oxygen consumption ( $\dot{V}O_2$ ) at the onset of a constant-load exercise rises progressively to an enhanced steady state level, with typical kinetics, that can be altered by aerobic training or by disease (cardiovascular, diabetes). Kinetics is typically studied by fitting procedures, including a time delay and a one, two or three component exponential model. Alternatively, mean response time (MRT) is calculated, as the ratio between the integral of  $\dot{V}O_2$  deficit during the transient phase and  $\dot{V}O_2$  at steady state. (figure 57)

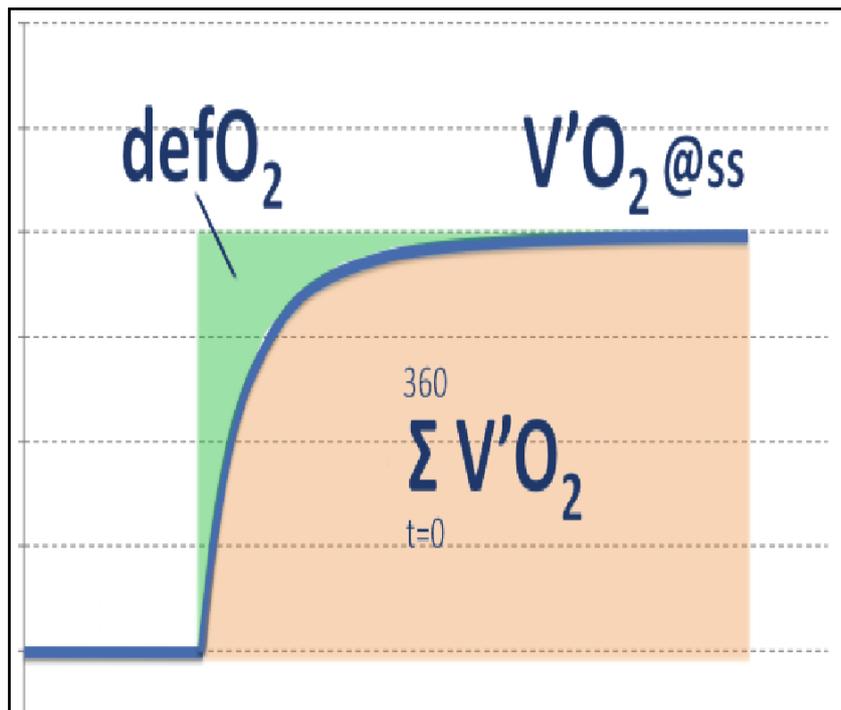


Figure 57: Computation descriptions

## Results

### Cardiovascular

The cardiovascular data describe only four populations HYF HEF D2F D2M, because HEM HYM and CHF data were collected in different moments without using the portapres.

In order to be clear with results description we report each cardiovascular parameter as absolute value, and as a percentage change relative to baseline.

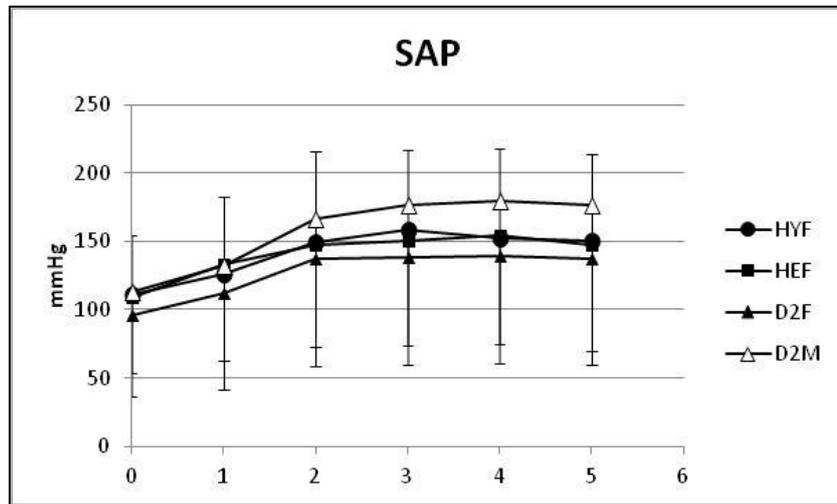


Figure 58: SAP response during Constant load Aerobic Test

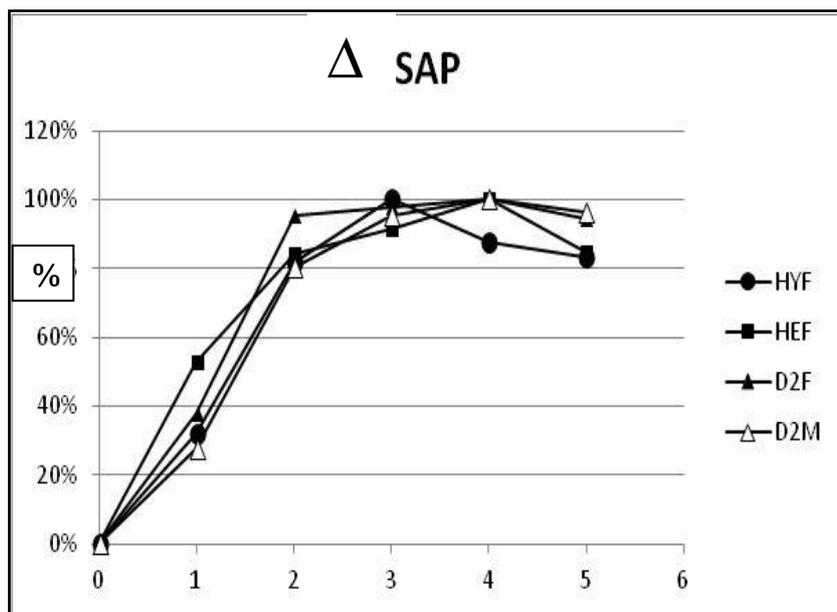


Figure 59: % SAP response during Constant load Aerobic Test

The figures 60-61 show a similar relative increase for all groups, no one gets a large pressure increase, as is typical in a sub maximal exercise.

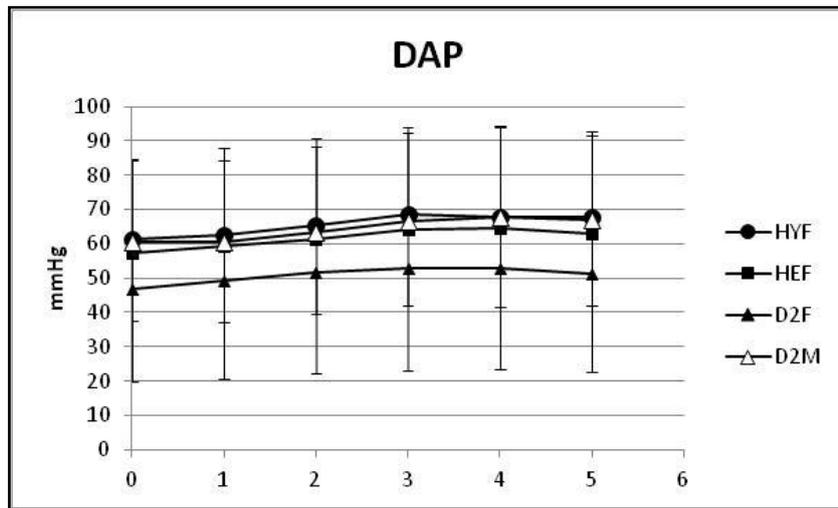


Figure 60: DAP response during Constant load Aerobic Test

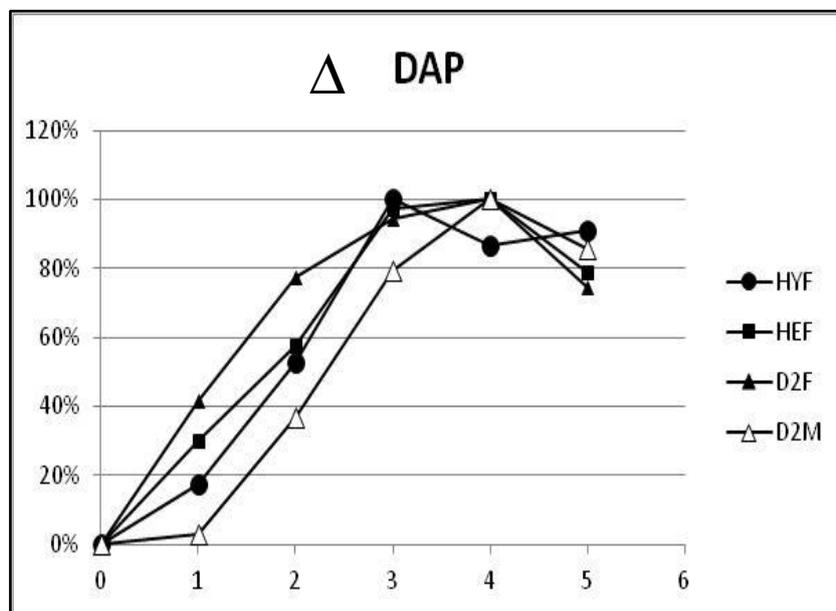


Figure 61: % DAP response during Constant load Aerobic Test

The following figures show a similar relative increase for all groups, no one gets high diastolic pressure values, as is typical in a sub maximal exercise.

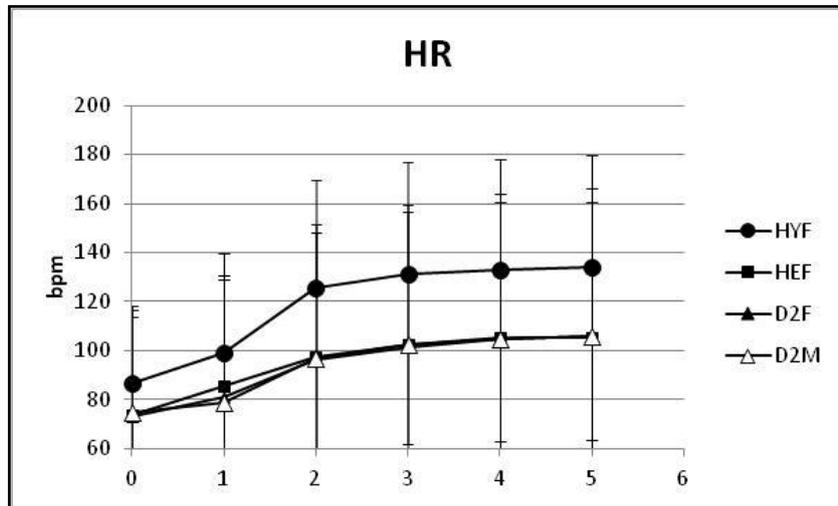


Figure 62: HR response during Constant load Aerobic Test

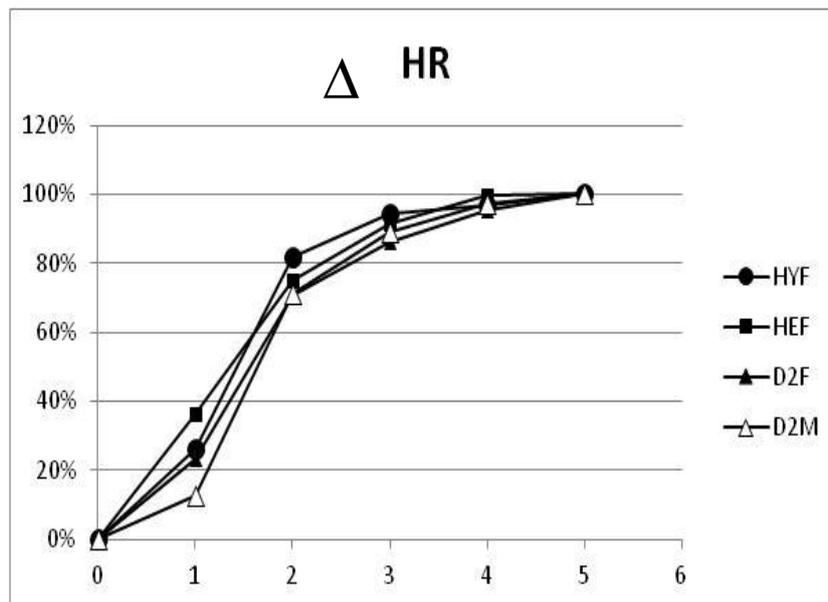


Figure 63: %HR response during Constant load Aerobic Test

HYF display higher steady state value (140 bpm) than other groups are at same steady state value (105 bpm), this response is an effect of age. The relative increase is similar, but HEF increases more at the beginning (in the first 2 minutes) than the others.

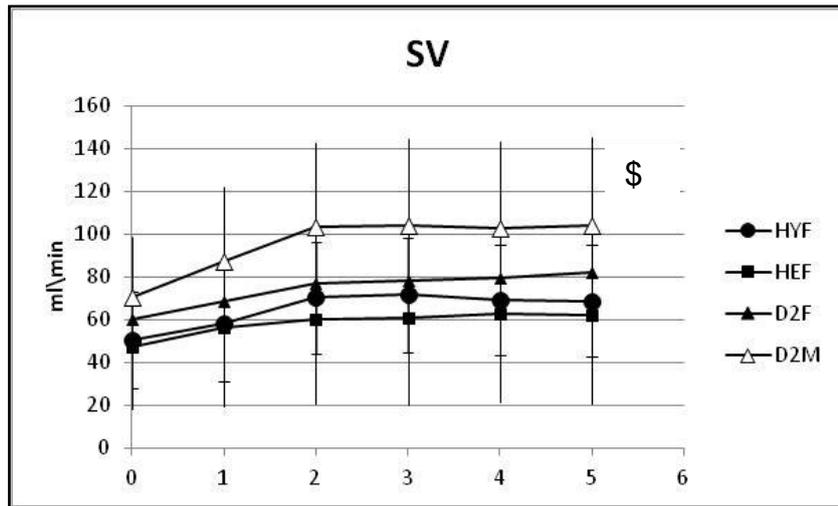


Figure 64: SV response during Constant load Aerobic Test

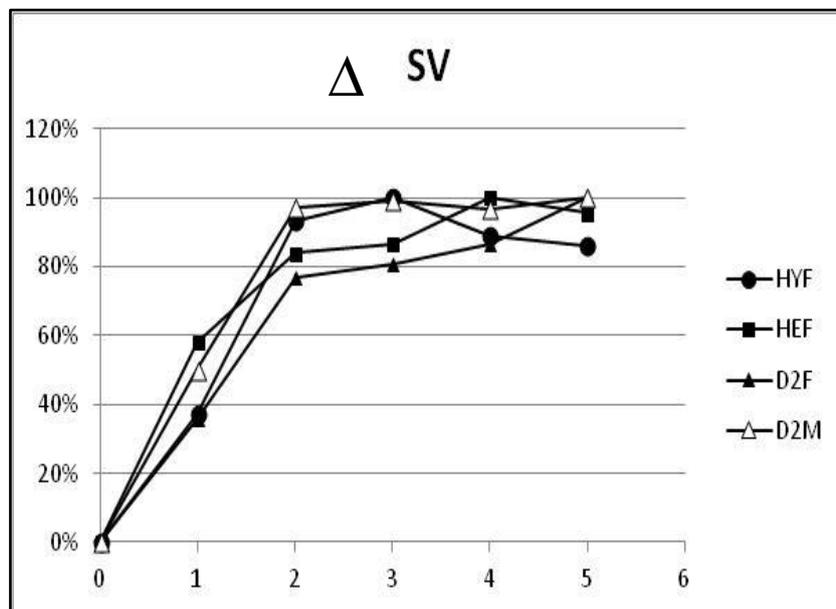


Figure 65: % SV response during Constant load Aerobic Test

In the figures, D2M display the higher steady state value (100 ml/min), while all female groups show lower increase: 55 ml/min (HEF) 65ml/min (HYF) to 80 ml/min (D2F). The relative increase is similar, but HEF increases more at the beginning (in the first 2 minutes) than the others, like in HR response.

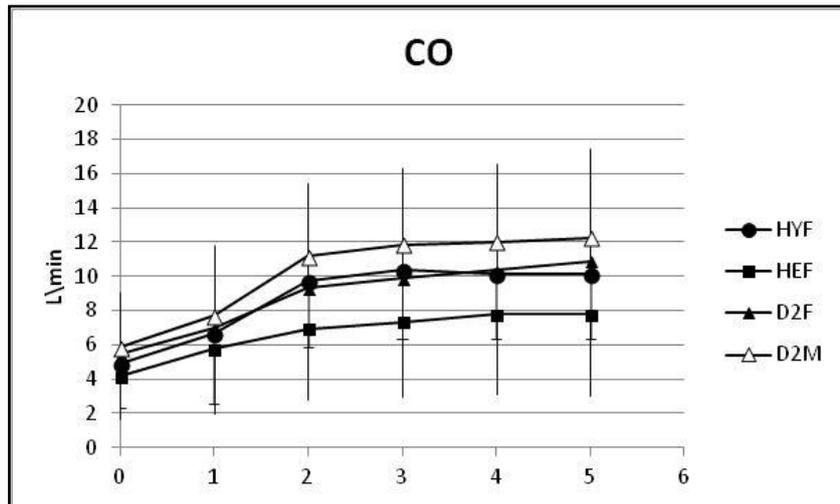


Figure 66: CO response during Constant load Aerobic Test

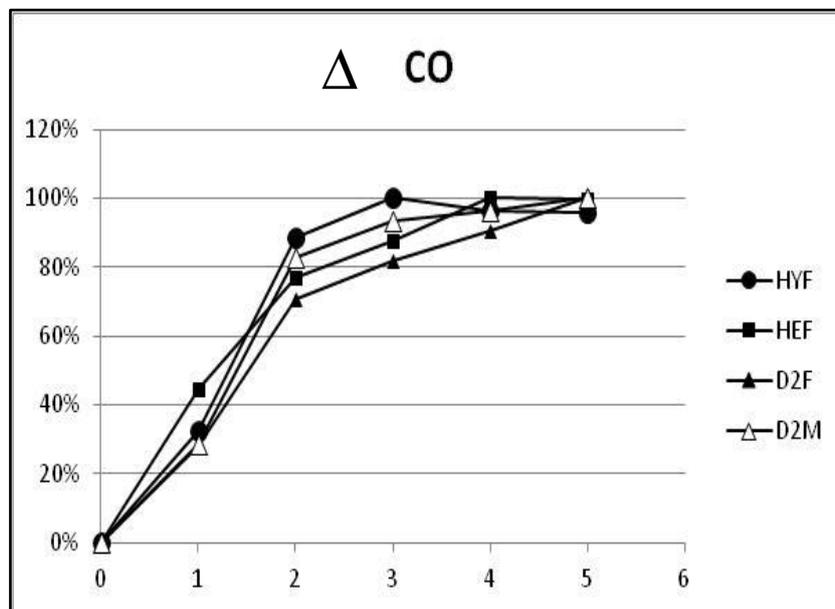


Figure 67: CO response during Constant load Aerobic Test

Cardiac output response follows SV adaptation; D2M displays the higher steady state value (12 l), while all female groups show lower increase, HEF rise to 5 l, while HYF and D2F stay around 10 l. The relative increase is similar, but HEF increases more at the beginning (in the first 2 minutes) than the others as in SV an HR.

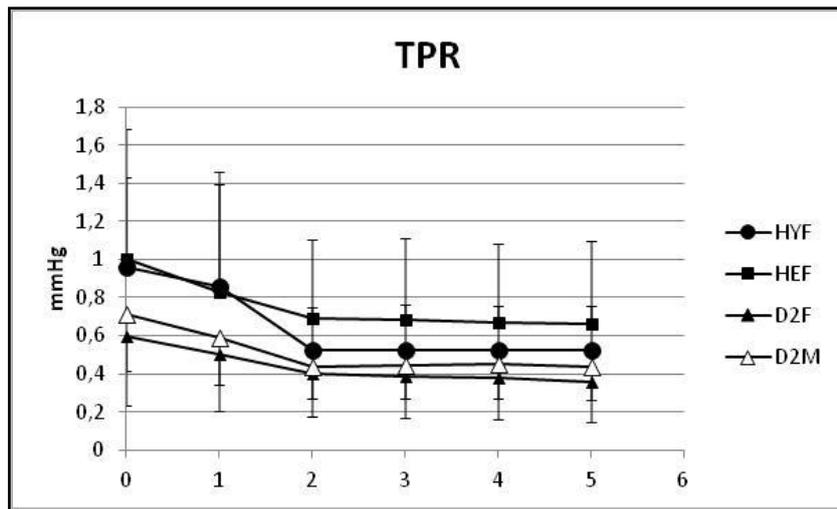


Figure 68: TPR response during Constant load Aerobic Test

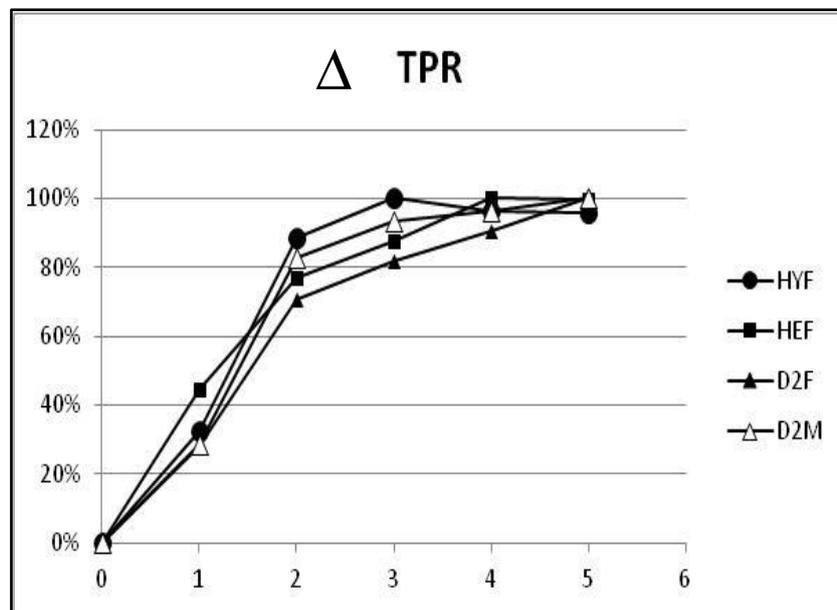


Figure 69: %TPR response during Constant load Aerobic Test

TPR drops down a lot at the beginning in HYF. HEF shows a modest decrease in comparison with others. HYF is in the middle. D2F/M show the lower values.

## Metabolic

All VO<sub>2</sub> kinetics looked similar in shape, so we reported a summary table with VO<sub>2</sub> at baseline condition (VO<sub>2</sub>base), VO<sub>2</sub> at steady state (VO<sub>2</sub>ss) and MRT in seconds. The results are described for 1<sup>st</sup> bout and 2<sup>nd</sup> bout.

	SW1	SW2	SW1	SW2	SW1	SW2	P<0,05
GROUP	VO <sub>2</sub> base	VO <sub>2</sub> base	VO <sub>2</sub> ss	VO <sub>2</sub> ss	VO <sub>2</sub> MRT	VO <sub>2</sub> MRT	Sign.
CHF <sub>M</sub>	271,4±86,1	318,1±103	1149,5±221	1142,6±228	44,9±11	34,5±11	∅ in all
D2 <sub>M</sub>	296,8±244	331,4±118	1608,6±223	1597,9±226	28,7±12	27,8±14	n.s
HE <sub>M</sub>	365,4±268,3	383,6±86	1662,2±461	1701,6±376	27,2±12	25,7±8	n.s
HY <sub>M</sub>	376,1±248	387,7±339	2235,3±769	2297,7±710	28,4±11	24,4±10	n.s
CHF <sub>F</sub>	171,6±15	244,0±36	936,3±186	960,7±169	45,6±3	32,5±4	∅ in all
D2 <sub>F</sub>	244±57	238,2±49	1158,4±161	1133,2±150	31,0±12	26,4±7	n.s
HE <sub>F</sub>	268,3±84	286,3±93	1103,4±179	1117,3±215	33,5±11	34,5±9	n.s
HY <sub>F</sub>	248,4±84	237,0±100	1516,5±211	1459,0±250	34,0±14	34,6±19	n.s

Table 20: comparison between first and second repetition on cycle ergometer, VO<sub>2</sub> at baseline (base), VO<sub>2</sub> at steady state (ss) and MRT values.

VO<sub>2</sub> response is quantitatively different among groups, which has been well documented in the literature, depending on age or presence of pathology. In the baseline condition VO<sub>2</sub> is around 350 l/min in male and 300 l/min in female, and the increase to the steady state during exercise is different among the groups. Young subjects display the greater increase: 2,0 l male, and 1,2 l female; elderly groups show lower increase, 1,3 l male and 0,7 l female; Diabetic groups behave like the Elderly. The kinetics tends to be similar per age but not per sex, HEM and HEF are significantly different than HYF and HYM.

In Fig 70 we have reported the MRT calculated for all 125 subjects who have repeated a SW trial, identified by different symbols for any group, in an identity diagram. A large scattering is evident, with the relevant exception of CHF (blue diamonds), who, with a single exception, all lay below the identity line, indicating that their MRT was consistently reduced at the second trial.

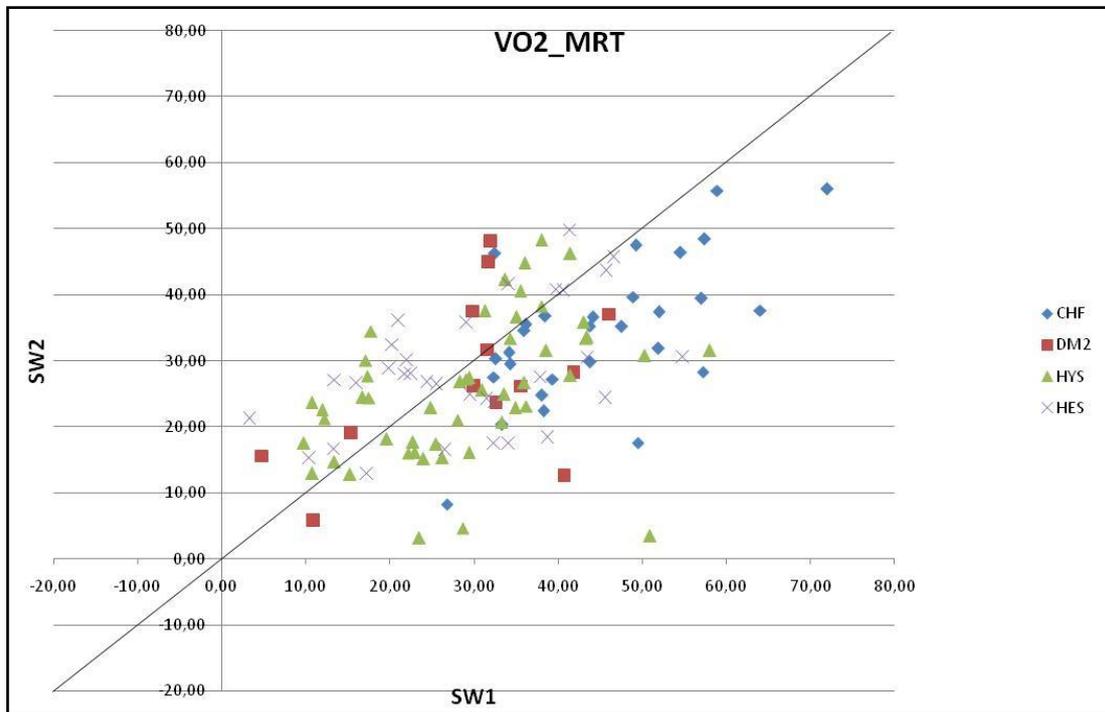


Figure 70: MRT of each subject in constant load aerobic tests in two repetitions (SW1, SW2)

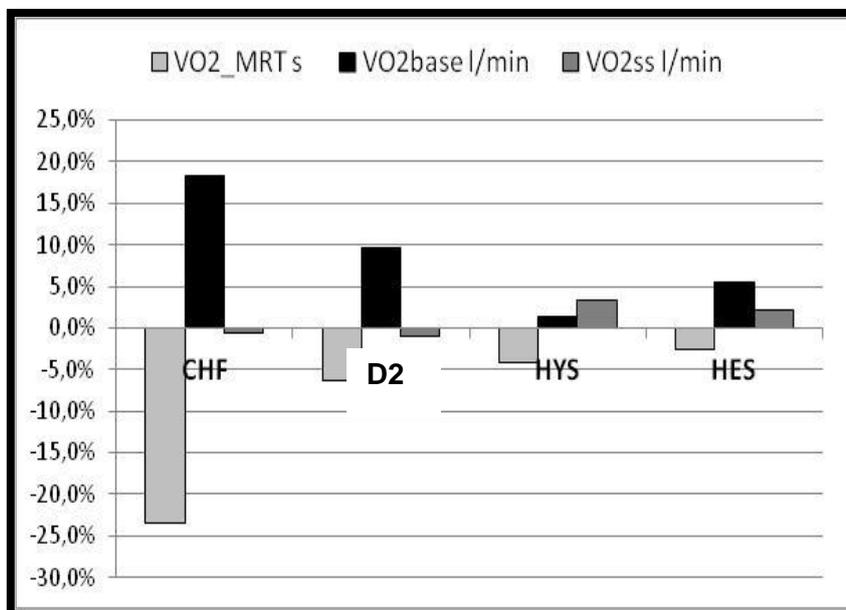


Figure 71: Percent changes of MRT, baseline  $VO_2$  and steady state  $VO_2$  of each group in the second bout of constant load aerobic test with respect to the first bout

To allow an easier interpretation, in Fig 72 we have reported the average MRT per group. Thus it becomes clear that Male (open symbols) adapt faster than Female (full symbols) and CHF much slower. In addition, if the male groups tend to speed up quite slightly their adaptation in the second trail, this tendency is overt in CHF. Notice that this was true also for CHFF, who were two subjects only and were generally excluded from further elaboration due to the excessively small number.

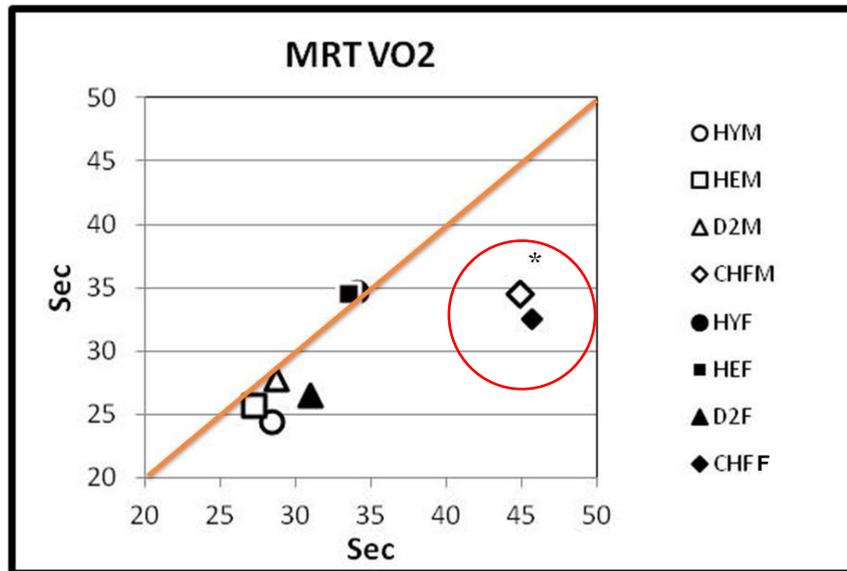


Figure 72: Average MRT of each group in two repetitions (SW1, SW2)

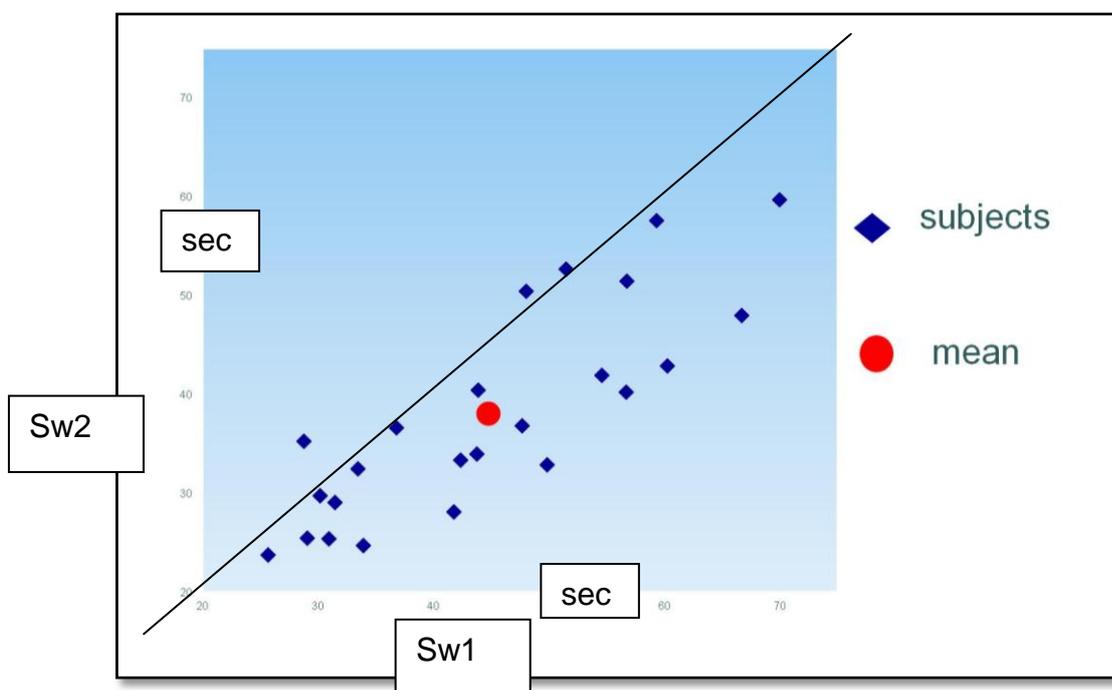


Fig 73: CHF (27 males and 2 females) MRT comparison between 1<sup>st</sup> stand and 2<sup>nd</sup> exercise bouts

Most CHF subjects increased the speed of VO<sub>2</sub> kinetics: the average values of MRT were 44,7 s in SW1 and 38,1 s in SW2, a significant decrease by 15%.

The calculation of MRT has been proposed to estimate the time course of VO<sub>2</sub> adaptation at the onset of a constant load exercise, but it can be extended to other variables. In table 21 we reported the percent changes in MRT calculated for some respiratory variables and for heart rate. As for the data described above, changes for all groups are rather scattered and small, while in CHF we observe a regular increase of kinetics in all the variables reported.

MRT SW2 vs SW1	HYS	HES	DM2	CHF
<b>VT</b>	↑ 1.1%	↓ 10.1%	↓ 9.4%	↓ 31.6%**
<b>VE</b>	↓ 7%	↓ 6%	=	↓ 24%**
<b>V'O<sub>2</sub></b>	↓ 10.1%	↑ 2.5%	↓ 6.9%	↓ 23.5%**
<b>V'CO<sub>2</sub></b>	↓ 7.7%	↑ 5.8%	↓ 1.9%	↓ 19.5%**
<b>R</b>	↓ 4.8%	↑ 3.4%	↓ 1.4%	↓ 21%**
<b>HR</b>	↓ 9%	↑ 1%	↓ 14%	↓ 22%**

Table 21: percent changes in MRT between SW1 and SW2 of some metabolic variables (column 1) in each group

## Discussion

### Cardiovascular

In literature it has been already reported that age-associated decline in maximal oxygen consumption can be attenuated by habitual aerobic exercise. This decline is proportional to a decreased cardiac output reserve, peak heart rate, and peak stroke volume in older subjects. For this reason we decided to evaluate all these parameters. In additions other works refer that Elderly women appear to adapt to exercise activity with similar increases in  $\dot{V}O_{2\max}$  as elderly men, but with a different mechanism<sup>(22, 23)</sup>.

Lambert reported that ~66% of the improvement in  $\dot{V}O_{2\max}$  in elderly men was due to an increase in cardiac output and more specifically in stroke volume. However, in elderly women these investigators reported that the improvement in  $\dot{V}O_{2\max}$  was due to an enhanced A- $\dot{V}O_2$  difference with no change in cardiac output<sup>(26)</sup>. Moreover, untrained people with type 2 diabetes have been shown to have a reduced  $\dot{V}O_{2\max}$  compared with non diabetic people;  $\dot{V}O_2$  and HR during constant load exercise is lower in elderly than in young. Overall cardiovascular results are similar among groups except for two items: CO is the highest in D2M, in substantial accordance with incremental test results. In HEF all cardiovascular parameters show a faster increase within the first minute.

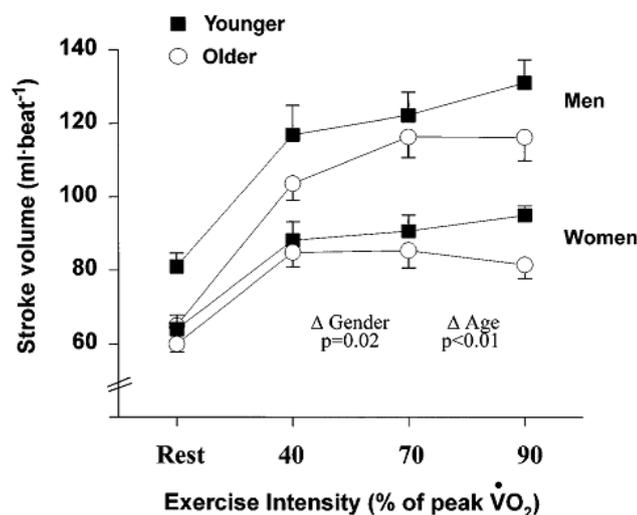


Fig. 2. Stroke volume (SV) responses of 4 subgroups during submaximal (40 and 70% of  $\dot{V}O_{2\text{peak}}$ ) and near-maximal (~90% of  $\dot{V}O_{2\text{peak}}$ ) intensities of leg cycling. Values are means  $\pm$  SE. SVs were higher in men than in women at all intensities. Additionally, SV increased during submaximal intensities (40–70%) of cycling in men, but not in women. However, older men and women showed an impaired ability, relative to their younger counterparts, to augment or maintain SV at 70–90% of  $\dot{V}O_{2\text{peak}}$ .

Figure 74: Proctor 1998, SV

## Metabolic

The pulmonary oxygen uptake ( $\text{VO}_2$ ) response to constant intensity exercise reflects the time course of the adjustment of muscle  $\text{O}_2$  consumption towards a steady state, following a short delay reflecting the transit time of blood flow from the exercising muscle to the lung<sup>(48)</sup>. It has been reported that a prior bout of heavy exercise (above the lactate threshold, LT) speeds the  $\text{VO}_2$  kinetics during subsequent heavy exercise<sup>(49,50)</sup>. Both of these studies characterized the heavy exercise  $\text{VO}_2$  response using a single dynamic parameter ('effective' time constant or Mean Response Time). Therefore the  $\text{VO}_2$  response to heavy exercise is dependent on the intensity of prior exercise and it increases the amplitude of the phase II response independently of changes in the baseline  $\text{VO}_2$ <sup>(51)</sup>.

The lower kinetics of adaptation to constant load exercise in CHF is well documented and probably stands form a generally poor fitness level, coupled to sluggish response of the heart.

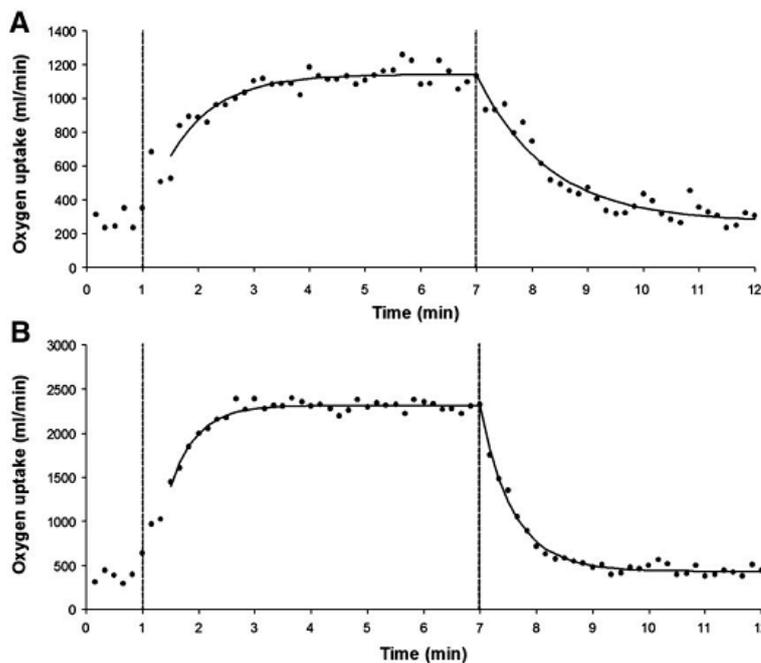


Figure 75: Changes in oxygen uptake during and after the constant load test in a patient with chronic heart failure (A) and a healthy control subject (B). The curved line represents the mono-exponential model fit. The first vertical line indicates onset of exercise and the second vertical line the end of exercise.

In summary, we may devise a sort of graduation in the preconditioning effect of previous bouts of exercise on the time course of a following repetition (Table 23). In the young, only heavy (not light) exercise is preconditioning, and only for a following heavy (not light) exercise bout. In the healthy

older, heavy exercise affects even a following light exercise bout. In CHF, even a light exercise affects a following light exercise bout.

This sort of graduation may offer some hint about the mechanisms underlying the preconditioning effect. As usual, the mechanisms limiting the basal oxygen consumption, as well as its adaptation to new steady states, may be classified as central or peripheral. For the young, who were the first population studied under this respect, an enhancement of peripheral mechanism was suggested, reflecting more prompt delivery of substrate to oxygen consuming enzymes. Thus, a supramaximal effort ought to produce changes in the intracellular environment of muscle fibers, which allows a more rapid increase in oxygen utilization during a following effort, provided this is also characterized by a metabolic demand exceeding maximal oxidative capabilities. This is also probably true for the healthy older, whose aerobic power is basically reduced and may be advantaged by a previous bout of heavy exercise even for a lighter exercise, with analogous mechanisms. Thus for these categories of subjects, peripheral mechanisms seem to prevail, even if central mechanisms may not be totally excluded. On the contrary, CHF patients are basically limited in their ability to raise cardiac output and enhance muscle blood flow during exercise. In this case, a previous bout of light exercise leaves the circulatory system in a hyper dynamic state that enables them to adjust the circulatory response to the following (light) exercise bout more efficiently, thus reducing MRT.

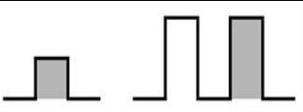
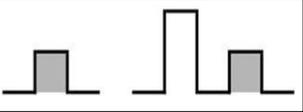
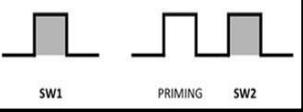
PRIMING EFFECT ON				
	HYM/F	HEM/F	D2M/F	CHF
<p>Intense/intense (I/I) [literature]</p> 	YES	YES	YES	YES
<p>Intense/moderate (I/M) [our data not shown]</p> 	NO	YES	YES	YES
<p>Moderate/moderate (M/M) [this study]</p> 	NO	NO	NO	YES

Table 23: Priming effect- considering different possibility, Intense/intense, Intense/moderate and moderate/moderate







## References cap. 4

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## Conclusion

To summarize, we need to pool together the main differences among our groups of subjects that characterize the response to acute exercise of different type. In incremental tests, we found an easily expected graduation in maximal load and  $\text{VO}_2$ , with young male attaining the top levels, followed by young females, elderly males and females, with the lowest values for diabetics. The unexpected differences regarded the HEM group for the cardiovascular response and the diabetics for oxygen extraction. The HEM subjects were unable to adapt their stroke volume to the increasing load and eventually reduced SV, while peripheral vasodilatation that characterized incremental tests in all other subjects, subsided. It is therefore tempting to conclude that the main limitation of maximal aerobic performance in HEM stems from inadequate adaptation of the microvasculature of working muscles. Diabetic subjects, both male and female, whose aerobic performance was similar to that of our elderly groups, showed the highest de-saturation of capillary blood in working muscles. The D2M group, and to a lesser extent the D2F group, showed the highest oxygen extraction values in all kinds of exercise. Thus, enhanced blood de-saturation seems to be a common feature linked to diabetes. This finding combines with the highest values of FBF (in males) in dynamic and isometric exercise. Therefore, the oxygen flow to exercising skeletal muscle cells is strongly enhanced in D2M, which raises the issue of a possible reduction in metabolic efficiency associated to the pathology.

Another unexpected finding was a delayed termination in cardiac output and oxygen consumption increase at the end of leg press exercises that characterize healthy males, not females nor diabetics. Such a persistence was also observed in the limb hyperemia (data for HEM not available). This may be due to inadequate adaptation of cardiovascular and respiratory mechanisms during this type of exercise, leading to persistence of enhanced metabolic demands after the effort was terminated. Of course, one reason for this difference may derive from the highest loads lifted by males, however diabetics males 1RM was higher than that of HEM, but this sort of overshoot was not seen in D2M. Therefore, the difference with the other groups cannot be only attributed to the absolute value of loads, but calls into play the overall cardiovascular and metabolic regulation in healthy males.

The last important finding is the reduction of MRT in a second bout of constant load moderate level work in CHF. Given the general low fitness level of these subjects, due to the limiting condition of the cardiovascular system associated with reduced physical activity, it is probable that the previous bout of moderate exercise keeps the circulatory system in a sort of hyper dynamic state that helps faster adaptation to subsequent exercise bout. The mechanism of the priming effect in CHF must be

different with respect to that of the other subjects, requiring high loads for the priming effect and pointing to peripheral rather than central mechanisms.

### Consideration

This study ought to be continued by pointing to the effects of training, rather than to the acute effects of exercise that were afforded in the present phase, and keeping different population groups, according to sex, age and pathologies. The main results of the present study (table 24, 25) should be transferred to training prescriptions based on important differences that may be crucial to work out the correct program of personalized exercise steps.

INCREMENTAL TEST							
	LOAD	VO2	HR	SV	CO	TPR	HHB
<b>HYM</b>	+++++	+++++	+++++	+++++	+++++	-----	+++
<b>HEM</b>	++++	+++	+++	+++	++	---	+++
<b>D2M</b>	+++	+++	+++	+++++	++	-----	+++++
<b>HYF</b>	++++	++++	+++	+++	++++	-----	+++
<b>HEF</b>	+++	+++	++	++	+	-----	++
<b>D2F</b>	++	++	+++	++	++	-----	+++++

Table 24: the overall adjustments to incremental test are synthesized: ( + ) indicates an increase ; ( - ) indicates a decrease, ( = ) indicate no change; the numbers of symbols indicates the magnitude of changing

LEG PRESS TEST							
DYNAMIC							
	VO2PRE	VO2POST	FBFPRE	FBFPOST	HR	SV	CO
<b>HYM</b>	+++++	+++++	+++++	+++++	+++++	+++++	+++
<b>HEM</b>	++++	+++	N.C.	N.C.	++	---	+-
<b>D2M</b>	+++	++	+++	-	++	---	+++++
<b>HYF</b>	++++	++	++++	+	++++	++++	+++
<b>HEF</b>	+++	++	+++	=	+	---	++
<b>D2F</b>	++	++	++	-	++	---	+++++
ISOMETRIC							
	VO2PRE	VO2POST	FBFPRE	FBFPOST	HR	SV	CO
<b>HYM</b>	+++++	+++++	+++++	+++++	+++++	-	++
<b>HEM</b>	N.C.	N.C.	N.C.	N.C.	N.C.	N.C.	N.C.
<b>D2M</b>	+++	++	+++	-	++	-	+
<b>HYF</b>	++++	++++	++++	+	++++	-	++
<b>HEF</b>	+++	+++	+++	=	+	-	+
<b>D2F</b>	++	++	++	-	++	-	+

Table 25: the overall adjustments to leg press test are synthesized: ( + ) indicates an increase ; ( - ) indicates a decrease, ( = ) indicate no change; the numbers of symbols indicates the magnitude of changing

For example, Diabetics subjects exhibited the highest oxygen extraction at muscular level among all subjects in all exercise types. A possible suggestion, in order to apply a differentiated training plan and to achieve safe and the good performance, might be to always perform at least 5 min of moderate exercise on a cardio machine (aerobic exercise), to set the cardiovascular system in the best conditions to bear the subsequent efforts in any sort of training session.

Elderly male show a different SV adaptation to incremental exercise. The strong decrease in SV of HEM could be caused by relatively compromised vasodilator function, which does not keep proportional to the effort. Although their muscle mass appears to be well preserved, in comparison with female, the muscle usage is not optimized and, maybe as a consequence, the microvascular response is impaired. A good solution might be to train them on cycle ergometer with an intermittent protocol that enhances angiogenesis and improves muscle vasodilatation.

The large quantitative differences between male and female must be seriously taken into account: in the general practice in gymnasiums such differences are too often overlooked, and training programs are exclusively based on HR and 1RM. Based on our study it is possible to understand how to proceed in order to produce specific adaptations and to improve performance.

For example, females are characterized, with respect to males, by lower muscular oxygen extraction, lower femoral blood flow, lower oxygen utilization. Therefore, it might be really important to introduce active recovery phases that modify the initial oxygen debt and improve the performance. It may also be suggested to prescribe higher volume and lower intensity, in order to allow longer periods for bodily adaptation to metabolic demands.

CHF, male and female, have similar adaptations to aerobic exercise. One specific item is highly slowed kinetics, as determined by the MRT, not only for oxygen consumption but for a variety of parameters (see Table 21). Therefore, MRT determination, which is relatively easy to obtain, could be proposed as a reliable tool to monitor clinical condition and physical fitness in these patients.

My utopian aim would be to tailor, by careful interpretation of the results, individualized training programs for all the categories of subjects I have tested.



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## **POSTER COMMUNICATIONS (P) AND ORAL COMMUNICATION (O)**

### **(P) SIF2009:**

#### **Skeletal muscle improvements in CHF patients after 16 week resistance training**

Tarperi C, Baraldo A, Schena F, Cevese A

The aim of this study was to evaluate chronic adaptations in skeletal muscle strength and function in 12 chronic heart failure (CHF: all males, NYHA-class II, ICD implanted) patients (ITG: 67±5 yy, 75±14 kg, 174±6 cm) after a 16 week controlled and progressive resistance training program (1:30 hour, 3 times/week) on different muscle groups using 6 isotonic machines, based on 70% 1RM (previously calculated by Brzycki's formula and recalculated every fortnight). Before and after training, we calculated, for each subject: 1RM at all machines; total force TFI as the sum of all 1RMs, and the maximal rate of force development (RFD) in the leg press machine. For comparison we also tested 6 more CHF patients (ATG: 66 ±5 yy, 76±13 kg, 1715±10 cm) who followed an aerobic training for a similar period. The 1RMs in each muscle group were significantly improved by 53% in ITG and by 20% in ATG. TFI passed from 403 to 598 Kg (+48.8%, P<0.001) in ITG and from 412 to 495 Kg in ATG (+18.8%, P=0.02). The RFD showed a doubling (P=0.001) in ITG an increase by 31% (P=0.04) in ATG. Resistance training is a valid strategy to improve muscle force and function in CHF. Therefore, by this means, it may be possible to contrast muscle wasting in CHF and improve their quality of life.

#### **(P) Changes in muscle oxygen extraction (NIRS) during exercise in chronic heart failure patients after a period of resistance training.**

Baraldo A, Cevese A, Tarperi C

Aim: monitoring changes in oxygen extraction by working muscles during an incremental cycle ergometer exercise in chronic heart failure (CHF) patients, before and after a 16 week period of resistance training, by a near infrared spectroscopy (NIRS) . Subjects: 12 CHF patients (age 45-75, all males, NYHA class II) carrying an implantable defibrillator. Incremental test to exhaustion with steps of 10W\*min<sup>-1</sup> before and after a 4 month resistance training. In comparison with pre training, post training NIRS recordings showed significant increases (about 100%, P<0.05) in oxygen extraction at workloads 40 W to 70 W (all subjects). At the peak load of 97±18 before and 108±35W after training, extraction was 45.7±29.8% and 65.3±35.22% (P<0.05), respectively.

Resistance training, which is seldom prescribed, and often even forbidden, to CHF patients, is expected to produce skeletal muscle hypertrophy or to prevent atrophy (a common, severe, evolution of chronic heart failure), but ought not to interfere with oxygen utilization. The present

results, to the contrary, demonstrate that resistance trained muscles in CHF patients significantly improve their oxygen utilization, as attested by enhanced extraction during similar absolute and relative workloads. This may be attributed either to build up of mitochondrial oxidative enzymes, or to enhanced capillarity, or both, although the precise mechanism cannot be disclosed in our experimental setup.

### **(P) Metabolic changes in chronic heart failure after resistance and aerobic training.**

Tarperi C, Schena F, Zanolla L, Baraldo A, Cevese A

Chronic changes induced by aerobic and resistance training in chronic heart failure patients (CHF) are not completely documented. In the present study we wanted to compare the metabolic changes obtained by two different exercise training in CHF. We trained 18 (all males, age  $66.5 \pm 5.2$ yy, NYHA class II) CHF patients carrying an implantable defibrillator, for safety reasons. Training lasted 16 weeks 3 times/week; 6 subjects (ATG) performed aerobic and 12 subjects (ITG) resistance training. Pre and post training incremental  $10W \cdot \text{min}^{-1}$  cyclergometer tests allowed evaluation of first (VT1) and second (VT2) ventilatory thresholds by Wasserman method. After the training, the mechanical and metabolic powers increased: VT1 54.2 to 73.3 watt ( $\text{VO}_2$  0.8 to 1.0 l/min) in ITG and 50.8 to 66.7 watt ( $\text{VO}_2$  0.9 to 1.1 l/min) in ATG; VT2 68.3 to 90 watt ( $\text{VO}_2$  1.1 to 1.2 l/min) in ITG and 79.2 to 90.8 watt ( $\text{VO}_2$  1.2 to 1.4 l/min) in ATG. All changes were significant ( $P < 0.05$ ). Resistance training seems to be as effective as classical specific aerobic training in inducing improvements both in VT1 and VT2. The results could reflect an improvement of  $\text{O}_2$  delivery and utilization systems (VT1) and a refinement of plasma bicarbonate lactic acid buffering capacity (VT2). Overall, this is a very important outcome in CHF patients.

### **(P) PHD DAY 2010**

#### **Acute cardiovascular responses during resistance exercise: comparison between Chronic Heart Failure Patients, Healthy Age Matched and Young Subjects**

Baraldo A, Cevese A, Tarperi C

The aim of the present project is to characterize hemodynamic acute responses during leg press exercise (resistance efforts), in different populations: Chronic Heart Failure Patients (CHF, 12 subjects  $\pm 66.3$ ), Healthy elderly (HES, 8 subjects  $\pm 65.2$ ) and Healthy Young Subjects (HYS, 8 subjects  $\pm 24.3$ ). We have collected: pressure values (systolic SAP and diastolic DAP), heart rate (HR), stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR). All subjects must raise a given load as many times as they can with Leg press machine (1RM INDIRECT TEST). In this way we will find a value in kg that will be used to perform strength Test (70% 1RM);

the session is divided into a warm-up phase (jogging), and a test phase, which lasts about 1 hour and is performed according to the formula of the 2 series (10 minute recovery between series) of 12 repetitions (each repetition should last about 5 sec).

Results of the two series and average measurements at control (C), at peak during exercise (E) and 20 seconds after the exercise (R): HES → SAP 163-228-180; DAP 74-108-71; HR 84-115-108; SV 92-65-97; CO 8-7-10; TPR → 0.91-1.35-0.64. CHF → SAP 127-162-129; DAP 63-86-56; HR 69-90-83; SV 91-67-102; CO 6-5-8; TPR 0.91-1.36-0.63. HYS → SAP 140-200-158; DAP 70-105-70; HR 90-133-110; SV 105-98-110; CO 9-12.5-12; TPR 0.6-0.6-0.5.

In all groups cardiovascular adaptations during and after resistance exercise appear adequate. Systolic and diastolic pressure are higher in HES than in HYS; in CHF they were pharmacologically reduced.  $\beta$ -blockade reduced HR in CHF, but HR was also lower in HES than HYS at peak exercise. HYS did not change TPR from base, contrary to HES and CHF, probably as an effect of a better microcirculatory adaptation at the active muscle level. As a consequence the overall cardiovascular response is different in young versus elderly subjects: SV decreased at peak and increased during recovery in CHF and HES, but did not change in HYS; CO decreased slightly in HES and more in CHF during exercise and rebounded at recovery. HYS can increase CO at peak and reduce it after the effort. The difference in SV response between CHF/HES and HYS probably represents an age-factor, depending on TPR (unchanged in HYS). It does not seem to be related to heart failure (CHF behave like HES).

### **(P) Manchester - Physiology 2010**

#### **V'O<sub>2</sub> kinetics is speeded up during a second bout of constant load cycle ergometer exercise in chronic heart failure humans.**

Anna Baraldo, Cantor Tarperi, and Antonio Cevese

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Oxygen consumption (V'O<sub>2</sub>) at the onset of a constant-load exercise rises progressively to an enhanced steady state level, with typical kinetics, that can be altered by aerobic training or by disease (cardiovascular, diabetes). Kinetics is typically studied by fitting procedures, including a time delay and a one, two or three component exponential model. Alternatively, mean response time (MRT) is calculated, as the ratio between the integral of V'O<sub>2</sub> deficit during the transient phase and V'O<sub>2</sub> at steady state. We sought to verify whether MRT can be reduced during a bout of constant load exercise preceded by an identical exercise, in chronic heart failure (CHF) patients, in which V'O<sub>2</sub> kinetics is known to be typically slowed with respect to healthy subjects. Twenty patients (mean±SD: 67±5 yy, 78±12 kg, 173±7 cm; V'O<sub>2</sub>max 17.35±5 ml kg<sup>-1</sup> min<sup>-1</sup>; peak work

96±23 W) with NYHA type II/III chronic heart failure, all wearing an automatic implanted defibrillator for safety reasons, performed two bouts of 6 min cycle ergometer exercise, separated by 6 min sitting rest, while connected to a QUARK b2 (COSMED, Italy) metabolimeter for breath by breath recording of respiratory variables. After two min stabilisation, the subjects started pedalling at 60-70 strokes/min against a load corresponding to the individual first ventilatory threshold (Wassermann (1999)), previously determined in an incremental trial. The steady state values of  $\dot{V}O_2$  during the first and the second exercise bouts were unchanged (1026±150 and 1035±175 ml min<sup>-1</sup>, ns, t-test), while the MRT decreased from 42.2 ±14.3 s to 34.7±13.8 s (p<0.01). Thus, a bout of constant load exercise sped up  $\dot{V}O_2$  kinetics by significantly decreasing MRT by about 18%. It may be suggested that the first exercise bout exerts a sort of preconditioning on active muscles, as previously described by others (Gurd BJ et al: J Appl Physiol, 2005) in normal subjects, albeit with a substantial difference, consisting in the use of a much higher-load preconditioning exercise. Although the precise mechanism cannot be determined at present, we believe that CHF patients suffer for a specific skeletal muscle deconditioning status deriving from their chronic cardiac disease, which can be quickly attenuated by a short aerobic exercise.

#### **(P) SIF 2010**

##### **Dynamic resistance exercise: cardiovascular, metabolic and extractive implications**

Baraldo A, Tarperi C, Cevese A

The cardiovascular effects of resistance exercise, matched with metabolic and peripheral O<sub>2</sub> utilisation data, are still poorly understood. The present project characterizes cardiovascular, metabolic and muscle functional responses during leg press resistance exercise in young subjects. Subjects were 8 males (25±2 yy; 177±5 cm; 72±12 kg): they were equipped with a K<sub>4</sub>B<sup>2</sup> metabolimeter to collect respiratory data, a PORTAPRES finger cuff on a free hand to collect hemodynamic data and a NIRS on the right vastolateral muscle, to test muscle oxygen extraction. A 1RM indirect test (Brzycki method) was performed to determine the individual maximal voluntary dynamic force, followed, in separate sessions by two sets of 3 series of leg extensions (10 minute recovery between series) of 12 repetitions at 70% and 80% 1RM, respectively. Averaged results of the 3 series of each set are reported at control, after 10 sec and at the end of each exercise. Most of the changes we documented were load related, since they were higher in the second set (80% 1RM) than in the first set (70% 1RM). Both systolic and diastolic pressures rose during the efforts, while stroke volume was slightly reduced and cardiac output did not change. Heart rate rose in parallel with oxygen consumption, that corresponded to a mild aerobic exercise. Muscle oxygen extraction

increased by 60%. We conclude that active muscles largely rely on increased extraction during isometric contractions

**(P) Preconditioning effect of heavy exercise on O<sub>2</sub> uptake kinetics, determined as MRT (mean response time), in chronic heart failure patients**

Tarperi C, Baraldo A, Cevese A

It has been demonstrated that oxygen consumption kinetics ( $\dot{V}O_{2cin}$ ) at the onset of aerobic exercise may be speeded up when preceded by a short bout of heavy exercise (*preconditioning heavy exercise*, PHE): PHE is effective only on subsequent high intensity exercise in young physically fit subjects, while it may be effective also in moderate intensity exercise in elderly individuals. It was proposed that the mechanism underlying PHE be related to increased muscle blood flow and heart rate after heavy exercise, which would speed up the enhancement of oxygen transport to active muscles after PHE. Whether this phenomenon operates also in patients with chronic heart failure (CHF) has not been determined, yet, and will be the subject of this presentation. 14 CHF male patients (68yy, 77kg, 172cm) performed a cycle ergometer (Sport Excalibur, Lode, NL) incremental test (20W+10W\*min<sup>-1</sup>) to exhaustion, to determine individual maximal aerobic power ( $\dot{V}O_{2max}$ ) and workload ( $W_{max}$ ). Workloads corresponding to the first ( $W_{vt1}$ ) and the second ( $W_{vt2}$ ) ventilator thresholds were also determined by Wasserman method.  $\dot{V}O_{2cin}$  was studied in two subsequent identical sessions (15 days apart) each comprising two moderate load exercises ( $SW_1$ ,  $SW_2$ ) at 80%  $W_{vt1}$ , separated by a high intensity exercise ( $SW_{PHE}$ ), with load equal to  $(W_{vt2} + (W_{max} - W_{vt2})/2)$ . Each exercise started with 3 min free wheeling at 30 RPM, followed by 6 min loaded pedaling at 70 RPM. Successive exercise periods were separated by 6 min sitting rest. Respiratory gas composition was continuously recorded (Innocor, Innovision, DK) during the entire experiment. Breath by breath oxygen values ( $\dot{V}O_{2bxb}$ ) were used to calculate oxygen deficit ( $def_{O_2}$ ) as the difference between theoretical and real  $\dot{V}O_2$  ( $def_{O_2} = (\text{mean steady state } \dot{V}O_2 * 360s - \int_1^{360} \dot{V}O_{2bxb})$ ). The mean response time (MRT) was calculated as the ratio between  $def_{O_2}$  and  $\dot{V}O_{2ss}$ . The mean workloads were 64w in  $SW_1$  and  $SW_2$ , and 96w in  $SW_{PHE}$ . Since there was no difference between the two sessions, we pooled the results.  $Def_{O_2}$  was 784, 924 and 669 ml at  $SW_1$ ,  $SW_{PHE}$  and  $SW_2$ , respectively, with a reduction by 14.8% ( $p=0.007$ ) from  $SW_1$  to  $SW_2$ , while  $\dot{V}O_{2ss}$  did not change at equal workloads (1.246 and 1.293 l\*min<sup>-1</sup>) and was 1.521 l\*min<sup>-1</sup> in PHE. Thus, MRT, which we used as an index of  $\dot{V}O_{2cin}$ , was significantly shortened by preconditioning, from 37.1s in  $SW_1$  to 30.6s in  $SW_2$  (-18.4%;  $p=0.001$ ).

Maximal aerobic power is generally hampered in CHF patients, as part of a reduced level of wellbeing. Also  $\dot{V}O_{2cin}$  is known to be more sluggish than in their age matched counterparts. Thus, it is important to highlight a means by which  $\dot{V}O_{2cin}$  can be speeded up, thus reducing the need to

rely on anaerobic mechanisms at the beginning of exercise. Even more important is recognizing that metabolic adjustments in CHF patients, although negatively influenced by the heart pathology, may still be modulated by appropriate physiological stimuli.

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It has been demonstrated that oxygen consumption kinetics ( $\dot{V}O_{2cin}$ ) at the onset of aerobic exercise may be speeded up when preceded by a short bout of heavy exercise (*preconditioning heavy exercise*, PHE). It was proposed that the mechanism underlying PHE be related to increased muscle blood flow and heart rate after heavy exercise, which would speed up the enhancement of oxygen transport to active muscles after PHE. This phenomenon operates also in patients with chronic heart failure (CHF) has not been determined, yet. 14 CHF male patients (68yy, 77kg, 172cm, Class II NYHA) performed a cycle ergometer incremental test to exhaustion, to determine individual maximal aerobic power ( $\dot{V}O_{2max}$ ), workload ( $W_{max}$ ) and workloads at the first ( $W_{vt1}$ ) and the second ( $W_{vt2}$ ) ventilator thresholds.  $\dot{V}O_{2cin}$  was studied in two moderate load exercises ( $SW_1$ ,  $SW_2$ ) at 80%  $W_{vt1}$ , separated by a high intensity exercise ( $SW_{PHE}$ ), with load equal to  $(W_{vt2} + (W_{max} - W_{vt2})/2)$ , separated by 6 min sitting rest. Breath by breath oxygen values ( $\dot{V}O_{2bxb}$ ) were used to calculate oxygen deficit ( $def_{O_2} = (\dot{V}O_{2SS} * 360s - \int_0^{360} \dot{V}O_{2bxb})$ ) and the mean response time ( $MRT = def_{O_2} * \dot{V}O_{2SS}^{-1}$ ).  $def_{O_2}$  was reduced by 14.8% ( $p=0.007$ ) from  $SW_1$  to  $SW_2$ , while  $\dot{V}O_{2SS}$  did not change at equal workloads. Thus, MRT, was significantly shortened by preconditioning (-18.4%;  $p=0.001$ ). The metabolic adjustments in CHF patients, although negatively influenced by the heart pathology, may still be modulated by appropriate physiological stimuli.

SISMES 2010

**(P) Cardiovascular responses in strength exercise: comparison between Total Peripheral and Femoral Vascular Resistance in healthy young females.**

Cantor Tarperi, Anna Baraldo, Federico Schena, Antonio Cevese

The aim of the present project was to characterize cardiovascular changes combined with  $O_2$  utilisation during and after resistance efforts, in young female subjects. **PURPOSE:** to collect, combine and analyze respiratory, cardiac and peripheral vascular data before, during and after a high-intensity two-leg extension exercise. **METHODS:** 10 healthy girls (mean $\pm$ SD: 24 $\pm$ 2 years, 165 $\pm$ 6 cm, 56 $\pm$ 5 kg, BMI 21 $\pm$ 2) performed repeated strength exercise at 70% MVF on a leg press machine. They moved their knee angle from 90° to 180° and back at angular velocity 45° s<sup>-1</sup> (concentric) and 30° s<sup>-1</sup> (eccentric). The resulting exercise at 0.2 Hz without pauses was protracted to exhaustion (79 $\pm$ 27s) and performed 3 times, with 10 min intervals. Metabolic ( $\dot{V}O_2$ ,  $\dot{V}CO_2$ ), cardiac (arterial pressure, HR, and CO - finger photo-plethysmography and modelflow algorithm),

and femoral artery blood flow (FBF - Doppler ultrasound) data were measured before, during exercise and up to 6 min recovery. **RESULTS** (at peak exercise and 20 s recovery):  $\dot{V}O_2$  rose to 945 and 1032 ml min<sup>-1</sup>;  $\dot{V}CO_2$  to 703 and 733 ml min<sup>-1</sup>; HR to 133 and 110 bpm; CO to 9700 and 9100 ml min<sup>-1</sup>; FBF to 1202 and 1421 ml min<sup>-1</sup>. Total peripheral resistance was decreased by 10 and 28%, while femoral vascular resistance fell by 50 and 68%. **DISCUSSION:** the metabolic and cardiovascular challenge associated with this kind of exercise was moderate, as attested by the relatively low values attained by oxygen consumption, HR and CO; it must however be remarked that after end exercise  $\dot{V}O_2$  further rose, indicating a delay in going back towards baseline conditions. This is explained by the large femoral vasodilatation during recovery, which must compensate for an insufficient rise in FBF during exercise. Discrepancies between the pattern of total peripheral and femoral vascular resistance indicate active neurovascular control aimed at avoiding the fall in arterial pressure that would be caused by the large femoral vasodilatation.

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### **Cardiac, Vascular And Metabolic Changes During Recovery From Resistance Effort**

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The aim of the present project was to characterize cardiovascular changes combined with O<sub>2</sub> utilisation during and after resistance efforts, such as weight-lifting, in young subjects.

**PURPOSE:** to collect, combine and analyze respiratory, cardiac and peripheral vascular data before, during and after a high-intensity knee-extension exercise (EXE).

**METHODS:** 9 male healthy subjects (mean±SD: 27±5 years; 75±7 Kg, 177±7 cm) performed repeated strength exercise at 70% MVF on a single leg extension machine. The subjects moved their right knee angle from 90° to 180° and back at angular velocity 45° s<sup>-1</sup> (concentric) and 30° s<sup>-1</sup> (eccentric). The resulting exercise at 0.2 Hz without pauses lasted 120 s. Metabolic ( $\dot{V}O_2$ ,  $\dot{V}CO_2$ , R - breath by breath metabolimeter), cardiac (arterial pressure, HR, SV, and CO - finger photo-plethysmographic system and modelflow algorithm), and femoral artery blood flow (FBF - Doppler ultrasound) data were measured before, during exercise and up to 6 min recovery.

**RESULTS:** (mean±SD at baseline and peak exercise): Metabolic:  $\dot{V}O_2$  from 4.9±0.3 to 9.2±0.2 ml/min/kg (+88%);  $\dot{V}CO_2$  from 5.2±0.3 to 9.2±0.2 l/min (+77%), R from 0.77±0.01 to 0.93±0.01. Cardiac: HR from 74±1 to 99±2 bpm (+33%); SV from 77±1 to 67±2 ml (-13%); CO from 5.0±0.1

to  $6.0 \pm 0.1$  l min<sup>-1</sup> (+20%). Peripheral vascular: FBF from  $94 \pm 8$  to  $202 \pm 51$  (+62%). During recovery we observed a further increase in  $\dot{V}O_2$  ( $10.6 \pm 0.1$  (+116%)),  $\dot{V}CO_2$  ( $10.4 \pm 0.1$  (+100%)) by 20 s recovery, and R ( $1.18 \pm 0.001$ ) after 80 s. HR immediately recovered, returning to baseline in 10-20 s.

SV rebounded after the effort, up to  $89 \pm 4$  ml (+16%) at 10 s recovery. During the effort CO increased, because of tachycardia, despite the fall in SV; after its cessation an additional light increase lead CO to  $7.0 \pm 0.1$  l/min (+40%) in 20 s. FBF showed a sharp increase within 20 s recovery, up to  $752 \pm 17$  ml/min (+495%); afterwards it declined progressively, however not reaching base levels after 6 min.

CONCLUSIONS: even with such a short duration, the kind of exercise proposed was of sufficient intensity as to induce large changes in metabolic and circulatory parameters. During the recovery, when the transmural pressure exerted by isometric contractions vanishes, a considerable oxygen deficit is unmasked, leading to further increases in  $\dot{V}O_2$  and  $\dot{V}CO_2$ . The femoral flow increases only slightly during the effort, but rises by almost 5 times during recovery as a consequence of reactive.

#### **(P) ECSS2010**

#### **Comparison of aerobic and resistance training effects on glycemic control in type 2 diabetes mellitus (T2DM)**

**Bacchi, E.1, Negri, C.1, Tarperi, C.2, Milanese, C.2, Baraldo, A.2, Rudi, D.2, Zancanaro, C.2, Cevese, A.2, Schena, F.2, Lanza, M.2, Moghetti, P.1**

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#### **Introduction**

Previous trials have evaluated the effects of aerobic training and resistance training on glycemic control in type 2 diabetes but there are only few data comparing these two types of exercise in these subjects (Sigal, 2007). The aim of this study was to compare the effects of aerobic and resistance training in T2DM patients.

#### **Methods**

27 diabetic patients, 9 females and 18 males (mean $\pm$ SD:55.8 $\pm$ 7.1 years, BMI 30.7 $\pm$ 3.7 kg/m<sup>2</sup>, HbA1c 7.3 $\pm$ 0.7%), treated with oral hypoglycemic agents and uncomplicated were randomized to

aerobic group (AER, n=14) or to resistance training (RES, n=13). The two groups had similar baseline characteristics. Exercise training was performed 3 times weekly, 60 minutes per session, for 4 month. AER group exercised at 60-65% heart rate reserve. FOR group performed 3 series of 8-10 repetition of 8 different exercise on weight machines each session, at 70-80% 1RM. Before and at the end of the study the following were assessed: HbA1c (primary outcome), BMI, waist circumference, blood pressure, body composition (by DEXA Total Body), insulin sensitivity by euglycemic hyperinsulinemic clamp (DeFronzo, 1979), peak oxygen uptake (VO<sub>2</sub>peak), leg and arm muscle 1RM tests.

## **Results**

Mean exercise training attendance was 86% in both group. Only 1 patient, in AER group, dropped-out. VO<sub>2</sub>peak increased by 8.5% after 4 month in AER (p<0.001), while leg and arm muscle strength increased by 21±23% and 28±10% in RES (p<0.01 for both). After 4 months of training, HbA1c decreased similarly in AER and RES groups (-0.36±0.45 vs -0.37±0.56). AER and RES groups showed similar changes in anthropometric features (BMI -0.81±0.8 vs -0.52 ± 0.72 kg/m<sup>2</sup>, waist circumference -3.3±2.9 vs -2.2±2.1 cm, total fat mass -2112±1750 vs -1924±1486 gr, total lean mass -175±1048 vs +496±1376 gr, respectively). Insulin sensitivity changes were also similar in AER and RES groups (+181±296 vs +128±229 μmol/min m<sup>2</sup> BSA). Blood pressure was lowered in both groups, without statistically significant differences between groups (systolic -9.8±19.4 vs -5.5±17.7 mmHg; diastolic -4.4±11.4 vs -1.5±10.4 mmHg, respectively). In multivariate analysis HbA1c improvement was independently predicted by baseline HbA1c, change in insulin sensitivity and reduction in total body fat.

## **Discussion**

These preliminary data suggest that aerobic exercise and resistance exercise can exert similar effects on metabolic control of T2DM despite their different effects on functional capacity improvement.

## **References**

- Sigal RJ et al.(2007). *Ann Intern Med*, 147, 357-69  
DeFronzo RA et al.(1979). *Am J Physiol*, 237,E214-23

## **(O) ECSS2010**

### **Acute cardiovascular responses during resistance exercise: comparison between Chronic Heart Failure Patients, Healthy Age Matched and Young Subjects**

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#### Introduction

Acute hemodynamic responses during resistance efforts are not well characterized. The aim of the present project was to characterize such responses during leg press exercise, in different populations.

#### Methods

Experiments were performed on: 8 Healthy Young Subjects (HYS, 25±5 yrs), 12 Chronic Heart Failure Patients (CHF, 66±5 yrs), 8 age-matched Healthy Elderly (HES, 66±4 yrs). All subjects were equipped with a Portapres device on a finger of a free hand. We analyzed: pressure values (systolic SAP and diastolic DAP), heart rate (HR), stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR) (by Modelflow software). All subjects performed a 1RM indirect test (Brzycki method) to determine the individual load in kg that was used during the strength test (70% 1RM); sessions were divided into a warm-up phase (jogging), and a test phase, which lasted about 1 hour and was performed according to the formula of 2 series (10 minute recovery between series) of 12 repetitions (each repetition lasting about 5 sec).

#### Results

Averaged results of the two series, with measurements taken at control (C), at peak changes during exercise (E) and 20 seconds after the exercise (R): HYS - SAP 140-200-158; DAP 70-105-70; HR 90-133-110; SV 105-98-110; CO 9-12.5-12; TPR 0.6-0.6-0.5. HES - SAP 163-228-180; DAP 74-108-71; HR 84-115-108; SV 92-65-97; CO 8-7-10; TPR 0.91-1.35-0.64. CHF - SAP 127-162-129; DAP 63-86-56; HR 69-90-83; SV 91-67-102; CO 6-5-8; TPR 0.91-1.36-0.63.

#### Discussion

In all groups cardiovascular adaptations during and after resistance exercise appeared adequate. Systolic and diastolic pressures were higher in HES than in HYS; in CHF they were pharmacologically controlled.  $\beta$ -blockade reduced HR in CHF, but HR was also lower in HES than HYS at peak exercise. TPR did not change from base in HYS, while it rose in HES and CHF, probably as an effect of a better microcirculatory adaptation at the active muscle level in the HYS. As a consequence the overall cardiovascular response was different in young versus elderly subjects: SV decreased at peak and increased during recovery in CHF and HES, but did not change in HYS at any phase; CO decreased slightly in HES and more so in CHF during exercise, and

rebounded at recovery. In HYS CO increased at peak and declined after the effort. The difference in SV response between CHF/HES versus HYS probably represents an age-factor, depending on TPR (unchanged in HYS). It does not seem to be related to heart failure (CHF behave like HES).

## **(O)ECSS2011**

### **Aerobic and Resistance training in Chronic Heart Failure and Type 2 Diabetes, central and peripheral limiting factors analysing**

Tarperi C., Bacchi E., Zanolla L., Baraldo A., Milanese C., Moghetti P., Cevese A.

#### **Introduction**

It is well known that aerobic and strength training specifically improve, respectively, central and peripheral limiting factors of skeletal muscle performance, and recent studies confirmed this trend also in the elderly healthy population. Type 2 Diabetes patients (DM2) are characterized, besides insulin resistance, by peripheral and metabolic limitations to skeletal muscle performance, while Chronic Heart Failure (CHF) patients are limited by cardiovascular factors. Therefore, the aim of the present research was to compare and characterize the effects of the two types of exercise on DM2 and CHF.

#### **Methods**

26 DM2 male patients (uncomplicated, treated with oral hypoglycaemic agents: age  $57 \pm 7.2$  yrs, HbA1c  $7.3 \pm 0.7\%$ ), and 20 CHF male patients (NYHA Class II-III, ICD implanted: age  $67 \pm 5.0$  yrs, EF 28.9%;) were randomized to aerobic ( $A_{DM2}=13$ ,  $A_{CHF}=8$ ) or resistance training ( $R_{DM2}=13$ ,  $R_{CHF}=12$ ). Supervised exercise sessions were performed 3 times weekly following the Recommendations for exercise prescriptions in DM2 (ACSM and ADA, 2010) and CHF (ACSM and NYHA), respectively. The following variables were assessed before and after 4 month treatments: BMI, body composition (Fat Total, Lean Mass by Total Body DEXA); peak oxygen uptake ( $VO_{2peak}$ ); muscle 1RM indirect tests (Brzycki method, chest press and leg press).

#### **Results**

At baseline, DM2 and CHF respectively showed the following values: BMI  $29 \pm 4.4$  and  $26 \pm 3.6$   $kg/m^2$  ( $p=0.008$ ), FAT  $24 \pm 7.7$  and  $20 \pm 5.4$   $kg$  ( $p=0.05$ ),  $VO_{2peak} * kg^{-1}$   $27 \pm 4.0$  and  $18 \pm 2.6$   $ml * kg^{-1} * min^{-1}$  ( $p<0.05$ ), 1RM at chest press  $48 \pm 9.8$  and  $34 \pm 6.6$   $kg$  ( $p<0.0001$ ), at leg press  $257 \pm 55$  and  $203 \pm 32$   $kg$  ( $p<0.001$ ). After aerobic training,  $V'O_{2peak} * kg^{-1}$  was increased by 19% both in DM2 and CHF ( $P<0,001$ ), while in resistance training it increased by 17% in CHF only ( $P=0,001$ ). Resistance

training increased by 23% in DM2 and by 52% in CHF the 1RM in upper limbs and by 17% in DM2 and by 44% in CHF in the lower limbs. Beyond, a statistically increased by 12% and 22% in arm and leg muscle respectively was found in CHF after resistance training.

## **Discussion**

Both treatments permitted health related benefit in CHF and DM2 populations. Aerobic training improve, central and peripheral limiting factors obtained an increased maximal aerobic power in both diseases.  $\dot{V}O_{2peak}$  enhances by resistance training too in CHF but not in DM2. The wasted cardio-circulatory and muscle condition at baseline in CHF, more than DM2, could explain these important results. Muscle training also improved the maximal voluntary dynamic force (1RM) in arm and leg in both groups. It is interesting to evaluate, the potential impact of cross-treatment on same populations.

### **(O)Effects of Aerobic Training and Resistance Training on Visceral and Ectopic Fat as measured by Magnetic Resonance Imaging in Subjects with Type 2**

**Bacchi, E.1, Negri, C.1, Faccioli, N.2, Di Sarra, D.1, Tarperi, C.3, Milanese, C.3, Baraldo, A.3, Schena, F.3, Cevese, A.3, Lanza, M.3, Moghetti, P.1**

Introduction Non-alcoholic fatty liver disease is an independent predictor of incident cardiovascular events in type 2 diabetes patients (DM2). Previous studies evaluated the effects of aerobic and resistance training on glycaemic control in DM2 (Sigal, 2007), but there are no data comparing the effects of these different types of exercise on ectopic fat and visceral adipose tissue in these patients. Methods 38 DM2, 11 females and 27 males (mean $\pm$ SD: age 56 $\pm$ 7 years, BMI 29.4 $\pm$ 4.6 kg/m<sup>2</sup>, HbA1c 7.3 $\pm$ 0.7%) were randomized to aerobic (AER, n=20) or to resistance (RES, n=20) training. In both groups exercise was performed 3 times weekly, for 4 months. The AER group exercised for 60 minutes at 60-65% heart rate reserve. The RES group performed 3 series of 8-10 repetitions of 8 different exercises on weight machines each session, at 70-80% 1RM. Before and after the intervention programs visceral adipose tissue (VAT) and fat accumulation in the liver were measured using Magnetic Resonance Imaging. In addition, the following were assessed: fat mass (FM, by DEXA Total Body), metabolic features, insulin sensitivity (by euglycemic hyperinsulinemic clamp), peak oxygen uptake( $\dot{V}O_{2peak}$ ), leg and arm muscle 1RM tests (leg extension, LE; and chest press, CP). Results The two groups had similar baseline characteristics. After 4 months of training HbA1c and triglycerides were significantly reduced in both groups. Changes in  $\dot{V}O_{2peak}$ , as well as in leg and arm strength showed significant differences between AER and RES groups ( $\dot{V}O_{2peak}$ \*kg<sup>-1</sup> 15 $\pm$ 10 vs 8 $\pm$ 10%, p=0.04; LE 4 $\pm$ 11 vs 19 $\pm$ 10%, p<0.0001;

CP  $4\pm 8$  vs  $24\pm 11\%$ ,  $p<0.0001$ ). AER and RES groups showed similar changes in total fat mass ( $-2.2\pm 1.7$  vs  $-1.7\pm 1.3$  kg). VAT and fat accumulation in the liver were also reduced to a similar extent in the two groups ( $-58\pm 68$  vs  $-30\pm 40$  cm<sup>2</sup>, and  $-8\pm 18$  vs  $-9\pm 18\%$ , respectively). Insulin sensitivity was significantly increased in both groups (by 30% and 19%, respectively). In the whole population, the change in VAT negatively correlated with change in insulin sensitivity ( $r=0.39$ ,  $p<0.05$ ). Discussion These data show that aerobic and resistance exercise can exert beneficial effects on both visceral adipose tissue and fat accumulation in the liver in subjects with DM2, with attenuation of insulin resistance and improved metabolic features. References Sigal RJ et al. Ann Intern Med 2007; 147:357–69.

## **(O)Cardiovascular Response During Incremental Cycle Ergometer Tests: Gender And Age Differences**

**Anna Baraldo, Cantor Tarperi, Antonio Cevese**

### **Introduction**

The literature on cardiovascular responses to aerobic exercise does not unanimously clarify the role of stroke volume changes in the enhancement of cardiac output. The aim of the present project was to characterize the cardiovascular response, in terms of Heart Rate (HR), Stroke Volume (SV) and Cardiac Output (CO), during cycle-ergometer incremental tests, in young and aged subjects of both sexes.

### **Methods**

We recruited 36 healthy volunteers: 8 Young Males (YM) ( $25 \pm 2$  yy, BMI  $22.3 \pm 3$ ); 8 Elderly Males (EM) ( $66.5 \pm 3.5$  yy, BMI  $29.09\pm 2.9$ ); 9 Young Females (YF) ( $23 \pm 2.4$  yy, BMI  $20.4 \pm 2.3$ ); 9 Elderly Females (EF) ( $67\pm 6.9$  yy, BMI  $23.1\pm 2.7$ ). We recorded cardiovascular data with Portapres TNO, during cycle ergometer incremental tests, starting with a load of 40 W for 3 min followed by 10 or 20 W increments each minute, for females and males, respectively, up to voluntary exhaustion. Since the time course of exercises was not identical among the subjects, data are presented as mean $\pm$ SD at 3 points: rest, 40% and 80% maximum load ( $VO_2$  max). Three way ANOVA was used to detect significant differences ( $P<0.05$ ).

### **Results**

In all groups HR (bpm) increased linearly and progressively with the effort, although the increase was limited in the elderly group, both males and females, but the difference was significant at 80%  $VO_{2max}$  only: YM  $74\pm 13.2$ ,  $110\pm 23.8$ ,  $165\pm 14.3$ ; EM  $83\pm 9.6$ ,  $108\pm 7.3$ ,  $144\pm 13.1$ ; YF  $88\pm 12.9$ ,  $112\pm 1.7$ ,  $167\pm 1.4$ ; EF  $87\pm 14$ ,  $101\pm 2.1$ ,  $144\pm 1.3$ . At rest, SV (ml) was higher in males than in females, and in young than in older subjects. Irrespective of the age, in the males it increased at

40% but declined slightly at 80%, while in the females it increased at 40% and increased further at 80%; differences between males and females were significant: YM  $95\pm 23$ ,  $135\pm 23$ ,  $128.7\pm 17$ ; EM  $65\pm 18.3$ ,  $84\pm 20.2$ ,  $82\pm 21.1$ ; YF  $62\pm 7.8$ ,  $66\pm 0.7$ ,  $77\pm 0.6$ ; EF  $52\pm 12.7$ ,  $60\pm 0.8$ ,  $70\pm 0.08$ . In all subjects, CO (l/min) significantly increased in proportion to the effort, and differences in changes were significant among the groups: YM  $7\pm 0.8$ ,  $14\pm 1.7$ ,  $21\pm 2.4$ ; EM  $5\pm 1.5$ ,  $9\pm 2.1$ ,  $12\pm 2.4$ ; YF  $6\pm 1.2$ ,  $7\pm 0.05$ ,  $12\pm 0.2$ ; EF  $5\pm 1.6$ ,  $6\pm 0.1$ ,  $9\pm 0.07$ .

## **Discussion**

While the overall cardiovascular response to exercise was similar in the 4 groups, if expected age and gender related differences are accounted for, all females appeared to apply a different strategy for CO enhancement during exercise, relying on continuous deployment of the pumping reserve function of their heart, while males used only tachycardia after the initial rise in SV. The mechanism underlying this remarkable gender related difference deserves further examination.

## **(P)SIF 2012**

### **Gender- and age-related factors in acute cardiovascular adjustments to dynamic resistance exercise**

Anna Baraldo, Cantor Tarperi, Antonio Cevese

Aim of this study was to characterize cardiovascular and metabolic changes during leg press dynamic resistance exercise in: 12 Young Males (YM;  $22.6\pm 1.3$ yy;  $68.6\pm 8.7$ kg;  $175\pm 10$ cm), and 12 Females (YF;  $23.7\pm 2.5$ yy;  $55.9\pm 5.7$ kg;  $164\pm 10$ cm), 12 Elderly Males (EM;  $67.3\pm 2.7$ yy;  $83.8\pm 8.5$ kg;  $171\pm 5$ cm), and 12 Females (EF;  $67.1\pm 7.1$ yy;  $58.2\pm 5.0$ kg;  $157\pm 1$ cm). We continuously recorded finger arterial pressure and calculated cardiac output (CO), stroke volume (SV) and heart rate (HR) during 3 series (10' recovery) of 12 leg-press repetitions at 70% of 1RM (previously estimated by the Brzycki method). The most evident age-related differences were found in SV adaptation to exercise; YM-YF slowly increased SV from baseline to peak (+11%; +8%) while EM-EF exhibited a decrease in SV during exercise (-11%; -3%) with a rebound at end exercise (+49%; +25%). As a consequence, since changes in HR (and in arterial pressure) were similar in all groups, CO increased during exercise by 30% in the young groups, while it was almost unchanged in the elderly, but with a delayed increase at recovery (EM +40%, EF +15%). Thus, at a difference with the young, elderly subjects were unable to manage the increased hindrance to the output of blood from the heart during essentially isometric muscle contractions and relied on delayed vasodilatation to overcome the metabolic unbalance accumulated during the exercise bouts; this was more prominent in the males.

(O)Aerobic versus resistance exercise, cardiovascular adaptations in young and elderly female subjects.

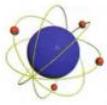
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**Purpose:** A comparison of cardiovascular adaptations to resistance (RE) and aerobic (AE) exercise in Elderly (EF) and Young Females (YF) is an important and not yet completely understood topic in Sports Science. The purpose of this work was to delineate and quantify changes in the cardiovascular system during AE and RE bouts in 12 YF ( $23.7\pm 2.5$ yy,  $56.0\pm 5.7$ kg,  $164\pm 1$ cm) and 12 EF ( $67.1\pm 7.1$ yy,  $58.2\pm 5.0$ kg,  $157\pm 1$ cm)

**Method:** RE was performed on a leg press machine with three series (10' recovery) of 12 repetitions at 70% of individual 1RM (previously assessed by the Brzycki method). AR was performed on a cycle ergometer at constant load (80%  $\dot{V}O_2$ max), at 60-70 rpm for 5 min and repeated 3 times, separated by 10 min recovery. During both tests, we continuously recorded the finger arterial pressure by photoplethysmography (portapres, TNO) and calculated heart rate (HR), cardiac output (CO), stroke volume (SV), and total peripheral resistance (TPR).

**Results:** arterial pressure values increased to the same extent in YF and EF, but the increase was greater in RE and was entirely due to changes in diastolic pressure. Heart rate increased more in YF than in EF, but the increase was unrelated to the exercise type. CO increased by 110% and 60% in YF and by 75% and 22% in EF, for AE and RE, respectively. These changes were caused by progressively decreasing vasodilatation, which turned into vasoconstriction in EF\_RE. Changes in TPR lead to corresponding changes in SV that increased by 40% in YF\_AR and decreased by 10% in EF\_RE.

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Anna Baraldo Cantor Tarperi Antonio Cevese

*Esercizio aerobico versus resistenza: adattamenti cardiovascolari  
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