UNIVERSITÉ DE REIMS CHAMPAGNE-ARDENNE UFR SCIENCES ET TECHNIQUES DES ACTIVITÉS PHYSIQUES ET SPORTIVES



Paramètres morphologiques, fonction, Doppler Tissulaire et analyse des contraintes du ventricule gauche chez les sportifs âgés de 45 à 55 ans

THESE

Soutenue le 17 Decembre 2007 en vue de l'obtention du titre de DOCTEUR DE L'UNIVERSITÉ DE REIMS CHAMPAGNE-ARDENNE

(Ecole Doctorale Sciences, Techniques et Santé)

Spécialité : Sciences des Activités Physiques et Sportives

Par

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List of abbreviations – Liste des abréviations

MTG	most trained group
LTG	less trained group
NTG	non trained group
AV	atrioventricular
LV	left ventricle
RV	right ventricle
LVOT	left ventricular outflow tract
RVOT	right ventricular outflow tract
IVST	interventricular septum thickness
LVID	left ventricluar internal diameter
PWT	posterior wall thickness
ECG	electrocardiogram
Age (years)	age expressed in years
Height (cm)	height expressed in cm
Weight (kg)	weight expressed in kg
Sex	1=man 2=woman
BSA (m ²)	body surface area
BMI (kg/m ²)	body mass index
Resting HR (pulse/min)	resting heart rate
Systolic BP (mmHg)	systolic blood pressure
Diastolic BP (mmHg)	diastolic blood pressure
Duration of training (years) DT	duration of training in years
Training intensity (hours/week) TI	hours of training per week
AOD (mm)	aorta diameter
LADS (mm)	left atrial diameter in systole
IVSd (mm)	interventricular septum thickness in diastole
LVIDd (mm)	left ventricular internal diameter in diastole
PWTd (mm)	posterior wall thickness in diastole
IVSs (mm)	interventricular septum thickness in systole
LVIDs (mm)	left ventricular internal diameter in systole
PWTs (mm)	posterior wall thickness in systole
E (m/s)	peak early mitral inflow velocity
A (m/s)	peak late mitral inflow velocity

ICT (msec)	isovolumic contraction time
IVRT (msec)	isovolumic relaxation time
AOV (m/s)	mean velocity in the aorta
	ratio of peak early mitral inflow in early and late
E/A	diastole
FS (%)	fractional shortening
	left ventricular muscle mass indexed for body surface
$LVM/BSA(g/m^2)$	area
LVM (g)	left ventricular muscle mass
EDV (ml)	end-diastolic volume
ESV (ml)	end-systolic volume
EF (%)	ejection fraction
SV (ml)	stroke volume
CO (l/min)	cardiac output
Lateral Ea (m/s)	peak early annular velocity of the basal inferior wall
Lateral Aa (m/s)	peak late annular velocity of the basal inferior wall
Lateral Ea/Aa	ratio of annular peak early and late velocity of the
Lateral Ea/Aa	basal inferior wall
Septal Ea (m/s)	peak early annular velocity of the middle inferior wall
Septal Aa (m/s)	peak early annular velocity of the middle inferior wall
Santal Ea/Aa	ratio of annular peak early and late velocity of the
Septar Ea/Aa	middle inferior wall
E/Ee	ratio of mitral E-wave peak velocity (E) to annular E
E/Ea	velocity (Ea)
LVH	left ventricular hypertrophy
DTI	Doppler Tissue Imaging

Résumé

Paramètres morphologiques, fonction, Doppler Tissulaire et analyse des contraintes du ventricule gauche chez les sportifs âgés de 45 à 55 ans

Le vieillissement est associé avec la détérioration de la fonction diastolique et l'effet de l'entraînement aérobie sur la fonction diastolique au repos reste inconnu. En effet, les données actuelles restent contradictoires en ce qui concerne ce paramètre puisque certaines recherches constatent que la détérioration de la fonction diastolique liée à l'âge, pourrait être partiellement évitée par l'entraînement, ce qui est infirmés par d'autres auteurs.

Par ailleurs, l'échocardiographie Doppler est largement utilisée en tant que méthode non invasive pour distinguer l'hypertrophie pathologique ou physiologique du ventricule gauche (VG). Cette méthode offre une information sur la fonction globale du VG, en particulier avec la nouvelle technique, le Doppler Tissulaire (DT). Le DT peut être couplé au Doppler pulsatile, au 2D Doppler couleur ou au M-mode Doppler couleur. Le DT pulsatile permet d'étudier la relation, en fonction du temps, des cycles systoliques et diastoliques du myocarde.

D'autre part, grâce au développement de la simulation numérique grâce à l'analyse des éléments finis, il est désormais possible de modéliser le ventricule gauche afin de valider les résultats expérimentaux.

Par manque d'information sur les pratiquants d'activités physiques et sportives âgés entre 45-55 ans, il a été décidé d'examiner la fonction diastolique du VG des personnes ayant un véritable passé sportif en utilisant une échocardiographie conventionnelle et DT pour obtenir l'information additionnelle sur les caractéristiques principales des contractions du VG chez les athlètes endurants et chez les sédentaires.

Notre population d'étude est composée de : i) 16 athlètes de haut niveau (15 hommes, 1 femme). Ils étaient membres du Stade George Hébert de Reims en France et suivaient un entraînement intensif (plus de 5 heures par semaine avec une moyenne de 17 ± 12 ans, mentionné comme Groupe Plus Athlétique = GPA) ; ii) 13 coureurs (11 hommes, 2 femmes) qui suivent un entraînement régulier (moins de 5 heures par semaine, mentionné comme Groupe Moins Athlétique = GMA) iii) et 16 sédentaires

(7 hommes, 9 femmes), ne pratiquant aucune activité physique (mentionné comme Groupe Non Athlétique = GNA). Les sujets ne présentaient pas de maladies cardiovasculaires, d'hypertension, de diabète et étaient tous non fumeurs. De plus, leurs échocardiographies n'ont révélé aucune pathologie.

Tous les sujets ont subi une échocardiographie de type traditionnel qui a été réalisée avec un échocardiographe de marque Siemens Acuson Aspen[®] couplé à un DT. Une sonde de 2.5-3.5 MHz était utilisée pour obtenir les images echo-Doppler et DT. Les sujets étaient dans une position partiellement latérale pendant toutes les mesures et la moyenne de 3-5 cycles cardiaques a été prise en compte. Les mouvements en M-mode ont été obtenus dans le respect du protocole établi par la Société Américaine d'Echocardiographie dans une vue parasternale et dans un axe longitudinal. Les diamètres du VG en systole et diastole, l'épaisseur du septum interventriculaire et la paroi postérieure du VG ont été ainsi mesurés. La masse musculaire du VG a été calculée par la formule de Penn.

Le Doppler pulsatile a été effectué avec la vue « 4 cavités ». Les pics E et A (m/s) et leurs ratios, les temps de relaxation isovolumétriques ont été mesurés comme paramètres de la fonction diastolique du VG. Le DT a été réalisé avec une sonde de 3.5 - 4.0 MHz. Les variables suivantes du DT ont été évaluées : Ea, Aa, Ea/Aa et le ratio E/Ea.

L'analyse statistique a été réalisée avec le logiciel STATISTICA 6.1[®] (Statsoft, France).

Les résultats sont exprimés comme moyenne \pm SD. Le test T de Student pour des échantillons indépendants a servi à évaluer les différences significatives entre les groupes, quand les variables étaient normalement distribuées. Le même test a servi à montrer des différences d'intragroupes entre les variables DT dans chaque groupe. Une corrélation partielle avec la méthode Pearson a servi à montrer les relations univariantes. Une régression multiple pas à pas a servi à montrer les effets indépendants des déterminants potentiels sur les variables dépendantes.

Parmi les trois groupes examinés, le GPA a montré une plus grande épaisseur de la paroi postérieure du VG, un diamètre final diastolique plus grand et une masse musculaire plus importante du VG comme cela était attendu. Il n'y avait pas de différences significatives entre les paramètres diastoliques (E, A, E/A) et la fraction d'éjection. Comparé au GMA et au GNA, le GPA n'a pas montré un Ea plus important, mais une baisse significative du Aa sur le côté latéral du cœur par rapport au GNA et aussi un plus grand ratio Ea/Aa sur le côté latéral et septal du coeur. En ce qui concerne la pression de remplissage du VG (E/Ea), chaque groupe avait une pression de remplissage normale (E/Ea<8).

Un modèle simplifié du ventricule gauche a été utilisé pour montrer les différences de stress et de déformation parmi le GPA et GNA analysés par ABAQUS/Explicit 6.5[®] en adaptant l'épaisseur du mur postérieur et le septum ventriculaire du ventricule gauche à la fin de la phase diastolique. Même avec ce modèle, il a été possible de mettre en évidence qu'en situation normale, l'influence du stress ne peut pas être négligée dans la mécanique ventriculaire et peut expliquer les résultats expérimentaux obtenus avec le Doppler Tissulaire.

L'augmentation physiologique du VG se manifeste surtout par l'épaississement du septum interventriculaire et de la paroi postérieure du VG, par la dilatation du VG en réponse à un exercice de plus de 5 heures par semaine dans le GPA. Et ceci associé à une augmentation du diamètre de l'oreillette gauche et à une baisse de Aa sur le côté latéral du cœur et ce, malgré les différences manquantes entre les résultats d'échocardiographie standard. La fonction systolique reste inchangée parmi les groupes.

Les conclusions de cette étude confirment l'hypothèse selon laquelle le déclin de la fonction diastolique du VG en relation avec le vieillissement est dû à un mode de vie, et non seulement au vieillissement en lui-même, ainsi qu'à l'aggravation des index diastoliques qui peuvent être préservés par un entraînement bien dosé. En plus, le DT peut être utile dans le dépistage des sujets d'âge moyen et pour distinguer la forme physiologique et pathologique de l'hypertrophie du VG.

Mots clés: fonction diastolique, vieillissement, Doppler Tissulaire, échocardiographie, cœur d'athlète

Summary

Left ventricular morphologic parameters, diastolic filling, pulsed Doppler Tissue Imaging and stress analyzes among 45-55 years old athletes and highly trained athletes.

Aging is associated with impaired early diastolic filling; however the effect of endurance training on resting left ventricular (LV) diastolic function remains unclear. There are certain contradictions considering this parameter since some articles states that the age-related impairment of diastolic function could be partly prevented by exercise while others show the contrary.

Doppler echocardiography is a widely used non invasive method to distinguish pathological and physiological LV hypertrophy. This tool provides information on LV global function, especially with the new upcoming technique, the Doppler Tissue Imaging (DTI). DTI can be performed with the use of pulsed Doppler, color 2D Doppler and color M-Mode Doppler. Pulsed Doppler Tissue Imaging offers a high temporal relation between myocardial systolic and diastolic waves.

Furthermore, thanks to the development of computer simulation, with the Finite Element Analyzis, there is the possibility to validate the experimental results on the left ventricle.

Lacking the information on the athletic people aged between 45-55 years old, it had been decided to investigate the LV diastolic function with a long-time athletic background by using conventional echocardiography and DTI to have additional information on the myocardial wall motion features of endurance athletes and sedentary people.

Sixteen highly competitive endurance runners enrolled into this study (15 men, 1 woman) members of the Stade George Hebert, Reims, who had been trained intensively more than 5 hrs/week for more than an average of 17±12 years (mentioned as Most Trained Group=MTG); 13 runners (11 men, 2 women) who had been trained less than 5 hours/week (mentioned as Less Trained Group=LTG) and 16 healthy controls (7 men, 9 women) (mentioned as Non Trained Group=NTG). Subjects were excluded for coronary artery disease, valvular and congenital heart disease, heart

failure, cardiomyopathy, arterial hypertension, diabetes mellitus, smoking and inadequate echocardiograms.

All study participants underwent standard echocardiography which was carried out with a Siemens ACUSON Aspen equipped with DTI. A variable frequency phased-array transducer (2.5 to 3.5 to 4.0 MHz) was used for echo-Doppler and DTI imaging. The subjects were in a partial decubitus position while all measurements were analyzed by 1 experienced reader, on an average of 3 to 5 cardiac cycles. Mmode measurements were obtained according to the American Society of Echocardiography in the parasternal long-axis view. LV end-diastolic and end systolic diameters (LVIDD and LVIDS), septal (IVST) and posterior end-diastolic wall thickness (PWT) were measured. LV mass was calculated using the Penn formula.

Pulsed Doppler LV inflow was performed in the apical 4 chamber view. E and A peak velocities (m/s) and their ratio, isovolumetric relaxation time (IVRT) were measured as parameters of the LV diastolic function. DTI was performed by transducer frequencies of 3.5 to 4.0 MHz. The sample volumes were located in each basal left ventricular segment in the apical view. The following variables of the tissue velocity curve were evaluated: peak early diastolic velocity, peak late diastolic velocity and ratio of E/Ea were obtained.

Statistical analyses were carried out by Statistica 6.1 (StatSoft, France). Data are expressed as mean±SD. The Student t test for independent samples was used to evaluate the significance of differences between groups when variables were normally distributed. The same test was used to show intragroup differences between the DTI variables in each group. Partial correlation test by Pearson's method was done to assess univariate relations. Stepwise forward, multiple regression analyses were performed to weigh the independent effects of potential determinants on the dependent variables.

Among the three examined groups, the MTG showed a greater left ventricular wall thickness, end diastolic diameter and left ventricular mass as it was expected. There were no significant differences on the diastolic indexes (E, A, E/A) and ejection fraction. Respect to the NTG and the LTG, the MTG did not exhibit a higher Ea, but a significantly lower Aa on the lateral side of the heart compared to the NTG and showed a higher Ea/Aa ratio of both lateral and septal wall. As for the LV filling pressure (E/Ea) each group showed a normal filling pressures (E/Ea<8).

A simplified model of the left ventricle had been used to show the differences of stress and strain among the MTG and NTG analyzed by ABAQUS/Explicit 6.5 by adapting the thickness of the posterior wall and the interventricular septum of the left ventricle at the end-diastolic phase. Even with this model, it was possible to show that under normal conditions the influence of stress can not be neglected in ventricular mechanics, and can explain the experimental findings with the Doppler Tissue Imaging.

The physiologic increase of LV which is manifesting in the thickening of IVST, dilatation of left ventricular internal diameter (LVID) and the thickening of posterior wall thickness (PWT), in response to exercise spent more than 5 hours/week among the MTG occurs in parallel with an augmentation of the diameter of the left atrium (LA) and with the decrease in late wave velocity (Aa) on the lateral side of the heart despite of the missing significative differences between standard echocardiographic indexes. Systolic function seems to be preserved among the three groups.

This finding underlines the hypothesis that the decline of the LV diastolic function related to aging is due in part of lifestyle, and not only to aging itself and the worsening of the diastolic indexes can be prevented by a well loaded training. Furthermore, DTI may be useful for the screening of middle aged athletes and to distinguish pathological form of hypertrophy from physiologic hypertrophy.

Key words: LV diastolic filling, aging, Doppler Tissue Imaging, echocardiography, athlete's heart

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1. Introduction

ardiovascular disease (CVD) accounts for approximately 30% of all deaths worldwide, and will only worsen as the world's population ages. It is well established that age is a major risk factor and contributor to all cardiovascular morbidities and mortalities (Shioi, T., 2006; Cutler et al., 2006; De Meersman et al., 2007). There are several factors that appear to play a critical role in the onset and progression of cardiovascular diseases such as: nutrition, stress and lack of exercise.

Many nutrients and phytochemicals in fruits and vegetables, including fiber, potassium, and folate, could be independently or jointly responsible for the apparent reduction in cardiovascular diseases (Ignarro et al., 2007; King et al., 2007).

As one of the low cost antioxidant therapy, exercise seems to be the best since exercise has been confirmed as a pragmatic countermesure to protect against cardiac injury (Ascensao et al., 2006).

Low-intensity exercise is generally better accepted by people naive to exercise training, those who are extremely deconditioned ("out of shape") and older people. Low-intensity exercise may result in an improvement in health status with little or no change in physical fitness even if it means only regular walking or moderate to heavy gardening as it has been shown to be sufficient in achieving these health benefits (Ignarro et al., 2007).

If today it is well established that practicing a physical activity regularly and at a low intensity is favorising a good cardiovascular health, it is not that sure for an intensive one. Carre, 2004 describes that a very intensive training can lead to the modifications of the autonome nervous system and can cause for example supraventricular arrhytmias and orthostatic intolerance. Furthermore, Gomez-Cabrera et al., 2006 revealed that exercise generates oxidative stress only when it is exhaustive, which means that when oxidants are produced at moderate levels they act as signals to adapt cells to exercise, on the contrary, when they are overproduced, they cause cellular damage.

Heamodynamic and/or pressure overload due to training usually involve left ventricle, inducing in cardiac structure as increase of internal cavity diameters, wall thickness and mass. These changes are usually described as "athlete's heart". A large meta-analysis on this has underlined how the combination of endurance- and strength training may determine both extreme volume and pressure load, thus explaining the athlete's heart increase in LV internal dimension and wall thickness (D'Andrea et al., 2007). On the contrary, pathologic left ventrcicular hypertrophy represents both a manifestation of the effects of hypertension and other cardiac risk factors over time as well as an intrinsic condition causing pathologic changes in cardiac structure and function (Krauser et al., 2006).

Thanks to the development of technology, the mechanical events, morphology of the heart can be described thoroughly (Ganong, 2001; Gowda et al., 2004). As such a mechanical event, diastolic function seems to have a great importance to identify the nature of physiologic and pathologic hypertrophy (D'Andrea et al., 2007). Furthermore, it seems that Doppler Tissue Imaging (DTI) will play an additional role in the differentiating of these two forms of hypertrophy (Toncelli et al., 2006; Weyman, 2007).

Advances in engineering and computer technology allowed bridging the gap between physiology and mechanics. Cardiomyocyte stress/strain relates to muscle energy expenditure, which dictates oxygen and substrate utilization. Furthermore, theory of finite element analyzis (FEA) can predict cardiac mechanics under normal and pathologic conditions (Tendulkar et al., 2006). In this study, it was meant to describe mechanical stresses and strain in the myocardium among the MTG and NTG group.

In the field of cardiologic research there are growing numbers of studies to show how the heart of aged people is reacting on exercise or training compared to pathologic and/or sedentary cases. Left ventricular diastolic function may be impaired in the elderly (Libonati, 1999; Oxenham et al., 2003), while others state the contrary thanks to training (Forman et al., 1992; Pavlik et al., 2001; Galetta et al., 2004). Doppler Tissue Imaging seems to solve this problem, even though there are still some confusing results (Fleg et al., 1995; Galetta et al., 2004). However, there hasn't been lots of article written on the question: what is happening before 'aging' since the articles chosen for this study and generally are indicating the aged group above 60 years. This was one of the reasons to choose the age group between 45-55 years old to see, what cardiovascular events are coming up with regular training.

None of the articles found for this study took into account the hours spent by training per week. There were several articles that explained the upcoming differences on the diastolic function comparing the aged athletes and sedentary people because of the years spent by training. This indication of years might not be reasonable since it had been shown that one can have the manifestation of the athletic heart followed by a regular training after three months (Ocel et al., 2003; Meyer et al., 2007) (maybe among the aged people it would take more time – no proof found on this hypothesis).

Therefore in this study it was meant to highlight the differences of cardiac parameters based on the hours spent by training per week and to see whether excessive hours of training is beneficial for the development of the cardiovascular system, especially the heart, or not in the chosen age group?

To answer these questions, a study carried out with 45 subjects aged between 45-55 years old, were divided into three groups: Most Trained Group (MTG), Less Trained Group (LTG) and Non Trained Group (NTG). The protocol established to carry out the measurements had been divided into two phases: *1*) a questionnaire to collect personal and anthropometrical data *2*) following the standardized approach of the American Society of Echocardiography to obtain morphologic, diastolic function and Doppler Tissue data on the hearts of the participants of the study.

Echocardiography provided information regarding cardiac morphology, function and hemodynamics non-invasively. It is the most frequently performed cardiovascular examination after electorcardiography and chest X-ray. Currently the technique called M-mode echocardiography is of particular use and it does not mean a "picture" of the heart, but rather a diagram that shows how the positions of the heart's structures change during the cardiac cycle where time resolution is necessary for the precise measurements, such as echo of derived systolic and diastolic time intervalls (Gowda et al., 2004). In most centers, measurement directly from 2-D echocardiography or two-dimensionally guided M-mode echocardiography has supplanted isolated M-mode recordings (Feigenbaum et al., 2005), as it happened in this study also. Although Doppler imaging can be regarded as being complementary to 2-D imaging, it is used primarily to examine the flow, the direction, and the velocity of blood flow (Feigenbaum et al., 2005). Furthermore, Doppler Tissue Imaging (DTI) was used as a useful echocardiographic tool for quantitative assessment of left ventricular (LV) systolic and diastolic function. From DTI analysis, a number of parameters (Sa, Ea, Aa, Ea/Aa, E/Ea) have been shown to be useful to predict long

term prognosis, while the use of threshold values of Ea (<3 cm/s) and E/Ea (>15) has provided independent and incremental prognostic information in a number of major cardiac diseases (Isaaz K., 2002; Yu et al., 2007).

Data were registered in a STATISTICA file, then were analysed with a program STATISTICA to characterise the best possible the three groups.

Then a Finite Element Analyzis (FEA) was used to validate some experimental results through a simplified heart model.

The results were then inserted into the literature chosen for this study, to see whether there is a concordance or dissonance.

A study limitation was stated to have a critical analyzis on the factors that can explain the similarities or differences obtained in the study through the literature.

Finally, a conclusion was written to highlight some suggestion of further research on this work in the same domain and combined with other research fields.

2. Aging and sport – Le vieillissement et le sport

The number of adult men and women over 40 years of age participating in competitive sports has increased dramatically over the past 25 years. Although many of these older competitors engage in competition for recreation and fitness, others train with the same enthusiasm and intensity as Olympians. Opportunities are now available for older athletes to compete in activities ranging from marathon running to weight lifting. The success and the standards of performance set by many older athletes are exceptional and often difficult to explain. However, although these older athletes exhibit strength and endurance capacities that are far greater than those of untrained people of similar age, even the most highly trained older person experiences a decline in performance after the fourth or fifth decade of life (Schulman et al., 1992; Wilmore and Costill, 1999).

2.1 The effects of sport on aging

In general, there is a decline in almost every sport events beyond our physical prime. Researchers showed as we age, peak performances in both endurance and strength events decrease by about 1% to 2% per year, starting after age 25 (Maron et al., 2001).

As physiological changes here are some major factors that have to be obligatory mentioned with aging:

• Vital capacity, forced expiratory volume, maximal expiratory ventilation decrease with age (Rogers et al., 1990; Katzel et al., 2001),

• Strength is reduced with aging. This is the result of decreases in both physical activity and muscle mass. Whereas endurance training does little to prevent the aging loss in muscle mass, strength training can maintain or increase the muscle fiber cross-sectional area in both men and women (Schuit, 2006),

• The amount of relative body fat increases as we age (Raguso et al., 2006).

It is well known that moderate exercise can significantly improve one's health and make life longer. The outstanding effects of doing sport/exercise are due to the followings and can be applied even for some, already existing pathological cases (hypertension, diabetes etc.) such as:

• Kelley et al., 1994 found in their study that lower extremity aerobic exercise has an antihypertensive effect on resting systolic and diastolic blood pressure in adults;

• Physical activity increases the fat burning enzymes in the muscles as it was found in the study of Sido et al., 2000 where their results indicated that physical training programs have a favorable effect on the echocardiographic parameters among obese women even without a pharmacological intervention;

• Helps stay fit which was confirmed in the study of Cottini et al., 1996 where they showed that physical activity of running and regular physical activity can attenuate the age-dependent decline of the explosive power of the inferior limbs in sedentary subjects, especially over the age of 65 years, and can slow down the deterioration of the coordinative neuromuscular capacity, and maintain weight;

• It strengthens heart muscles and improves circulation of blood thereby reducing the risk of heart disease even among diabetic women, where increased physical activity, including regular walking, is associated with substantially reduced risk for cardiovascular events (Hu et al., 2001; Dugan, 2007);

• The results of Tran et al., 1985 suggested that reductions in cholesterol and LDL-C levels were greatest when exercise training was combined with body-weight losses even though there was a decrease on these parameters simply with weight loss also;

• Physical training improves the effect of exercise on insulin sensitivity through multiple adaptations in glucose transport and metabolism. In addition, training may elicit favorable changes in lipid metabolism and can bring about improvements in the regulation of hepatic glucose output, which is especially relevant to NIDDM (Non Insulin Dependent Diabetes Mellitus). It is concluded that physical training can be considered to play an important, if not essential role in the treatment and prevention of insulin insensitivity (Borghouts et al., 2000).

• Rogers et al., 1990 found that the age-related decrease in VO₂max of master athletes (aged 62 ± 2.3 yrs) who continue to engage in regular vigorous endurance exercise training is approximately one-half the rate of decline seen in age-matched sedentary subjects. Furthermore, the importance of regular exercise was emphasized in the work of Katzel et al., 2001 where they showed that the longitudinal decline in

 VO_2 max is highly dependent upon the continued magnitude of the training stimulus. The majority of the athletes, who reduced their training levels over time, resulted in a longitudinal reduction in VO_2 max two to three times as large as their sedentary peers.

• It creates the feeling of self-confidence and control over one's body and life (Duclos, 2006; Themanson et al., 2006).

Briefly, regular physical moderate activity is associated with many health benefits and due to all these, physical activity is considered to be essential for those who want to prolong their life span (Gielen et al., 2005; Tuomainen et al., 2005; Rajendran et al., 2006; Dua et al., 2007). Different studies have attempted to show how exactly exercise affect's one health as it happened in the study of Huang et al., 1998 where they studied a group of middle-aged and older men and women (40 years and more) followed for an average of 5.5 years to examine the association between physical fitness, physical activity, and the prevalence of functional limitation. The result of their work showed that physically fit and physically active participants reported less functional limitation than unfit or sedentary participants. After controlling for age and other risk factors, the prevalence of functional limitation was lower for both moderately fit and high fit men compared with low fit men. So did Blair et al., 2001 in their work where «they identified articles by PubMed search (restricted from 1/1/90 to 8/25/00) using keywords related to physical activity, physical fitness, and health». An author scanned titles and abstracts of 9831 identified articles. After having analyzed these articles they arrived to the following conclusions:

i) There is a consistent gradient across activity groups indicating greater longevity and reduced risk of CHD (Coronary Heart Disease), CVD (CardioVascular Disease), stroke and colon cancer in more active individuals and

ii) The studies are compelling in the consistency and steepness of the gradient across fitness groups. Most show a curvilinear gradient, with a steep slope at low levels of fitness and an asymptote in the upper part of the fitness distribution.

Furthermore, improvements have been observed in patients with mild depression and anxiety thanks to the physiological changes with regular exercise. There was also an improvement considering the self esteem, psychomotor development, memory, calmness and sleep (Fentern, 1996; Blanco-Centurion, et al., 2006).

On the contrary, the benefits of high-intensity exercise are not as clear as in the case of moderate exercise. Kemi et al., 2005 demonstrated that cardiovascular adaptations to training are intensity-dependent. A close correlation between VO₂max, cardiomyocyte dimensions and contractile capacity suggests significantly higher benefit with high intensity, whereas endothelial function appears equivalent at moderate levels. Laursen et al., 2005 supports the above mentioned statement, but they tought that peripheral adaptations rather than central adaptations are likely responsible for the improved performances witnessed in well-trained endurance athletes following various forms of high-intensity interval training programs. Nevertheless, Esteve-Lanao et al., 2007 found that the value of a relatively large percentage of low-intensity training is great, while the contribution of high-intensity exercise remains only sufficient. Jansen et al., 2007 seems to support this theory, because in their study highintensity weight training is not able to produce adaptive improvement in cardiovascular function. Therefore, they support previous studies where they showed that the lack of cardiovascular adaptation may be due to the low percentage of VO₂max elicited by this form of training. Thus, exercise intensity emerges as an important variable in future (clinical) investigations.

2.2 The effects of sport on the cardiovascular system while aging

2.2.1 HR, HRmax, blood pressure and morphological changes due to sport and while aging

Even though the resting heart rate shows little alteration with age, the heart rate of the trained heart is becoming less compared to the non-trained heart while aging (Arbab-Zadeh et al., 2004). This phenomenon is also called bradycardia which means a heart rate less than 60 beats/min. Stratton et al., 1994 were screening healthy older men aged between 60 to 82 years compared to younger men aged between 24 to 32 years before and after 6 months of training and they found that among all subjects the resting heart rate (HR) reduced by 12%. On the contrary, this adaptation on training is not so evident since some studies have found that there is hardly any difference from the baseline resting heart rate and on the resting heart rate reached with exercise when master athletes are compared to sedentary controls (Wilmore et al., 1996; Pavlik et al., 2001; Baldi et al., 2003).

A person's maximum heart rate (HRmax) tends to be stable and usually remains relatively unchanged following endurance training and the heart rate recovery period decreases with endurance training (Wilmore and Costill, 1999).

Following endurance training, arterial blood pressure (resting blood pressure) changes very little during submaximal or at maximal work rates (Ehsani et al., 1991, Giada et al., 1998, Wilmore and Costill, 1999, Baldi et al., 2003).

Even though, systolic left ventricular function measured at rest by echocardiography, is unaffected by aging itself (Fleg, 1986), as a result of endurance training, stroke volume (SV) shows an overall increase because after training, the left ventricle fills more completely during diastole that it does in an untrained heart (Ehsani et al., 1991). The reason of it is that the blood plasma volume increases therefore more blood is available to enter the ventricle which results in an increased end-diastolic volume (EDV) (Ehsani et al., 1991; Levy et al., 1993; Seals et al., 1994; Baldi et al., 2003). The increase of the EDV can be 'followed' by the thickening of the interventricular septum and posterior wall thickness (Baldi et al., 2003; Owen et al., 2004) but Gates et al., 2003 concluded that regular aerobic-endurance exercise does not consistently modulate the changes in LV structure among middle aged and older men. As for the cardiac output, that remains unchanged or decreases slightly after training, on the contrary, while training at a maximal level of exercise increases considerably (Ehsani et al., 1991; Levy et al., 1993). See Table 1.

Table 1	. The	effects	of	sport	on	the	cardi	ovascu	lar	system	1
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•	Stroke volume increases
•	End-diastolic volume increases
•	Blood plasma volume increases
•	Heart rate decreases (bradycardia)
•	Maximum heart rate rest stable
•	Heart rate recovery period decreases

- Cardiac output rest unchanged
- Blood pressure remains unchanged or decreases very little

Furthermore, age-related structural alterations include a decrease in myocyte number (because of apoptosis) and an increase in myocyte size, while on the extracellular level, the morphologic changes of aging include increases in matrix connective tissue (e.g., collagen) leading to interstitial fibrosis. Thus, these structural changes are leading to increased myocardial stiffness and reduced ventricular compliance, translating into impaired passive left ventricular filling (Groban, 2005). Another interpretation of diastolic dysfunction showed that vascular and ventricular wall thickness increase, whereas arterial compliance, endothelial function and ventricular contractility decline which is resulting in an increased viscoelastic myocardial stiffness (Tanaka et al., 2000; Arbab-Zadeh et al., 2004).

It is unclear how much of the decrease in cardiovascular function with aging is due to physical aging alone and how much is due to deconditioning because of the decreased activity. In the study of Arbab-Zadeh et al., 2004 they referred to the fact that for example a simple bed rest deconditioning leads to many of the apparent manifestations of the aging process, such as decreased work capacity, increased work sympathetic nerve activity and muscle atrophy. On the contrary, in the same study they compared 12 healthy sedentary seniors (69 ± 3 years old), 12 masters athletes (67±3 years old) and 14 young but sedentary control subjects (28.9±5 years old) and they found that stroke volume for any given filling pressure was greater in masters athletes compared with aged matched sedentary subjects, whereas contractility, was similar. Therefore, their conclusion was that a sedentary lifestyle during healthy aging is associated with decreased left ventricular compliance, leading to diminished diastolic performance but prolonged sustained endurance exercise training preserves ventricular compliance with aging and may help to prevent heart failure in the elderly. Moreover, Mc Guire et al., 2001 showed in their 30-year follow up study that 3 weeks of bedrest among healthy men at 20 years of age (in 1966) had a more profound impact on physical work capacity than did 3 decades of aging.

2.2.2 The heart as a pump

2.2.2.1 Mechanical events of the cardiac cycle

2.2.2.1.1 Events in late diastole

Late in diastole, the mitral and tricuspid valves between the atria and ventricles are open and the aortic and pulmonary valves are closed. Blood flows into the heart throughout diastole, filling the atria and ventricles. The rate of filling declines as the ventricles becomes distended, and – especially when the heart rate is low – the cusps of the atrioventricular valves drift toward the closed position. The pressure in the ventricles remains low.
2.2.2.1.2 Atrial systole

Contraction of the atria propels some additional blood into the ventricles, but about 70% of the ventricular filling occurs passively during diastole. Contraction of the atrial muscle that surrounds the orifices of the superior and inferior vena cava and pulmonary veins narrows their orifices, and the inertia of the blood moving toward the heart tend to keep blood in it; however, there is some regurgitation of blood into the veins during atrial systole.

2.2.2.1.3 Ventricular systole

At the start of ventricular systole, the mitral and tricuspid valves (AV) close. Ventricular muscle initially shortens relatively little, but intraventricular pressure rises sharply as the myocardium presses on the blood in the ventricle. This period is the isovolumic ventricular contraction and lasts about 0.05 sec, until the pressures in the left and right ventricles exceed the pressures in the aorta (80 mmHg) and pulmonary artery (10 mmHg) and the aortic and pulmonary valves open. During isovolumic contraction, the AV valves bulge into the atria, causing a small but sharp rise in atrial pressure. When the aortic pulmonary valves open, the phase of ventricular ejection begins. Ejection is rapid at first, slowing down as systole progresses. The intraventricular pressure rises to a maximum and then declines somewhat before ventricular systole ends. Peak left ventricular pressure is about 120 mmHg. Late in systole, the aortic pressure actually exceeds the ventricular, but for a short period momentum keeps the blood moving forward. The AV valves are pulled down by the contractions of the ventricular muscle, and atrial pressure drops. The amount of blood ejected by each ventricle per stroke at rest is 70-90 ml. The end-diastolic ventricular volume is about 130 ml. Thus, about 50 ml of blood remains in each ventricle at the end of systole (end-systolic ventricular volume), and the ejection fraction, the percent of the end-diastolic ventricular volume that is ejected with each stroke, is about 65%. The ejection fraction is a valuable index of ventricular function (Ganong, 2001).

2.2.2.2 Physiology of diastole

The physiology of diastole can be divided into cellular and mechanical definitions (Groban, 2005) but knowing that the purpose of this work to show the

echocardiographic findings on the aged heart, it is not a matter of interest to get involved with the biological explanation of this functioning.

Diastole can be divided into four phases: isovolumic relaxation, early filling, diastasis, and atrial systole. The amount of LV filling that occurs during each of these phases depends on the myocardial relaxation, the passive characteristics of the LV, the characteristics of the left atrium, pulmonary veins, and mitral valve, and the heart rate (Little et al., 1990). Therefore, on the mechanical level it begins with aortic valve closure when the pressure within the left ventricle begins to fall, termed the isovolumic relaxation phase (later on mentioned as IVRT). The left ventricular pressure will continue to fall even after the opening of the mitral valve. In fact, left ventricular pressure falls below left atrial pressure as a result of elastic recoil, creating a "suction" effect. Rapid filling of the left ventricle occurs during this phase. Normally, left ventricular relaxation ends in the first third of rapid filling (e.g., estimated change in left ventricular (LV) volume is 80-100mL) so that the majority of left ventricular filling (e.g., from 100 to 145 mL) (slow, passive filling) is dependent on such properties as left ventricular compliance, ventricular interaction and pericardial restraint. Finally, atrial systole contributes to the rest of left ventricular volume (e.g., 145-160 mL of LV volume). In the young heart, approximately 80% of LV filling is complete by the end of the passive filling phase, with the remainder occurring during active atrial transport. In contrast, with advanced age, impairments in early diastolic relaxation and ventricular compliance alter filling dynamics such that atrial transport becomes the more important contributor to diastolic volume (Groban, 2005).

2.3 Arterial pulse

The blood forced into the aorta during systole not only moves the blood in the vessels forward but also sets up a pressure wave that travels along the arteries. The pressure wave expands the arterial walls as it travels, and the expansion is palpable as the pulse. With advancing age, the arteries become more rigid, and the pulse wave moves faster (Ganong, 2001).

2.4 Diastolic function

Normal mitral inflow consists of biphasic flow from the left atrium into the left ventricle. In healthy, disease-free individual, the early flow, coincident with the mitral E-wave, exceeds the later flow, which occurs with atrial systole (the A-wave) both in velocity and volume (Feigenbaum et al., 2005) (Figure 1).



Figure 1 Schematic representation of the diastolic function. LVOT, left ventricular outflow tract (m/s); IVRT, isovolumic relaxation time (sec); IVCT, isovolumic contraction time (sec); DT, deceleration time (sec); Em, early peak (m/s); Am, late peak (m/s) (Feigenbaum et al., 2005)

The magnitude of these flows, as well as their ratio, varies with age in the normal population. In healthy, young, disease-free individuals the E-wave exceeds the A-wave and therefore the E/A ratio is more than 1.0 as it was found in numerous studies.

In adolescents and young adults, there may be a disproportionate contribution of active ventricular relaxation to ventricular filling, which results in a markedly accentuated E-wave velocity. In this instance, E/A ratio can exceed a value of 2.0 in a normal, disease-free individual especially in the case of athletes (Pavlik et al., 2001).

Numerous investigations have shown that peak early diastolic mitral inflow velocity (E) is reduced in aged individuals and to maintain ventricular filling and stroke volume, peak late diastolic filling velocity (A) increases with age, resulting an

age related decline in the E/A ratio (Spirito et al., 1988; Safar, 1990; Badano et al., 1991; Prasad, et al., 2007). Furthermore, many pathological processes, such as cardiac or systemic diseases, can increase the incidence of diastolic dysfunction which manifests in the reduction of E-wave, the increase of A-wave and the inversion of E/A. These pathological conditions can be even worsen when pathologic hypertrophy is present (Macor et al., 1991; Mockel, et al., 1996; Palmieri et al., 1999; Schanwell et al., 2002; Caserta et al., 2007; Borlaug et al., 2007). Nevertheless, as it had been described previously, regular training has positive effects on the human body, which, in the case of the diastolic function raised some problem in this field of research.

In fact, there had been some authors who found that doing sport has a beneficial effects on the E/A with aging. Pavlik et al., 2001 carried out in their study a two dimensionally guided M mode and Doppler echocardiographic measurement on 578 male subjects. They made their analysis from two aspects: a, in the young adult category competitors in different groups of sports were studied and b, in the different age groups (10-14 years, 15-18 years, 19-30 years, 31-44 years and 45-60 years) were compared through athletic and non-athletic backgrounds. They showed that with the respect of public health, the most important fact seems to be that the E/A quotient was much higher in the older athletes than in the non-athletic subjects. As in their study, older athletes had mostly performed at the top level in their youth, they suggested that a more effective positive influence of regular physical training on diastolic function can be expected when athletic conditioning is sufficiently intense at a younger age and has been continuously maintained throughout the years. So did Bouvier et al., 2001 who concluded that by endurance training, a high level of physical capacity can be maintained late in life (their subjects were 10 male veteran athletes aged 73±3 years and 12 sedentary subjects aged 75 ± 2 years) and the superior cardiovascular function in the veteran athletes, compared with the untrained controls was due to both better systolic and diastolic left ventricular function. Furthermore, Brenner et al., 2001 found in their study carried out with rats, that some age-associated changes in diastolic function are reversible and thus may not be intrinsic to aging but instead secondary to other processes, such as deconditioning. On the contrary, some authors stated that doing sport regularly doesn't have effect on the diastolic function when comparing the athletic and sedentary aged people (Jungblut et al., 2000; Prasad et al., 2007). Fleg et al., 1995 found that with the participation of 16 older competitive male endurance athletes (52-76 years old), 17 young (less than 40 years) and 23 older (52-76 years old) sedentary control subjects that older men with a long history of intensive endurance training demonstrate impaired early diastolic LV filling similar to that of their sedentary peers. Thus, impairment of early diastolic filling appears to be intrinsic to normative aging and not secondary to the reduction in aerobic capacity that accompanies the aging process. Highlights the above mentioned finding the study of Baldi et al., 2003 where they enrolled 20 older untrained men (60-80 years), 19 older male athletes, 19 young untrained men (20-30 years) and 13 male athletes into their study to determine whether endurance training is associated with an attenuation of age-associated changes in diastolic filling. In their findings peak early mitral inflow velocity (E) and early-to-late mitral inflow velocity ratios were lower in older vs. young men; however, there was no training effect. Finally, they suggested that early diastolic filling is not affected by training in older men, and the effect of training on tissue Doppler variables (Aa and Sa) is different in young and older men.

2.5 Isovolumic relaxation time

The isovolumic relaxation time (IVRT) represents the earliest phase of diastole. It is defined as the time from aortic valve closure to mitral valve opening and normally averages 76±13 ms in adults. If an IVRT greater than 90 ms is detected, there is a genuine concern that pathological left ventricular hypertrophy exists if it is associated with deceleration time more than 240 ms and the E/A ratio <1 (Hildick-Smith et al., 2001). During this time, systolic contraction has ceased, but left ventricular filling has not yet begun. Libonati et al., 2002 studied the effect of two exercise training modalities, i.e. low-intensity endurance running and sprint running, in vitro on rats. They suggested that LV diastolic isovolumic relaxation is improved with exercise training (Libonati, 2000) and that the impact of exercise training on the LV diastolic pressure/volume relationship is, in part, related to the intensity/mode of exercise. So far, there is no reported pathological case on this parameter among athletic and non athletic healthy, aged individuals, even though Nottin et al., 2005 found that long-term training does not reduce the age-related decline in LV relaxation properties in human. Their finding implied that other mechanisms, such as increased LV filling pressures due to expanded blood volume, are probably responsible for the higher contribution of early diastolic filling to LV filling in master athletes compared with their sedentary controls.

2.6 Physiologic and pathologic hypertrophy

Cardiac hypertrophy is one of the main ways in which cardiomyocytes respond to mechanical and neurohormonal stimuli. It enables myocytes to increase their work output, which improves cardiac pump function. However, this compensatory mechanism can become overwhelmed by biomechanical stress, thereby resulting in heart failure (Grossman, 1980; Carreno et al., 2006). Left ventricular hypertrophy is typically characterized as being pathologic or physiologic. It should be recognized that the calculation of left ventricular mass is a determination of the actual mass of the ventricular muscle and may not be related to overall cardiac enlargement. Increases in left ventricular mass can occur with chamber enlargement and relatively normal wall thickness (eccentric hypertrophy). When evaluating patients for left ventricular hypertrophy, it is important to characterize the hypertrophy as being due to either chamber enlargement or increased wall thickness (Abergel et al., 2006). One additional index of hypertrophy is relative wall thickness (RWT) defined as: posterior wall thickness /left ventricular interior dimension (Narayan et al., 2006). Relative wall thickness more than 0.44 is used as a threshold of pathologic left ventricular hypertrophy. This ratio is also useful in characterizing the physiologic hypertrophy of the athletic heart and distinguishing it from pathologic hypertrophy (Pellicia et al., 1999).

Pathologic hypertrophy can be associated with hypertensive cardiac disease, hypertrophycally obstructive cardiomyopathy and valvular aortic stenosis (Smith et al., 1985; Schannwell et al., 2002; Bountioukos et al., 2006).

The other form of hypertrophy, the physiologic hypertrophy can be seen in highly trained athletes. In general, this is a physiologic adaptation in which there is a slight increase in both wall thickness and chamber dimension. Wall thickness more than 13mm is unusual in physiologic hypertrophy. Because the hypertrophy is a physiologic adaptation to training, wall stress tends to be normal. If interventricular septal thickness is ≥ 13 mm, then left ventricular mass index should be calculated. If the result is > 134 g/m² in men or > 110 g/m² in women, then left ventricular hypertrophy can truly be said to be present (Granger et al., 1985; Hammond et al., 1986; Pellicia et al., 1997; Hood et al., 1999; Hildick-Smith et al., 2001).

As a result of increased wall thickness and diastolic dimension, overall left ventricular mass rises with training (Child et al., 1984). In elite athletes, this increase averages 40-50% in comparison with sedentary controls. Left ventricular mass and more particularly mass index are the benchmarks by which left ventricular hypertrophy should be judged. Mass can be calculated by transthoracic echocardiography using either Devereux's classic M mode formula or two dimensional estimation. The upper limit of physiological left ventricular hypertrophy is considered to be approximately 500 gr (Hildick-Smith et al., 2001).

In athletes, left ventricular hypertrophy (LVH) can mimics disease states (hypertrophic cardiomyopathy, hypertension); therefore, the distinction may have important implications, particularly when adults practice regular physical activity. Schannwell et al., 2002 revealed in their work, while comparing 49 athletes with LVH due to training, 49 patients with LVH and 26 controls, a higher LV muscle mass index in the two study groups compared with controls. But they stated that, the group of athletes had a normal diastolic filling pattern, while the hypertension group had a delayed relaxation pattern with a decrease in E and an increase in A. Limongelli et al., 2006 studied 30 master athletes (MA), 24 subjects with hypertension (HYP), 20 patients with hypertrophic cardiomyopathy (HCM) and 30 normal individuals (CG) aged between 40-50 years. The LV wall thickness and LV end-diastolic dimensions were higher in MA than controls, but significantly lower than other groups (HYP, HCM). LVH/height^{2.7} was increased in 79% of HYP and in 95% of HCM, but was within the normal limits in MA. As for the diastolic filling, all HYP and 95% of HCM showed abnormal relaxation pattern, but was normal in all MA. It seems that improved understanding of LV relaxation and filling helps to differentiate pathological and physiological myocardial hypertrophy (Mockel et al., 1996; Urhausen et al., 1996, 1997).

2.7 Doppler Tissue Imaging

2.7.1 Basic principles of DTI

Doppler Tissue Imaging targets the tissue rather than the conventional Doppler which targets the red blood system. For this purpose, filters are set to parameters opposite those needed to accurately detect red blood cell motion. Because tissue has a greater reflectivity and slower motion, instrumentation filters are set to exclude high velocities and low-intensity reflectors. With this technic, either the myocardium or fibrous skeleton of the heart can be targeted and weaker reflections from the higher velocity blood cells relatively excluded. More commonly for the determination of function, a pulsed Doppler sample volume is placed within an area of the myocardium or the anulus and the velocities at that point are then displayed for quantitation. Virtually any area of the myocardium can be evaluated in this manner. When evaluating global performance, as it was performed in this study, DTI velocities can show some regional variation based on which area of the mitral annulus is interrogated (septal vs. lateral) (Cardim et al., 2001; Ho et al., 2002). The annular velocity in systole has shown a good correlation with the left ventricular ejection fraction as it happened in the work of Gulati et al., 1996, where they found an excellent correlation between the average velocity of mitral annular motion and the ejection fraction.

Most commonly, DTI of the mitral annulus is employed and the data used as a marker of global systolic or diastolic function. In sinus rhythm, there are two annular motions (Ea and Aa) that parallel the transmitral flow. In normal, disease-free states, Ea is greater than Aa, similar to the relationship of the mitral E- and A-waves (E and A). With diastolic dysfunction, there is a reduction in Ea such that the annular ratio (Ea/Aa) reverses. With increasing age the Ea/Aa decreases, moreover, the reversal of E/A with increasing age occurs in the seventh decade, reversal of the Ea/Aa ratio occurs in the fifth decade. The annular velocity is not volume dependent, as opposed to mitral inflow and it remains depressed in the pressure of a pseudo-normal or restrictive mitral inflow pattern (Sohn et al., 1997; Oxenham et al., 2003).

Since DTI as a technique is coming into practice not a long time ago, and used to characterize myocardial patterns mainly in heart diseases (such as hypertrophic cardiomyopathy), there hasn't been as much article written on the athletic heart measured with this method than on the athletic heart measurement with the Doppler echocardiography. Derumeaux et al., 2002 found that myocardial contraction and relaxation assessed by tissue Doppler imaging were impaired in pathological hypertrophy but not in physiological hypertrophy among rats, while Galetta et al., 2003 showed in their human study that athletes can exhibit a higher Ea, a lower Aa and an increased Ea/Aa both lateral wall and septum among elderly aged 67.6 ± 4.5 years. Last, but not least, it can be stated, that DTI is very useful to identify myocardial diastolic properties, because this method is unrelated to preload, left atrial pressure, heart rate and aortic pressure (Dincer et al., 2002; Oxenham et al., 2003).

Briefly, DTI is a useful method to detect regional changes in myocardial function in pathologic and physiologic adaptations in the heart as it happened in the work of Kosmala et al., 2004, where they found DTI superior to other echocardiographic techniques as well as to measurements of plasma BNP (a type of neurohormon generally used for routine diagnosis of LV dysfunction) in identification of impairment in myocardial function in diabetic patients. Their results considerably enabled to detect deterioration of LV systolic and diastolic functions in normotensive and hypertensive diabetics compared with healthy subjects and patients with systemic hypertension and diabetes mellitus, respectively. Furthermore, Di Bello et al., 2000 found that DTI allows the differentiation of the two left ventricular hypertrophy model (physiologic and pathologic), and hypertensive cardiomyopathy showed an impairment of diastolic function, while athlete's heart shows a normal behavior at age 31.6 ± 3.5 years. It must be mentioned, that advancing age is characterized by structural and functional changes of the left ventricle. This finding was underscored by the study of Caso et al., 2000 and Zoncu et al., 2002, who found DTI a useful tool for detecting myocardial function induced by training among young athletes (age 22.5±5.3 and 20.7±4.5 years), because athletes presented an improvement in the diastolic passive properties of myocardium. The higher early diastolic velocity of the inferior wall and its relation to increased preload may represent an indicator of aerobic training, allowing quantification of the degree of LV adaptation to endurance exercise. Studies have already shown also that, with aging myocardial atrioventricular annular velocity and regional Ea decrease in both ventricles, whereas Aa increases (Nikitin et al., 2003; Thomas et al., 2003; Innelli et al., 2007).

On the contrary, the effects of training are still unclear among the aged athletes. Giada et al., 1998 carried out in their study among elderly athletes and controls vs. youngs (age: 55 ± 6 vs. 58 ± 6 years in the elderly group) found no significant differences between athletes and sedentary subjects but they noted that in the trained elderly subjects Doppler curve morphology of ventricular filling seems to resemble that of young people, with an increase in the E wave and a reduction in the A wave. So did Baldi et al., 2003, who showed also that early diastolic filling is not affected by training in older men. On the contrary, Galetta et al., 2003 and 2004 supported the hypothesis that age-related decline in LV diastolic function is due in part to lifestyle and not solely to aging and long-term endurance training throughout life

determines changes in myocardial diastolic properties in a prognostic favorable direction, which may contribute to the better LV diastolic function.

2.8 Left ventricular filling pressure

It occurs during diastole as left atrial pressure increases, causing mitral valve opening and creating a pressure gradient between the left atrium and left ventricle. The mitral E-wave peak velocity is another indirect measure of left atrial pressure. The Ewave velocity correlates with the difference between left atrial and left ventricular pressure at the time of mitral valve opening. Thus, the higher the left atrial pressure at the time of mitral valve opening, the higher the E velocity is going to be. Furthermore, the rate of left ventricular relaxation and atrial contractility influence this relationship. Recently, thanks to the technical developments, Doppler Tissue Imaging starts to be used to estimate left atrial pressure. This approach relies on the Doppler technique to measure the velocity in early diastole of the mitral annulus. This velocity profile appears to be more dependent on left ventricular relaxation and less dependent on the transmitral pressure gradient. The ratio of mitral E-wave peak velocity (E) to annular E velocity (Ea) has been shown to correlate well with left atrial pressure. A normal E/Ea is less than 10 and a ratio over 15 predicts a left ventricular pressure more than 15 mmHg. This simple ratio combines the influence of mitral driving pressure and left ventricular relaxation. Nevertheless, it appears to work well in the presence of normal hearts and/or preserved systolic function (Feigenbaum et al., 2005). De Sutter et al., 2005 evaluated the effects of age, gender, and left ventricular hypertrophy on the early diastolic mitral annulus velocity (Ea) assessed by Doppler Tissue Imaging and the ratios of the transmitral early peak velocity (E) assessed by conventional Doppler imaging over Ea (E/Ea) in a wide age range of normal patients and in patients with LV hypertrophy due to hypertension. In their results age appeared to be the strongest determinant of Ea and E/Ea and women in general had slightly higher values for E/Ea compared with men. Moreover, patients with LV hypertrophy had slightly higher E/Ea values for each age category compared with normal patients (age 45-54: normal (9.1±2.9 vs. 10.5±2.2).

2.9 Finite Elements

With the development of techniques, computer simulation is becoming an important tool for biological research. In such research, biological model is constructed and evaluated with variety of parameters. There have been lots of models of the heart constructed by many research groups while investigating different point of views of the functioning of the heart (Akira et al., 2004). Bovendeerd et al., 1992 studied the dependence of local left ventricular (LV) mechanics on myocardial muscle fiber orientation while using a finite element model. In the model they considered anisotropy of the active and passive components of myocardial tissue, dependence of active stress on time, strain and strain rate. They concluded that a physiological transmural distribution of the helix fiber angle can be found, at which active muscle fiber stress and muscle fiber strain are distributed approximately homogeneously across the LV wall. Gibbons et al., 2006 showed through their finite element analyzis that the pericardium has a significant influence on the structural behavior of the septum and LV and right ventricular (RV) free walls. It is possible also to generate complex left ventricular simulation models with 3D shape model, cell orientation model, cell electrophysiological model, coronary artery model and tissue mechanical property model (Dorri et al., 2006; Augenstein et al., 2006; Domenichini et al., 2007). Ingrassia et al., 2007 illustrated a model-based approach to designing wall motion measures using published finite element models of altered cardiac activation to screen wall-motion-based measures of synchrony of contraction. They indicated in their results that early systolic events and specifically early systolic rates of endocardial motion are likely the best wall-motion-based indicators of synchrony of contraction, confirming that fully 4D wall motion analyses will be essential for their clinical application. In this study, a Finite Element Analyzis is going to be used to validate some experimental results.

3. Hypothesis – Hypothèse

Healthy aging might results in changes in morphology, Doppler and Doppler Tissue measurements of the heart. It is unclear whether these alterations are a specific manifestation of the aging process or reflect a cardiac adaptation to a more sedentary lifestyle. However, there hasn't been lots of article written on the question: what is happening before 'aging' since the articles chosen for this study and generally are indicating the aged group above 60 years. This was one of the reasons to choose the age group between 45-55 years old to see, what cardiovascular events are coming up with regular training.

In this study it was meant to highlight the differences of cardiac parameters based on the hours spent by training per week and to see whether excessive hours of training is beneficial for the development of the cardiovascular system, especially the heart, or not in the chosen age group?

Therefore it was hypothesized that:

- Healthy, but sedentary aging would result in slowing of diastolic filling and Doppler Tissue variables,
- > Low- and high intensity endurance training would prevent such changes.

4. Materials and methods – Matériels et méthodologie

4.1 Study population

Fifty-one subjects were enrolled into this study, 6 had been excluded because of missing data, hypertension and smoking. Therefore finally, 16 healthy subjects (NTG (non-trained group)): 7 men and 9 women, (mean age 49.2 ± 4.0 years) and 29 matched athletic subjects (MTG (most trained group)): 15 men and 1 women, (mean age 50.1 ± 4.8 years) and LTG (less trained group): 11 men and 2 women, (mean age 46.9 ± 6.0 years) were participating in this study. All the subjects were free of cardiovascular diseases such as hypertension, coronary artery disease, valvular and congenital heart disease, heart failure, cardiomyopathy, diabetes mellitus, inadequate ECG (electrocardiogram), they were non-obese and non-smokers.

Athletes were selected on the basis of the hours spent with training per week which meant more or less 5 hours per week (MTG=more than 5 hours/week, LTG=less than 5 hours/week). Those who were practicing running had been recruited from the Stade Georges Hébert, Reims, France and cyclists had been recruited from the Cyclo Club Rémois and Pédale Rémoise, Reims, France. As for the runners recruited from the Stade George Hébert, they were following training sessions 4-5 times a week on a 60 to 90 minutes basis. Their training sessions followed the general guidelines of training which meant: warming up, exercise, and stretching. Their training sessions are guided by a professional trainer and the duration of their training in years is 14 ± 12 years (meant from childhood and not related only to the years spent with running). The cyclists were recruited from the two clubs mentioned earlier and followed training sessions 4-5 times a week with 10 ± 2.4 hrs of training. Their training sessions were guided by a professional trainer and their duration of training in years is 23 ± 12 years (meant from childhood and not related only to the years spent with cycling). They were all active at the time of the measurements in national and international running and cycling races. Athletes chosen for the less trained group (LTG) were doing running, cycling as a free time activity, some of them joined the above mentioned clubs but were not competitors. These athletes followed training sessions 3-4 times a week. Sedentary subjects (NTG=non trained group) had been searched through various forms of advertisement. Written informed consent was obtained from each subject entering the study.

All the measurements took place at the Department of Cardiology, Clinique de Courlancy, Reims, France. Generally the examinations were executed every two weeks on Fridays, between 14:00-19:00 pm.

Their height was measured with an height rod SECA model 202, Made in Germany before the examine and also their weight was measured with Balance Medicale, CK SECA, Made in Germany. Body surface area (BSA) (1) had been measured by using the Du Bois and Du Bois formula:

$$BSA(m^2) = 0.007184 x Height(cm)^{0.725} x Weight(kg)^{0.425}$$
(1)

This formula is one of the most frequently used for children >5 years and for non obese adults. Furthermore, this equation adequately predicted BSA but failed with obesity (Wang et al., 1992; Livingston et al., 2001).

Body Mass Index (BMI) (2) has been defined as weight in kilograms divided by the square of the height in meters (kg/m^2) and is a surrogate measure of overweight and obesity in clinical practice and in epidemiological studies (James et al., 2001).

$$BMI=Weight/Height (m^2)$$
⁽²⁾

Classification	BMI (kg/m ²)
Underweight	<18.5
Normal range	18.5 to 24.9
Overweight	≥25
Pre-obese	25 to 29.9
Obese class 1	30 to 34.9
Obese class 2	35 to 39.9
Obese class 3	≥40

Table 2 World Heart Organization (WHO) classification of obesity

The blood pressure had been measured 2 times (at the beginning, 3 minutes after being lied down on the examination table and at the end of the examen on the left arm) with Critikon DinamapTM 8100 DRE, Inc., Louisville, KY, USA and the average of these numbers were used as systolic and diastolic parameters. The Critikon Dinamap 8100 Adult/pediatric non-invasive blood pressure monitor measures systolic, mean, and diastolic pressures at preset levels, as well as pulse rate.

(<u>http://www.dremed.com/catalog/product_info.php/products_id/135</u>) Various cuff sizes were available.

The data obtained was registered on an individual questionnaire planned by Kispeter Zsofia (Annexe III)

4.2 The echocardiographic examination of the left ventricle

Orientation of the echocardiographic image has been addressed by the American Society of Echocardiography who recommended a standardized approach to two-dimensional echocardiographic imaging. The Society further suggests that all two-dimensional imaging transducers have an index mark that clearly indicates the edge of the ultrasonic plane, i.e., the direction in which the ultrasound beam is swept. For example, in parasternal long-axis view, the index mark should be oriented in the direction of the aorta and the aorta should appear to the observer's right of the image display. The effect of this convention is to position the parasternal long-axis view so that the aorta is to the right, the short-axis view so that the right ventricle is to the left side, and the apical four-chamber view so that the left heart is to the right. Recently, the same Society has made recommendations regarding the measurements and descriptive items that constitute a standard report of an adult transthoracic echocardiogram (Gardin et al., 2002). This document offers a comprehensive listing of the various features that should be routinely analyzed and which were applied in this study also. In general, the goal of this listing is to encourage standardization of echocardiographic reports and to ensure that examinations are thorough, comprehensive and carried out in the same way worldwide which helps the development and understanding of the cardiologic research also (Figure 2).



Figure 2 Schematic representation of a parasternal long-axis view of the left ventricle depicting linear measurements. LVOT, left ventricular outflow tract; LA, left atrium; RVOT, right ventricular outflow tract; IVS, interventricular septum; LVIDd, left ventricular internal diameter in diastole; LVIDs, left ventricular internal diameter in systole; PW, posterior wall thickness. (Feigenbaum et al., 2005)

The study was carried out with an Acuson Aspen Echo, Mountain View, California, USA phased-array echocardiograph with M-mode, two dimensional, equipped with pulsed, continuous and color-flow Doppler possibilities. The echocardiograms were evaluated according to the recommendations suggested by the American Society of Echocardiography (Sahn DJ et al., 1978). Left ventricular mass was calculated according to the Penn formula: LV mass=1.04 [(IVS + LVEDD + PWT)³ – (LVEDD)³] – 13.6, where IVS = interventricular septal thickness, LVEDD = internal end-diastolic dimension, PW = posterior wall thickness.

4.2.1 Left ventricular wall segments

Although the left ventricle could be divided into any number of segments, the American Society of Echocardiography has adopted a set of standards and recommended terminology. The scheme begins by dividing the left ventricle into thirds along the major axis from base to apex.

The most basal third of the left ventricle extends from the atrioventricular groove to the tip of the papillary muscles. The middle third is identified as that portion of the left ventricle containing the papillary muscles, and the apical third begins at the base of the papillary muscle and extends to the apex. The Society also identifies the left ventricular outflow tract as the area extending from the free edge of the anterior mitral leaflet to the aortic valve annulus.

The next step is to divide each region into segments around the circumference of the minor axis. The basal and mid thirds are customarily divided into six segments each, and the apical region is divided into four segments. The result is the creation of 16 segments that comprise the left ventricle. The practical advantage of this model is that each segment can be visualized in both a long-axis and a corresponding short-axis projection. After all, this model is commonly referred to as the 16-segment model and has become the standard approach for assessing regional left ventricular function and wall motion analysis (Cerqueira et al., 2002).

4.2.2 M-mode examination

With the development of two-dimensional and Doppler echocardiography, the M-mode examination has been subjugated to a supporting role but there are still lots of laboratories where M-mode measurements are still performed with two-dimensional echocardiography or two-dimensionally guided echocardiography, particularly to measure chamber dimension, left ventricular wall thickness and left ventricular of two-dimensional fractional shortening; moreover, with the advent echocardiography, area measurements and their derived volume calculations were also employed. As it was mentioned previously, M-mode echocardiogram is not a picture of the heart, but rather a diagram that shows how the positions of the heart's structures change during a cardiac cycle. In each case, the ultrasound first penetrates the chest wall, then the right ventricular cavity and finally into the left heart structures (Sahn et al., 1978). See also Annex I.

Its importance is highlighted in the study of hypertrophic cardiomyopathy and physiologic hypertrophy.

By convention, linear measurement of the left ventricle is made at the level of the mitral valve chordae. Furthermore, many of the linear measurements that can be made for assessment of left ventricular function such as left ventricular outflow tract. When ventricular septal thickness had been measured, caution were made to avoid measuring the most proximal portion of septum, which is frequently an area of isolated hypertrophy and angulation that does not truly represent ventricular wall thickness (Feigenbaum et al., 2005).

In all of the cases, imaging was performed with the patient either supine and/or tilted in the left lateral decubitus position. By tilting the patient to the left, the heart is brought forward to the chest wall and more to the left side of the sternum thereby improving the ultrasound windows. The degree to which the patient should be rotated to the left must have been individualized and the patients' cooperation was excellent (Figure 3 and 4).



Figure 3 Proper patient positioning for the echocardiographic examination. (Feigenbaum et al., 2005)



Figure 4 Various transducer locations used in echocardiography. (Feigenbaum et al., 2005)

All the measures were started with the parasternal long-axis view (Figure 5) which means that the transducer was placed on the third left intercostal space (sometimes moved up or down one or two intercostal spaces) to have an optimized image.



Figure 5 The parasternal long axis view. Ao, aorta; LA, left atrium; LV, left ventricle; RV, right ventricle. (Feigenbaum et al., 2005)

When it was properly recorded and shown on the screen, the mid portion and the base of the left ventricle, both leaflets of the mitral valve, the aortic valve and the aortic root, the left atrium, and the right ventricle had been seen. The transducer position has to be adjusted so that the scanning plane is parallel to the major axis of the left ventricle and passes through the center of the left ventricular chamber. From this view, an M-mode cursor can be placed to record the full excursion of the mitral valve, aortic valve opening and closing, right ventricular free wall motion, and the left ventricular septal and posterior wall motion had been viewed. Therefore the following parameters could have been determined: Aorta diameter (Ao), left atrial size (LA), interventricular septal thickness (IVST), left ventricular diastolic dimension (LVIDD), posterior wall thickness (PWT), all had been determined in systole and diastole (Figure 6 and 7).



Figure 6 The parasternal long axis view from the two-dimensional image, an M-mode display at the basal level. Ao, aorta; LAD, left atrial diameter. (Kispeter, 2006)



Figure 7 The parasternal long axis view from the two dimensional image, an M-mode display at the mid ventricular level. IVSs, interventricular septum in systole; LVIDs, left ventricular internal diameter in systole; PWTs, posterior wall thickness in systole; IVSd, interventricular septum in diastole; LVIDd, left internal diameter in diastole; PWTd, posterior wall thickness in diastole. (Kispeter, 2006)

4.3 Measuring systolic and diastolic function of the left ventricle

When the patient is rotated to the left and the transducer placed at the cardiac apex (Figure 8), a long-axis image is available. This occurs when the full excursion of both mitral and tricuspid valves is recorded and the "true" apex of the left ventricle lies in the near field. The normal true apex had been identified by its relatively thin walls and lack of motion. From the apical five-chamber view, simultaneous recording of aortic outflow and mitral inflow can be performed. From the four chamber view, the Doppler sample volume is first placed at the tips of the mitral leaflets to record mitral inflow.



Figure 8 The apical four- chamber view. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. (Feigenbaum et al., 2005)

There are numerous echocardiographic techniques for evaluating left ventricular diastolic function. In the contemporary practice, Doppler techniques evaluating mitral inflow and pulmonary vein flow and DTI of the mitral annulus have had the most clinical utility. All can be easily evaluated using standard commercially available equipment and the data can be recorded in most patients presenting for evaluation. On the contrary, two-dimensional echocardiography serves a lot in the evaluation of the anatomic description and assessment of systolic function. There are a number of Doppler approaches for determining diastolic function, including determination of mitral inflow patterns with pulsed Doppler imaging, evaluation of pulmonary vein flow, and the newer technique of DTI, which can be used as a stand alone technique or combined with mitral inflow patterns. It has to be mentioned that the accuracy and validity of Doppler markers of diastolic function are greatest in the presence of systolic dysfunction and individual parameters may lose their validity in the presence of normal systolic function. For the evaluation of diastolic properties of the left ventricle, the mitral inflow pattern is evaluated from an apical transducer position with the sample volume placed at the tips of the mitral valve. Normal mitral inflow consists of biphasic flow from the left atrium into the left ventricle. In healthy, disease-free individual, the early flow, coincident with the mitral E-wave, exceeds the later flow, which occurs with atrial systole (the A-wave) both in velocity and volume

(Figure 9). This permits to measure: transmitral E and A peak velocities (m/s), which were then calculated as diastolic indexes, E/A ratio and isovolumetric relaxation time, which was measured as the time interval occurring between the end of systolic output flow and the transmitral E-wave onset, by placing pulsed Doppler sample volume between outflow tract and mitral valve. There are multiple parameters that can be derived from the inflow pattern including E and A velocities and the time velocity integral of the E-wave and A-wave separately as well as their ratios. An additional commonly used measurement is the deceleration time of the E-wave. With delayed left ventricular relaxation there is a prolongation of deceleration time (Feigenbaum et al., 2005).



Figure 9 Example of a pulsed wave Doppler image with the sample positioned to record mitral inflow. E, peak early mitral inflow velocity; A, peak late mitral inflow velocity. (Kispeter, 2006)

In the absence of valvular regurgitation or intracardiac shunt, flow through all four valves should be equal. Although flow can theoretically be measured at any site, in practice, it is customary to measure blood flow through the aortic valve. The Doppler recording is performed using either the apical five-chamber or apical long-axis view and the sample volume is positioned at the level of the aortic annulus, approximately 3 to 5mm proximal to the valve. Therefore, Doppler echocardiography is able to measure blood flow through its ability to quantify blood velocity. It is known that the rate of flow through an orifice is equal to the product of flow velocity and cross-sectional area. In the cardiovascular system, however, flow is pulsatile and

therefore individual velocities during the ejection phase must be sampled and then integrated to measure flow volume.

4.3.1 Evaluation of systolic function

As a measure of systolic function (Figure 10), ejection fraction is computed according to the following formulas:

$$EF(\%) = \frac{SV}{EDV} \times 100 \tag{1}$$

where EDV is End-Diastolic Volume and SV is Stroke Volume.

Ejection fraction, the percent of the end-diastolic ventricular volume that is ejected with each stroke, is about $65\pm10\%$ (Ganong, 2001). See Annex II.



Figure 10 From the apical four chamber view, simultaneous recording of aortic outflow and mitral inflow can be performed. On this picture only the aortic outflow can be seen where the IVRT (isovolumic relaxation time) can be measured also. LVOT, left ventricular outflow tract; IVRT, isovolumic relaxation time. (Kispeter, 2006)

4.3.2 Evaluation of Doppler Tissue Imaging

Pulsed wave Doppler Tissue Imaging (DTI) was performed by using special software available on the Acuson Aspen Echo, Mountain View, California, USA. With this method there was the possibility to have measurements of ventricular wall motion velocity by positioning the sample volume within the myocardium. DTI of diastolic velocities of the basal lateral segment and of the basal interventricular septum in the apical four-chamber view were measured at the end of the examinations. The lower case "a" for annulus or "m" for myocardial (Ea or Em) and the superscripted prime symbol (E') are used to differentiate tissue Doppler velocities from conventional mitral inflow (Ho et al., 2006) and uniquely the Ea, Aa, Ea/Aa symbols are used in this study to describe tissue Doppler velocities in the part of the study carried out by the author. Therefore, early (Ea) and atrial (Aa) diastolic waves (m/s) were measured as diastolic indexes (Figure 11 and 12).



Figure 11 Diagrammatic representation of the processing required for Doppler tissue versus blood pool imaging. (Feingenbaum et al., 2005)



Figure 12 Patterns of mitral inflow and mitral annulus velocity from normal to restrictive physiology. (Sohn et al., 1997)

All parameters were measured during three consecutive cardiac cycles and their mean value calculated (Figure 13).



Figure 13 An example of mitral annulus velocity by pulsed-wave tissue Doppler with sample volume placed on the lateral wall. Ea, peak early annular velocity; Aa, peak late annular velocity. (Kispeter, 2006)

Figure 14 gives a brief summary on the echocardiographic measurements.



Figure 14 Schema showing each step while carrying out echocardiographic data (for abbreviations see List of abbreviations)

4.4 Finite Element Analyzis

As it was described previously, the heart is the pump that circulates blood through all organs of the body. It consists of four chambers: two ventricles situated below the two atria. The cardiac cycles is constituted by two successive phases: the systole and the diastole. During systole, both ventricle contract and at the end begins the diastolic phase, where both ventricles relax and are filled with blood. Ventricular filling begins with blood flowing in rapidly from the atria into the ventricles in a short period called the rapid filling phase that represents the first third of diastole. During this period, more than half of the subsequent stroke volume has entered the ventricles. The internal volumes of both cavities approximately double, while the ventricular pressures rise typically only by an amount of less than 1kPa. In view of such low pressures, the question arises whether they can provide the driving force for the large inflow of blood entering the ventricles during this phase. If it is not the case, it is important to understand which other mechanisms could play a role in the rapid filling phase as it happened in the study of Bettendorff-Bakman et al., 2006 where they investigated whether the ventricular filling pressures measured under physiological conditions can give a rise to such an extensive augmentation in ventricular volumes. They developed a finite element model of the right and left ventricles, taking into account the nonlinear mechanical behavior and effective compressibility of the myocardial tissue. They arrived to a conclusion that the ventricular pressure measured during the rapid filling phase cannot be the sole cause of the rise of the observed ventricular volumes and they indicated that under normal conditions the influence of the viscoelasticity of the tissue should not be disregarded in ventricular mechanics.

Local wall stress is a major determinant of the heart muscle's systolic function. Under in vivo conditions, however, such stresses cannot be measured systematically and quantitatively. In contrast, imaging techniques allow the deformation pattern of the left ventricle in vivo with high accuracy. Dorri et al., 2006 found as a conclusion of their study that a realistic geometry and fiber architecture lead to typical and substantially inhomogeneous deformation patterns as they are recorded in real hearts, therefore, they expect that the measurement of systolic deformation might provide useful diagnostic information.

4.4.1 Hypothesis

In order to investigate the non existing difference considering the echocardiographic measurements of the early filling peak (E) and the existing difference of Aa between the Most Trained Group (MTG) and Non Trained Group (NTG), nonlinear elastic Finite Element (FE) analyses with various types of cavity pressure functions applied as boundary conditions were performed by adapting the thickness of the posterior wall and septum of the left ventricle at the end-diastolic phase. Since the hypertrophy of the myocardium is one of the most evident sign of the adaptation of training (and were significant in my echocardiographic study), a thickness of 9.5mm of the interventricular septum (IVS) and posterior wall (PW) was

applied in the case of the NTG and a thickness of 11.5mm of IVS and PW was applied in the case of MTG.

4.4.2 Evaluation with ABAQUS/Explicit

A simplified finite element model of the human left ventricle was proposed as a 3D shape model to carry out this simulation, which generates complex left ventricular simulation. The model is constructed from extracted region of left ventricle from a 2D image (Figure 15). The model consists of 834 nodes and 677 elements in wall thickness. It must be mentioned that the models represent the NTG and MTG groups which corresponds to the population average measured in my echocardiographic study.



Figure 15 As a pre-processing a 2D image of the left ventricle was used to construct FE.

Mechanical property of the myocardial tissue is known to be strongly nonlinear. However, as the in vivo measurement of such property is very difficult and the results are not reliable enough, therefore, in the case of both groups the myocardium was considered to be a homogenate isotropic material with a Poisson's ratio 0.49 (is a measure of a tendency when a sample of material is stretched in one direction, tends thinner the other directions it to get in two (http://en.wikipedia.org/wiki/Poisson%27s_ratio) and with a 20 kPa Young's modulus. The pressure changes during systole of the LV were used in agreement with general physiology (Figure 16).



Figure 16 Physiologic changes of ventricular pressure (red line) and volume (white line) (http://library.med.utah.edu/kw/pharm/hyper_heart1.html)

Basically, to construct a simplified mechanical model of the left ventricle, the following models were taken into consideration:

- 2D shape model of the left ventricle
- o fluid dynamics model of blood inside the left ventricle

o mechanical property model of the myocardium

To carry out the measurements ABAQUS version 6.5 was used. ABAQUS is a commercial software package for finite element analysis developed by ABAQUS, Inc. ABAQUS was initially designed to address non-linear physical behavior; as a result, the package has an extensive range of material models.

A complete ABAQUS/Explicit analysis (that was used to perform the analysis) usually consists of three distinct stages: preprocessing, simulation, and postprocessing. These three stages are linked together by files as shown below (Figure 17).



Figure 17 The three stages carried out usually by ABAQUS/Explicit

Preprocessing (ABAQUS/CAE)

In this stage it has to be defined the model of the physical problem and create an ABAQUS input file. The model is usually created graphically using ABAQUS/CAE or another preprocessor, although the ABAQUS input file for a simple analysis can be created directly using a text editor.

Simulation (ABAQUS/Explicit)

The simulation, which normally is run as a background process, is the stage in which ABAQUS/Explicit solves the numerical problem defined in the input file. Examples of output from a stress analysis include displacements and stresses that are stored in binary files ready for postprocessing. In this study ABAQUS/Explicit had been used because it allows the resolution of the pression with the changes of time.

Postprocessing (ABAQUS/CAE)

It is possible to evaluate the results once the simulation has been completed and the displacements, stresses, or other fundamental variables have been calculated. The evaluation is generally done interactively using the Visualization module of ABAQUS/CAE or another postprocessor. The Visualization module, which reads the neutral binary output database file, has a variety of options for displaying the results, including color contour plots, animations, deformed shape plots, and X-Y plots.

Loads and boundary conditions

Loads distort the physical structure and, thus, create stress in it. ABAQUS/Explicit provides a variety of loading options, the most common of which include:

- point loads;
- pressure loads on surfaces;
- body forces, such as the force of gravity; and
- thermal loads.

Boundary conditions are used to constrain portions of the model to remain fixed (zero displacements) or to move by a prescribed amount (nonzero displacements). In this study, the Figure 18 shows how boundary conditions were used (shown with red colour on Figure 18) and Figure 19, how load was applied as a pressure of the interior part of the left ventricle (shown with red arrows on Figure 19).



Figure 18 Boundary conditions used on the left ventricle



Figure 19 Application of pressure of the interior part of the left ventricle as a load

4.5 Statistical analysis

Analyzes were performed with a Statistica 6.1 (StatSoft Inc., Maisons-Alfort, France).

4.5.1 Descriptive statistics

A descriptive statistics was used to show the average characteristics of the three groups. Descriptive statistics generally are calculated separately for each variable, and they provide such basic information as the mean, minimum and maximum values, different measures of variation, as well as data about the shape of the distribution of the variable. The measures of variation included the standard deviation, and the standard error. Numerous tests of whether the distribution of variables follows the normal distribution are also provided and in this study the Kolmogorov-Smirnov was used.

4.5.2 Pearson correlation

Correlation is a measure of the relation between two or more variables. The measurement scales used should be at least interval scales, but other correlation

coefficients are available to handle other types of data. Correlation coefficients can range from -1.00 to +1.00. The value of -1.00 represents a perfect negative correlation while a value of +1.00 represents a perfect positive correlation. A value of 0.00 represents a lack of correlation.

Pearson correlation assumes that the two variables are measured on at least interval scales, and determines the extent to which values of the two variables are "proportional" to each other. The value of correlation (i.e., correlation coefficient) does not depend on the specific measurement units used; for example, the correlation between height and weight will be identical regardless of whether inches and pounds, or centimeters and kilograms are used as measurement units. Proportional means linearly related; that is, the correlation is high if it can be "summarized" by a straight line (sloped upwards or downwards).

4.5.3 *T*-test for independent samples

The *t*-test is the most commonly used method to evaluate the differences in means between two groups. For example, the *t*-test can be used to test for a difference in test scores between a group of patients who were given a drug and a control group who received a placebo. Theoretically, the *t*-test can be used even if the sample sizes are very small (e.g., as small as 10; some researchers claim that even smaller numbers are possible), as long as the variables are normally distributed within each group and the variation of scores in the two groups is not reliably different. As mentioned before, the normality assumption can be evaluated by looking at the distribution of the data (via histograms) or by performing a normality test (via the descriptive statistics option). The equality of variances assumption can be verified with the *F*-test (which is included in the *t*-test output), or you can use the more robust Levene test option (as well as the Brown-Forsythe modification of this test). If these conditions are not met, then you can evaluate the differences in means between two groups using one of the nonparametric alternatives to the *t*-test.

The *p*-level reported with a *t*-test represents the probability of error involved in accepting our research hypothesis about the existence of a difference. Technically speaking, this is the probability of error associated with rejecting the hypothesis of no difference between the two categories of observations (corresponding to the groups) in the population when, in fact, the hypothesis is true. Some researchers suggest that if

the difference is in the predicted direction, you can consider only one half (one "tail") of the probability distribution and thus divide the standard *p*-level reported with a *t*-test (a "two-tailed" probability) by two. Others, however, suggest that you should always report the standard, two-tailed *t*-test probability.

In this study a student *t* test was used to evaluate the significance of differences between groups when variables were normally distributed with approximately equal variations.

4.5.4 Multiple regression

The general purpose of multiple regression (the term was first used by Pearson, 1908) is to learn more about the relationship between several independent or predictor variables and a dependent or criterion variable. It is possible to choose to analyze the data using a *Standard, Forward stepwise*, or *Backward stepwise* regression method. The popular *Forward stepwise* method evaluates the independent variables at each step, adding or deleting them from the model based on user-specified criteria as it happened in this study also (STATISTICA Electronic manual, Statistica 6.1, StatSoft, Inc. 1984-2004). Sex differences were coded as 1 for men and 2 for women in the Statistica database created for this study.

All values are expressed as a mean \pm SD (standard deviations) unless otherwise stated. Statistical significance was set at p < 0.05 for all tests.

5. Results – Résultats

5.1 Most Trained Group (with training hours more than 5 hrs per week):

5.1.1 Anthropometric and physiological data

Average age of this group was 50.0 ± 5.0 years. Their average height, weight and body surface area were 176.0 ± 6.0 cm, 72.0 ± 10.0 kg and 1.9 ± 0.14 respectively. Their body mass index was 23.3 ± 2.2 which shows that nobody suffered of obesity. Their heart rate was 60.2 ± 9.3 bpm that shows a regulatory adaptation to exercise. This phenomena is also called *bradycardia*, which indicates a resting heart rate lower than 60 beats/min (Feigenbaum et al., 2005). Their systolic and diastolic blood pressure was 123.4 ± 14.3 mmHg and 75.5 ± 12.4 mmHg respectively. None of the subjects suffered from hypertension at the time of examination.

As for their training hours, they trained 9.9 ± 2.0 hours per week and they had training background 17.4 ± 12.2 years.

5.1.2 Echo M-mode and Doppler measurements

As for the morphological signs the AOD and LADS are 34.9 ± 6.1 mm and 37.7 ± 5.7 mm respectively. The IVSD was 10.8 ± 1.5 mm; LVIDD 50.1 ± 5.0 mm and the PWD 10.4 ± 1.5 mm were respectively. The IVSS was 14.2 ± 2.4 mm, LVIDS 30.7 ± 4.2 mm, PWS 17.6 ± 2.7 mm were, respectively. The LVM is 235.2 ± 54.0 g, the LVM/BSA is 134.8 ± 30.8 g/m². The diastolic signs are the following: E 0.81 ± 0.19 m/s, A 0.62 ± 0.12 m/s and E/A 1.31 ± 0.27 . The systolic functions were the following: AOV 1.15 ± 0.16 m/s and EF 76.5 ± 7.2 %. The prevalence of LV hypertrophy (LVM/BSA>134 g/m²) in this group was 38% (Hildick-Smith et al., 2001).

The functional parameters gave the following results: SV 98.9±33.4ml, CO 5.9±1.9 L, EDV 129.2±41.1ml and ESV 30.3±11.8ml.

These results are considered to be normal values regarding to the international findings mentioned previously in this work.
5.1.3 Doppler Tissue Imaging

As for their DTI values the results were the following: the Ea was 0.21 ± 0.04 m/s, Aa was 0.16 ± 0.03 m/s on the basal inferior wall. Their Ea/Aa ratio was 1.42 ± 0.4 on the same side. The Ea was 0.17 ± 0.03 m/s, the Aa 0.14 ± 0.03 m/s on the middle inferior wall. The Ea/Aa ratio was 1.22 ± 0.3 on the same side. The E/Ea was 5.05 ± 1.7 . The descriptive statistics are presented in Table 3.

	Mean	±	SD
Anthropometric and physiological data			
Age (yrs)	50.0	±	5.0
Height (cm)	176.0	±	6.0
Weight (cm)	72.0	±	10.0
$BSA(m^2)$	1.9	±	0.14
BMI (kg/m ²)	23.3	±	2.2
Resting HR (pulse/min)	60.2	±	9.3
Sytolic BP (mmHg)	123.4	±	14.3
Diastolic BP (mmHg)	75.5	±	12.4
Duration of training (years)	17.4	±	12.2
Training intensity (hours/week)	9.9	±	2.0
Echo M-mode and Doppler measurements			
AOD (mm)	34.9	±	6.1
LADS (mm)	37.7	±	5.7
IVSD (mm)	10.8	±	1.5
LVIDD (mm)	50.1	±	5.0
PWD (mm)	10.4	±	1.5
IVSS (mm)	14.2	±	2.4
LVIDS (mm)	30.7	±	4.2
PWS (mm)	17.6	±	2.7
E (m/s)	0.81	±	0.19
A (m/s)	0.62	±	0.12
IVRT (msec)	86.5	±	18.8
AOV (m/s)	1.15	±	0.16
E/A	1.31	±	0.27
LVM (g)	235.2	±	54.0
LVM/BSA (g/m ²)	134.8	±	30.8
RWT	0.21	±	0.04
Functional data			
EDV (ml)	129.2	±	41.1
ESV (ml)	30.3	±	11.8
EF (%)	76.5	±	7.2
SV (ml)	98.9	±	33.4
CO (L/min))	5.9	±	1.9
Doppler Tissue measurements			
Lateral Ea (m/s)	0.21	±	0.04
Lateral Aa (m/s)	0.16	±	0.03
Lateral Ea/Aa	1.42	±	0.40
Septal Ea (m/s)	0.17	±	0.03
Septal Aa (m/s)	0.14	±	0.03
Septal Ea/Aa	1.22	±	0.33
E/Ea	5.05	±	1.7

 Table 3 Descriptive statistics of the Most Trained Group (MTG) (n=16) (SD, standard deviation)

5.2 Less Trained Group (with training hours less than 5 hrs per week):

5.2.1 Anthropometric and physiological data

Average age of this group was 47.0 ± 6.0 years. Their average height, weight and body surface area were 173.0 ± 5.0 cm, 71.0 ± 7.0 kg and 1.9 ± 0.11 respectively. Their body mass index was 23.7 ± 2.2 which shows that nobody suffered of obesity. Their heart rate was 62.5 ± 9.5 bpm that shows a regulatory adaptation to exercise. Their systolic and diastolic blood pressure was 120.2 ± 9.1 mmHg and 70.2 ± 13.4 mmHg respectively. None of the subjects suffered from hypertension at the time of examination.

As for their training hours, they trained 4.7 ± 1.5 hours per week and they had training background 8.3 ± 10.9 years.

5.2.2 Echo M-mode and Doppler measurements

As for the morphological signs the AOD and LADS are 32.6 ± 3.9 mm and 34.8 ± 3.0 mm respectively. The IVSD 10.5 ± 2.0 mm, LVIDD 46.8 ± 5.4 mm and the PWD 9.9 ± 2.1 mm were respectively. The IVSS was 16.6 ± 3.5 mm, LVIDS 28.1 ± 4.6 mm, PWS 17.1 ± 3.1 mm were respectively. The LVM is 194.9 ± 46.2 g, the LVM/BSA is 114.1 ± 24.6 g/m². The diastolic signs are the following: E 0.77 ± 0.18 m/s, A 0.63 ± 0.14 m/s and E/A 1.25 ± 0.31 . The systolic functions were the following: AOV 0.93 ± 0.2 m/s and EF 76.9 ± 10.0 %. The prevalence of LV hypertrophy (LVM/BSA>134 g/m²) in this group was 15% (Hildick-Smith et al., 2001).

The functional parameters gave the following results: SV 82.2±29.3ml, CO 5.2±2.1 L, EDV 106.0±35.2ml and ESV 23.8±11.23ml.

These results are considered to be normal values regarding to the international findings mentioned previously in this work.

5.2.3 Doppler Tissue Imaging

As for their DTI values the results were the following: the Ea was 0.23 ± 0.03 m/s, Aa was 0.18 ± 0.04 m/s on the basal inferior wall. Their Ea/Aa ratio was 1.35 ± 0.4 on the same side. The Ea was 0.19 ± 0.04 m/s, the Aa 0.16 ± 0.03 m/s on the middle inferior wall. The Ea/Aa ratio was 1.24 ± 0.3 on the same side. The E/Ea was 4.21 ± 1.2 . The descriptive statistics are presented in Table 4.

	Mean	±	SD
Anthropometric and physiological data			
Age (yrs)	50.0	±	6.0
Height (cm)	173.0	±	5.0
Weight (cm)	71.0	±	7.0
$BSA(m^2)$	1.9	±	0.11
BMI (kg/m^2)	23.7	±	2.2
Resting HR (pulse/min)	62.5	±	9.5
Sytolic BP (mmHg)	120.2	±	9.1
Diastolic BP (mmHg)	70.2	±	13.4
Duration of training (years)	8.3	±	10.9
Training intensity (hours/week)	4.7	±	1.5
Echo M-mode and Doppler measurements			
AOD (mm)	32.6	±	3.9
LADS (mm)	34.8	±	3.0
IVSD (mm)	10.5	±	2.0
LVIDD (mm)	46.8	±	5.4
PWD (mm)	9.9	±	2.1
IVSS (mm)	16.6	±	3.5
LVIDS (mm)	28.1	±	4.6
PWS (mm)	17.1	±	3.1
E (m/s)	0.77	±	0.18
A (m/s)	0.63	±	0.14
IVRT (msec)	78.7	±	20.4
AOV (m/s)	0.93	±	0.20
E/A	1.25	±	0.31
LVM (g)	194.9	±	46.2
$LVM/BSA (g/m^2)$	114.1	±	24.6
RWT	0.21	±	0.06
Functional data			
EDV (ml)	106.0	±	35.2
ESV (ml)	23.8	±	11.2
EF (%)	76.9	±	10.0
SV (ml)	82.2	±	29.3
CO (L/min))	5.2	±	2.1
Doppler Tissue measurements			
Lateral Ea (m/s)	0.23	±	0.03
Lateral Aa (m/s)	0.18	±	0.04
Lateral Ea/Aa	1.35	±	0.37
Septal Ea (m/s)	0.19	±	0.04
Septal Aa (m/s)	0.16	±	0.03
Septal Ea/Aa	1.24	±	0.30
E/Ea	4.21	±	1.2

Table 4 Descriptive statistics of the Less Trained Group (LTG) (n=13) (SD, standard deviation)

5.3 Non Trained Group (sedentary group):

5.3.1 Anthropometric and physiological data

Average age of this group was 49.0 ± 4.0 years. Their average height, weight and body surface area were 168.0 ± 10.0 cm, 66.0 ± 12.0 kg and 1.8 ± 0.2 respectively. Their body mass index was 23.3 ± 2.9 which shows that nobody suffered of obesity. Their heart rate was 74.5 ± 11.3 bpm. Their systolic and diastolic blood pressure was 122.9 ± 9.4 mmHg and 70.4 ± 7.8 mmHg respectively. None of the subjects suffered from hypertension at the time of examination.

As for their training hours, they were not trained at the time of examination and they were not following any organized training program or free time activity in their lifetime.

5.3.2 Echo M-mode and Doppler measurements

As for the morphological signs the AOD and LADS are 32.7 ± 5.2 mm and 29.8 ± 5.5 mm respectively. The IVSD 9.1 ± 2.0 mm, LVIDD 46.4 ± 5.0 mm and the PWD 9.2 ± 1.6 mm were, respectively. The IVSS was 13.7 ± 3.1 mm, LVIDS 27.9 ± 5.0 mm, PWS 16.6 ± 2.8 mm were, respectively. The LVM is 167.0 ± 52.4 g, the LVM/BSA is 102.9 ± 20.4 g/m². The diastolic signs are the following: E 0.77 ± 0.15 m/s, A 0.68 ± 0.14 m/s and E/A 1.16 ± 0.2 . The systolic functions were the following: AOV 1.05 ± 0.14 m/s and EF 77.1 ± 9.2 %.

The functional parameters gave the following results: SV 79.4±26.2ml, CO 5.7±2.0L, EDV 103.3±32.4ml and ESV 23.8±14.3ml.

These results are considered to be normal values regarding to the international findings mentioned previously in this work.

5.3.3 Doppler Tissue Imaging

As for their DTI values the results were the following: the Ea was 0.22 ± 0.04 m/s, Aa was 0.18 ± 0.04 m/s on the basal inferior wall. Their Ea/Aa ratio was 1.22 ± 0.26 on the same side. The Ea was 0.17 ± 0.03 m/s, the Aa 0.16 ± 0.03 m/s on the middle inferior wall. The Ea/Aa ratio was 1.09 ± 0.21 on the same side. The E/Ea was 4.73 ± 1.1 . The descriptive statistics are presented in Table 5.

	Mean	±	SD			
Anthropometric and physiological data						
Age (yrs)	49.0	±	4.0			
Height (cm)	168.0	±	10.0			
Weight (cm)	66.0	±	12.0			
$BSA(m^2)$	1.8	±	0.20			
BMI (kg/m ²)	23.3	±	2.9			
Resting HR (pulse/min)	74.5	±	11.3			
Sytolic BP (mmHg)	122.9	±	9.4			
Diastolic BP (mmHg)	70.4	±	7.8			
Duration of training (years)	0.9	±	3.8			
Training intensity (hours/week)	0.2	±	0.8			
Echo M-mode and Doppler measurements						
AOD (mm)	32.7	±	5.2			
LADS (mm)	29.8	±	5.5			
IVSD (mm)	9.1	±	2.0			
LVIDD (mm)	46.4	±	5.0			
PWD (mm)	9.2	±	1.6			
IVSS (mm)	13.7	<u>+</u>	3.1			
LVIDS (mm)	27.9	±	5.0			
PWS (mm)	16.6	±	2.8			
E (m/s)	0.77	±	0.15			
A (m/s)	0.68	<u>+</u>	0.14			
IVRT (msec)	79.4	<u>+</u>	10.6			
AOV (m/s)	1.05	<u>+</u>	0.14			
E/A	1.16	±	0.20			
LVM (g)	167.0	<u>+</u>	52.4			
$LVM/BSA (g/m^2)$	102.9	<u>+</u>	20.4			
RWT	0.20	±	0.04			
Functional data						
EDV (ml)	103.3	±	32.4			
ESV (ml)	23.8	±	14.3			
EF (%)	77.1	±	9.2			
SV (ml)	79.4	±	26.2			
CO (L/min))	5.7	±	2.0			
Doppler Tissue measurements						
Lateral Ea (m/s)	0.22	±	0.04			
Lateral Aa (m/s)	0.18	±	0.04			
Lateral Ea/Aa	1.22	±	0.26			
Septal Ea (m/s)	0.17	±	0.03			
Septal Aa (m/s)	0.16	±	0.03			
Septal Ea/Aa	1.09	±	0.21			
E/Ea	4.73	±	1.1			

Table 5 Descriptive statistics of the Non Trained Group (NTG) (n=16) (SD, standard deviation)

	MTG			LTG			NTG		
	Mean	±	SD	Mean	±	SD	Mean	±	SD
Anthropometric and physiological data									
Age (yrs)	50,2	±	4,8	46,9	±	6,1	49,3	±	4,0
Height (cm)	176,1	\pm	6,2	173,5	±	5,0	168,3	\pm	9,8
Weight (cm)	72,3	±	9,6	71,3	±	7,4	66,5	±	12,3
BSA (m ²)	1,9	±	0,14	1,9	±	0,11	1,8	±	0,20
BMI (kg/m^2)	23,3	±	2,2	23,7	±	2,2	23,3	±	2,9
Resting HR (pulse/min)	60,2	±	9,3	62,5	±	9,5	74,5	±	11,3
Sytolic BP (mmHg)	123,4	±	14,3	120,2	±	9,1	122,9	±	9,4
Diastolic BP (mmHg)	75,5	±	12,4	70,2	±	13,4	70,4	±	7,8
Duration of training (years)	17,4	\pm	12,2	8,3	\pm	10,9	0,9	\pm	3,8
Training intensity (hours/week)	9,9	\pm	2,0	4,7	\pm	1,5	0,2	\pm	0,8
Echo M-mode and Doppler mea	suremen	ts							
AOD (mm)	34,9	±	6,1	32,6	±	3,9	32,7	±	5,2
LADS (mm)	37,7	±	5,7	34,8	±	3,0	29,8	±	5,5
IVSD (mm)	10,8	\pm	1,5	10,5	±	2,0	9,1	\pm	2,0
LVIDD (mm)	50,1	\pm	5,0	46,8	±	5,4	46,4	\pm	5,0
PWD (mm)	10,4	±	1,5	9,9	±	2,1	9,2	±	1,6
IVSS (mm)	14,2	±	2,4	16,6	±	3,5	13,7	±	3,1
LVIDS (mm)	30,7	\pm	4,2	28,1	±	4,6	27,9	\pm	5,0
PWS (mm)	17,6	\pm	2,7	17,1	±	3,1	16,6	\pm	2,8
EV (m/s)	0,81	±	0,19	0,77	±	0,18	0,77	±	0,15
AV (m/s)	0,62	\pm	0,12	0,63	±	0,14	0,68	\pm	0,14
IVRT (msec)	86,5	\pm	18,8	78,7	±	20,4	79,4	\pm	10,6
AOV (m/s)	1,15	±	0,16	0,93	±	0,20	1,05	±	0,14
E/A	1,31	\pm	0,27	1,25	±	0,31	1,16	\pm	0,20
LVM (g)	235,2	\pm	54,0	194,9	±	46,2	167,0	\pm	52,4
LVM/BSA (g/m ²)	134,8	±	30,8	114,1	±	24,6	102,9	±	20,4
LVM/height (g/m ^{2.7})	51,6	±	14,2	43,8	±	9,5	40,4	±	9,3
Functional data									
EDV (ml)	129,2	±	41,1	129,2	±	35,2	103,3	±	32,4
ESV (ml)	30,3	±	11,8	30,3	±	11,2	23,8	±	14,3
EF (%)	76,5	±	7,2	76,5	±	10,0	77,1	±	9,2
SV (ml)	98,9	±	33,4	98,9	±	29,3	79,4	±	26,2
CO (L/min))	5,9	±	1,9	5,9	±	2,1	5,7	±	2,0
Doppler Tissue measurement									
Lateral Ea (m/s)	0,21	±	0,04	0,21	±	0,03	0,22	±	0,04
Lateral Aa (m/s)	0,16	±	0,03	0,16	±	0,04	0,18	\pm	0,04
Lateral Ea/Aa	1,42	\pm	0,40	1,42	±	0,37	1,22	±	0,26
Septal Ea (m/s)	0,17	\pm	0,03	0,17	±	0,04	0,17	±	0,03
$\mathbf{C} = (1 \mathbf{A} + (1 \mathbf{A}))$	0.14	±	0,03	0.14	±	0,03	0,16	±	0,03
Septal Aa (m/s)				- >					
Septal Ea/Aa	1,22	±	0,33	1,22	±	0,30	1,09	±	0,21

Table 6 Summary of Descriptive statistics among the three groups

5.4 Results of the T-test for impaired data on the lateral and septal velocity by Doppler Tissue Imaging

5.4.1 Most Trained Group

There was a significant difference between the lateral Ea and septal Ea (0.21m/s vs. 0.17 m/s). There was no significant difference between the lateral Aa and septal Aa even though on the lateral side the Aa peak was higher. Considering the Ea/Aa ratio on the lateral and septal side, the lateral side showed a higher ratio (1.42 vs. 1.22) (Figure 20).



Figure 20 T-test paired data in the MTG

5.4.2 Less Trained Group

There was a significant difference between the lateral Ea and septal Ea (0.23m/s vs. 0.19 m/s). There was no significant difference between the lateral Aa and septal Aa even though on the lateral side the Aa peak was higher. Considering the Ea/Aa ratio on the lateral and septal side, the lateral side showed a higher ratio (1.35 vs. 1.24) (Figure 21).



Figure 21 T test for paired data in the LTG

5.4.3 Non Trained Group

There was a significant difference between the lateral Ea and septal Ea (0.22 m/s vs. 0.17 m/s). There was also a significant difference between the lateral Aa and septal Aa (0.18 m/s vs. 0.16 m/s). Considering the Ea/Aa ratio on the lateral and septal side, the lateral side showed a higher ratio (1.22 vs. 1.09) (Figure 22).



Figure 22 T test for paired data in the NTG

5.5 Results of the T-test for impaired data on training background, morphologic data, diastolic function and DTI

The groups were comparable for age $(50.2\pm4.8 \text{ yrs}, 46.9\pm6.1 \text{ yrs}, 49.2\pm4.0 \text{ yrs})$, body surface area $(1.88\pm0.14, 1.85\pm0.1, 1.76\pm0.2 \text{ m}^2)$ and blood pressure $(123.4\pm14.3/75.5\pm12.4 \text{ mmHg}, 120.1\pm9.1/70.1\pm13.35 \text{ mmHg}, 122.9\pm9.4/70.4\pm7.7 \text{ mmHg})$ respectively (MTG-LTG-NTG) (Table 6).

5.5.1 T-test for the MTG-LTG groups

Significant differences were found in the following variables: training intensity $(9.9\pm1.9 \text{ vs. } 4.6\pm1.4 \text{ hrs}; \text{ p}<0.05)$, IVSS $(14.2\pm2.3 \text{ vs. } 16.5\pm3.5 \text{ mm}; \text{ p}<0.04)$, AOV $(1.1\pm0.2 \text{ vs. } 0.9\pm0.2 \text{ m/s}; \text{ p}<0.008)$ and LVM $(235.2\pm54.0 \text{ vs. } 194.9\pm46.1 \text{ g}; \text{ p}<0.04)$ respectively. Even though the difference was not significant, the MTG showed less HR compared to the LTG $(60.2\pm9.3 \text{ vs. } 62.4\pm9.5 \text{ bpm})$, and showed higher values among the following variables: duration of training $(17.4\pm12.15 \text{ vs. } 8.33\pm10.9 \text{ yrs})$, LADS $(37.7\pm5.7 \text{ vs. } 34.8\pm3.0 \text{ mm})$, IVSD $(10.8\pm1.5 \text{ vs. } 10.5\pm1.9 \text{ mm})$, LVIDD $(50.1\pm5.0 \text{ vs. } 46.8\pm5.3 \text{ mm})$, PWD $(10.4\pm1.5 \text{ vs. } 9.8\pm2.0 \text{ mm})$, E $(0.81\pm0.2 \text{ vs. } 0.77\pm0.2 \text{ m/s})$, E/A $(1.3\pm0.3 \text{ vs. } 1.2\pm0.3)$, LVM/BSA $(134.8\pm30.8 \text{ vs. } 114.1\pm24.6 \text{ vs. } 10.5\pm1.9 \text{ vs. } 10.5\pm1$

g/m²), LVM/height (51.6±14.2 vs. 43.8±9.5 g/m^{2.7}), EDV (129.2±41.0 vs.106.0±35.2 ml), SV (98.9±33.4 vs. 82.1±29.3 ml), lateral Ea/Aa (1.42±0.4 vs.1.35±0.4).

5.5.2 T-test for the MTG-NTG groups

Significant differences were found in the following variables: HR (60.2 \pm 9.3 vs.74.5 \pm 11.2 bpm; p<0.0007), duration of training (17.4 \pm 12.1 vs. 0.9 \pm 3.7 years), training intensity (9.9 \pm 1.9 vs. 0.2 \pm 0.7 hrs), LADS (37.7 \pm 5.7 vs. 29.8 \pm 5.5 mm), IVSD (10.8 \pm 1.4 vs. 9.0 \pm 2.0 mm), LVIDD (50.1 \pm 5.0 vs. 46.4 \pm 4.9 mm), PWD (10.4 \pm 1.5 vs. 9.2 \pm 1.6 mm), LVM (235.2 \pm 54.0 vs. 167.0 \pm 52.4 g), LVM/BSA (134.8 \pm 30.1 vs. 102.9 \pm 20.4 g/m²), LVM/height (51.6 \pm 14.2 vs. 40.4 \pm 9.3 g/m^{2.7}), DTI A lat (0.16 \pm 0.03 vs. 0.18 \pm 0.03 m/s) respectively. Even though the difference was not significant the MTG had higher values compared to the NTG among the following variables: E (0.81 \pm 0.2 vs. 0.77 \pm 0.1 m/s), E/A (1.3 \pm 0.3 vs. 1.2 \pm 0.2), EDV (129.2 \pm 41.0 vs. 103.3 \pm 32.3 ml), SV (98.9 \pm 33.4 vs. 82.1 \pm 29.3 ml), lateral Ea/Aa (1.42 \pm 0.4 vs. 1.22 \pm 0.3), septal Ea/Aa (1.22 \pm 0.3 vs. 1.09 \pm 0.2).

5.5.3 T-test for the LTG-NTG groups

Significant differences were found in the following variables at p<0.05: HR (62.4 ± 9.5 vs. 74.5 ± 11.2 bpm), duration of training (8.3 ± 10.9 vs. 0.9 ± 3.7 years), training intensity (4.7 ± 1.5 vs. 0.2 ± 0.7 hrs), LADS (34.8 ± 3.0 vs. 29.8 ± 5.5 mm), IVSS (16.5 ± 3.5 vs. 13.6 ± 3.1 mm) respectively. Even though the difference was not significant the LTG had higher values compared to the NTG among the following variables: IVSD (10.5 ± 1.9 vs. 9.0 ± 2.0 mm), EDD (46.8 ± 5.4 vs. 46.4 ± 4.9 mm), 9.8 ± 2.0 vs. 9.2 ± 1.6 mm), E/A (1.2 ± 0.3 vs. 1.2 ± 0.2 m/s), LVM (194.9 ± 46.2 vs. 167.0 ± 52.4 g), LVM/BSA (114.1 ± 24.6 vs. 102.9 ± 20.4 g/m²), LVM/height (43.8 ± 9.5 vs. 40.4 ± 9.3 g/m^{2.7}), EDV (105.9 ± 35.2 vs. 103.3 ± 32.3 ml), SV (82.2 ± 29.3 vs. 79.5 ± 26.2 ml), lateral Ea (0.23 ± 0.03 vs. 0.22 ± 0.04 m/s), lateral Ea/Aa (1.35 ± 0.4 vs. 1.22 ± 0.3), septal Ea/Aa (1.24 ± 0.3 vs. 1.09 ± 0.2).

	T-test for independent samples			
	MTG-LTG	MTG-NTG	LTG-NTG	
Anthropometric and physiological data				
Age (yrs)	↑	<u>↑</u>	Ļ	
Height (cm)	↑	↑ p<0.001	1	
Weight (cm)	↑		1	
$BSA(m^2)$, ↑	, ↑	1	
BMI (kg/m^2)	ļ	, ↑	1	
Resting HR (pulse/min)	, I	⊥ p<0.0007	⊥ p<0.005	
Svtolic BP (mmHg)	↓ ↑			
Diastolic BP (mmHg)	, ↑	, ↑	Ļ	
Duration of training (vears)	, ↓	↑ p<0.000	↑ p<0.02	
Training intensity (hours/week)	↑ p<0.05	↑ p<0.000	↑ p<0.000	
Echo M-mode and Doppler measurements				
AOD (mm)	1	1		
LADS (mm)	↑	↑ p<0.0004	Ť	
IVSD (mm)	↑	↑ p<0.008	1	
LVIDD (mm)	, ↑	↑ p<0.009	1	
PWD (mm)	, ↑	↑ p<0.01	1	
IVSS (mm)	↑ p<0.04	↑ 1	↑ p<0.03	
LVIDS (mm)	↑	1		
PWS (mm)	, ↑	, ↑	1	
EV (m/s)	, ↑	, ↑	\leftrightarrow	
AV (m/s)	ļ	L	.L.	
IVRT (msec)	↓ ↑	Ť	↓	
AOV (m/s)	↑ p<0.008	↑	↓	
E/A	↑ ¹	↑	↓	
LVM (g)	↑ p<0.04	↑ p<0.001	1	
$LVM/BSA (g/m^2)$	↑	↑ p<0.002	1	
$LVM/height (g/m^{2.7})$, ↓	↑ p<0.003	1	
RWT	\leftrightarrow	1	1	
Functional datas				
EDV (ml)	↑	↑	1	
ESV (ml)	1	1	1	
EF (%)	\downarrow	\downarrow	\downarrow	
SV (ml)	1	1	1	
CO (L/min)	1	1	Ļ	
Doppler Tissue measurements				
Lateral Ea (m/s)	\downarrow	\downarrow	1	
Lateral Aa (m/s)	↓	↓ p<0.05	\leftrightarrow	
Lateral Ea/Aa	↑ I	1	1	
Septal Ea (m/s)	\downarrow	\leftrightarrow	1	
Septal Aa (m/s)	\downarrow	\downarrow	\leftrightarrow	
Septal Ea/Aa	\downarrow	↑	↑	
E/Ea	↑	Ţ	\downarrow	

Table 7 T-test for impaired data between the three examined groups (p<0.05 were considered statistically significant)

 \uparrow the value of the first group is higher compared to the second group

 \downarrow the value of the first group is less compared to the second group

5.6 Correlation

5.6.1 Correlation in the overall population

	Age (yrs)	BSA (m2)	Sex	Resting HR (pulse/min)	Duration of training (yrs)	Training Intensity (hrs/week)
AOD (mm)	0.15	0.27	-0.36	-0.38	0.37	0.28
LADS (mm)	0.04	0.64	-0.59	-0.26	0.33	0.53
IVSD (mm)	0.33	0.51	-0.41	-0.49	0.19	0.35
LVIDD (mm)	0.07	0.21	-0.29	-0.24	0.42	0.38
PWD (mm)	0.37	0.40	-0.35	-0.32	0.04	0.25
E	-0.44	0.07	0.01	-0.16	-0.05	0.15
Α	-0.08	0.09	-0.05	0.17	-0.11	-0.06
IVRT (msec)	0.15	0.07	0.06	0.04	0.11	0.12
E/A	-0.41	0.02	0.06	-0.31	0.01	0.19
LVM (g)	0.36	0.52	-0.52	-0.50	0.37	0.54
LVM/BSA (g/m2)	0.35	0.25	-0.36	-0.44	0.44	0.52
LVM/height (g/m2.7)	0.33	0.20	-0.27	-0.39	0.38	0.46
RWT	0.27	0.22	-0.14	-0.16	-0.17	0.01
Lateral Ea (m/s)	-0.35	-0.34	0.01	0.04	0.05	-0.05
Lateral Aa (m/s)	-0.07	0.00	0.10	0.21	-0.29	-0.22
Lateral Ea/Aa	-0.12	-0.17	-0.13	-0.13	0.31	0.20
Septal Ea (m/s)	-0.31	-0.26	0.02	-0.00	0.27	-0.01
Septal Aa (m/s)	-0.12	-0.03	0.09	0.26	-0.25	-0.09
Septal Ea/Aa	-0.08	-0.20	-0.07	-0.25	0.49	0.11
E/Ea	-0.07	0.28	-0.06	-0.14	-0.16	0.15

Table 8 Correlation between anthropometric, physiologic, echo M-mode, Doppler and DopplerTissue measurements in the overall group (Correlations level of significance is marked at p < 0.05)

In the overall population age related to IVSD, PWD, PWS (r=0.33, r=0.37, r=0.41); E, E/A (r=-0.44, r=-0.41); LVM, LVM/BSA, LVM/height (r=0.36, r=0.35, r=0.36); lateral Ea, septal Ea (r=-0.35, r=-0.31) respectively at p<0.05. Sex was negatively related almost all the morphologic parameters at p<0.05, except LVIDD, LVIDS, LVM/height and was not related to any functional parameters, such as diastolic function and Doppler Tissue measurements. Resting HR was related to the following morphologic parameters: AOD, IVSD, PWD, E/A, LVM, LVM/BSA, LVM/height (r=-.0.38, r=-0.49, r=-0.32, r=-0.31, r=-0.50, r=-0.44, r=-0.44, r=-0.39) respectively. As for the duration of training, it was related to AOD, LADS, LVIDD,

LVIDS, LVM, LVM/BSA, LVM/height, septal Ea/Aa (r=0.37, r=0.33, r=0.42, r=0.47, r=0.37, r=0.44, r=0.38, r=0.49). Finally, the training intensity was related to LADS, IVSD, LVIDD, LVIDS, LVM, LVM/BSA, LVM/height (r=0.53, r=0.35, r=0.38, r=0.30, r=0.54, r=0.52, r=0.46) respectively (Table 7).

In the overall population the correlation between morphologic variables and Doppler Tissue variables showed the following results: the LVIDD and EDV were related only to septal Aa (r = -0.36, p<0.05 and r = -0.39, p<0.01) (Figure 23) and age was related to lateral Ea (r=-0.35, p<0.05) and septal Ea (r=-0.31, p<0.05).



Figure 23 Correlation between LVIDD and septal Aa in the overall group

As for the intragroup correlations between morphologic variables and Doppler Tissue variables, the results were the following.

5.6.2 Correlation in the Most Trained Group

In the MTG the LVIDD and EDV were related only to septal Aa (r = -0.53, p<0.04 and r = -0.53, p<0.05) (Figure 24).



Figure 24 Correlation between LVIDD and septal Aa in the MTG group

5.6.3 Correlation in the Less Trained Group

No significant correlation found between DTI and morphologic variables.

5.6.4 Correlation in the Non Trained Group

In the NTG the LVIDD and EDV were related only to septal Ea (r = -0.57, p<0.05 and r = -0.55, p<0.05) (Figure 25).



Figure 25 Correlation between LVIDD and septal Ea in the NTG

5.7 Stepwise, forward multiple regression

Stepwise, forward multiple regressions were performed to learn more about the relationship between several independent predictor variables and a dependent variable. Therefore, morphologic variables such as resting HR, LADS, IVST, LVIDD, LVIDS, PWT, LVM; DTI were chosen in the overall population. It is assumed in multiple regression that the residuals are distributed normally, therefore the following variables were entered: age, sex, training intensity, duration of training were included into the model as potential determinants to allow a researcher to ask:"What is the best predictor of a chosen variable?"

Resting heart rate was independently associated with the intensity of training (β =-0.37, p<0.03); duration of training was the only independent predictor of LVIDD and LVIDS (β =0.36, p<0.03 and β =0.47, p<0.002; respectively). Age and sex was independently associated with PWT (β =0.33, p<0.03; β =-0.31, p<0.04; respectively). LADS was independently associated with sex and duration of training (β =-0.48, p<0.002; β =0.26, p<0.08). Finally, LVM was independently associated with the intensity of training, age and sex (β =0.36, p<0.02; β =0.28, p<0.08; β =-0.31, p<0.04, respectively).

Age was the only independent predictors of lateral Ea (β =-0.35, p<0.03). However, age (β =-0.32, p<0.04) and duration of training (β =0.47, p<0.02) were independently associated with septal Ea. As for the lateral and septal Aa, none of the chosen variables showed an association with them, even though the duration of training showed a negative, non significant association on these variables.

5.8 Results on the Finite Element Analyzis

5.8.1 Stress of von Mises

Stress is the internal distribution of force per unit area that balances and reacts to external loads applied to a body. It is a second-order tensor with nine components, but can be fully described with six components due to symmetry in the absence of body moments. Stress is often broken down into its shear and normal components as these have unique physical significance (http://en.wikipedia.org/wiki/Stress_%28physics%29).

Von Mises stress, σ_v is a scalar function of the components of the stress tensor that gives an appreciation of the overall 'magnitude' of the tensor. This allows the onset and amount of plastic deformation under triaxial loading to be predicted from the results of a simple uniaxial tensile test (Lodini et al., 2003).

In 3D, the Mises stress can be expressed as:

$$\sigma_v = \sqrt{\frac{(\sigma_1 - \sigma_2)^2 + (\sigma_2 - \sigma_3)^2 + (\sigma_3 - \sigma_1)^2}{2}}$$

Where $\sigma_1, \sigma_2, \sigma_3$ are the principal stresses. In 1-D, this reduces to the uniaxial stress.

Or, in terms of a local coordinate system:

$$\sigma_v = \frac{1}{\sqrt{2}}\sqrt{(\sigma_x - \sigma_y)^2 + (\sigma_y - \sigma_z)^2 + (\sigma_z - \sigma_x)^2 + 6(\tau_{xy}^2 + \tau_{yz}^2 + \sigma_y)^2 + 6(\tau_{xy}^2 + \sigma_y)^2 + 6(\tau_{xy}^$$

(http://en.wikipedia.org/wiki/Von Mises stress).

5.8.1.1 Stress of Von Mises in the Non Trained Group



Figure 26 Stress of Von Mises with a Young's modulus E=0.3 MPa (which is a measure of the stiffness of a given material) and a Poisson's ratio v=0.49 at t=0 msec in the NTG





Figure 27 Stress of Von Mises with a Young's modulus E=0.3 MPa (which is a measure of the stiffness of a given material) and a Poisson's ratio v=0.49 at t=0.12 msec in the NTG

The stress is maximal at the apex, decreases from the apex toward the base of the heart and decreases from the endocardium toward the epicardium at t=0.12 msec in the NTG.



Figure 28 Stress of Von Mises with a Young's modulus E=0.3 MPa (which is a measure of the stiffness of a given material) and a Poisson's ratio v=0.49 at t=0.24 msec in the NTG

The stress has its highest value at the apex and at the level of septal and lateral valves, and increases from the endocardium toward the epicardium at t=0.24 msec in the NTG.

5.8.1.2 Stress of Von Mises in the Most Trained Group



Figure 29 Stress of Von Mises with a Young's modulus E=0.3 MPa (which is a measure of the stiffness of a given material) and a Poisson's ratio v=0.49 at t=0 msec in the MTG



The LV wall is hypothesized to be stress free at t=0 msec in the MTG.

Figure 30 Stress of Von Mises with a Young's modulus E=0.3 MPa (which is a measure of the stiffness of a given material) and a Poisson's ratio v=0.49 at t=0.12 msec in the MTG

The stress is maximal at the apex, decreases from the apex toward the base of the heart, except on the septal side, where there is an increase of the stress at the level of aortic valves. There is also an increases from the endocardium toward the epicardium at t=0.12 msec in the MTG.



Figure 31 Stress of Von Mises with a Young's modulus E=0.3 MPa (which is a measure of the stiffness of a given material) and a Poisson's ratio v=0.49 at t=0.24 msec in the MTG

The stress has its highest value at the level of aortic valves on the septal side and at the level of mitral valves on the lateral side. There is an increases from the endocardium toward the epicardium all along the LV wall at t=0.24 msec in the MTG.

5.8.2 Strain

Strain is the geometrical expression of deformation caused by the action of solicitation of external pressure on a physical body. Strain is calculated by first assuming a change between two body states: the beginning state and the final state. Then the difference in placement of two points in this body in those two states expresses the numerical value of strain. Strain therefore expresses itself as a change in size and/or shape (http://en.wikipedia.org/wiki/Strain %28materials_science%29).

The (relative) strain, ε , is given by:

Where \mathcal{E} is strain in measured direction, ℓ_o is the original length of the material and ℓ is the current length of the material.

5.8.2.1 Strain in the Non Trained Group



Figure 32 Strain of the left ventricle at t=0.0 msec in the NTG

This stimulation showed that at time=0.0 msec the maximal principal strain (Emax) is the largest at the middle of the left ventricular wall and smaller at the level of the septum while the apex remains static.



Figure 33 Strain of the left ventricle at t=0.12 msec in the NTG

As for time=0.12 msec, just in the middle of the myocardial contraction, the Emax is the largest at the apex, then it is increased at the middle of the left ventricular wall and the smallest at the basal level. The deformation takes place from the endocardial muscle fibers toward the epicardial muscle fibers. The lateral and septal basal parts move toward each other, so does the middle of the left ventricular wall and septum, while the apex remains quasi static.



Figure 34 Strain of the left ventricle at t=0.24 msec in the NTG

Finally, at time=0.24 (end-systolic phase), the contraction took place, the Emax is growing from the apex toward the basal level of the lateral and septal side of the left ventricle at the level of the mitral valves through the myocardium and seems to be the same among the endocardial muscle fibers and epicardial muscle fibers. Interestingly, there is an augmentation of the Emax at the level of the septal side, just above the origin of the aortic valve.

5.8.2.2 Strain in the Most Trained Group



Figure 35 Strain of the left ventricle at t=0.0 msec in the MTG

This stimulation showed that at time=0.0 msec the maximal principal strain (Emax) is about the same all along of the left ventricular wall while the apex remains static.



Figure 36 Strain of the left ventricle at t=0.12 msec in the MTG

As for time=0.12 msec, in the middle of the myocardial contraction, the Emax is the largest at the apex and getting smaller from it toward the lateral and septal side of the left ventricle and compared to the NTG the activation takes places somehow slower among the left ventricular wall. The middle of the left ventricular wall and septum moves toward each other while the apex moves slightly toward the basal part of the heart.



Figure 37 Strain of the left ventricle at t=0.24 msec in the MTG

At time=0.24 msec, the full contraction takes place, the wall of the heart is contracted all along the left ventricle. At this time it can be clearly seen compared to the NTG, how the deformation passed through from the endocardium toward the epicardium. Interestingly, there is an accumulation of strain at the septal and basal sides at the level of the mitral valves, just like in the case of the NTG, even though in this case is more evident on both sides.

6. Discussion – Discussion

The normal aging process is known to be associated with a decline in cardiac performance, often manifested as impaired left ventricular diastolic function, with little or no change in systolic performance. Specifically in diastole, left ventricular relaxation slows and the peak rate of early rapid filling decreases, whereas the relative late atrial filling of the left ventricle increases with age. However, it seems that with regular moderate- to high intensity endurance exercise training this aging process can be slowed down and even aged athletes can induce cardiac adaptations.

6.1 Echo M-mode and Doppler measurements

6.1.1 The left atrium

The left atrium serves as both a reservoir and a conduit for passage of blood from the pulmonary veins to the left ventricle and as a contractile chamber that augments left ventricular filling. Moreover, some studies showed that the left atrium (LA) contribute up to 30% of left ventricular filling and cardiac output (Thomas et al., 2003). One of the most interesting finding of this work was the difference shown between the three examined groups considering their LADS where the MTG and LTG had a more increased but non pathologic left atrium size (≤ 40 mm). This result is similar to the finding of Giada et al., 1998, where they found a significant increase of left atrium size only among elderly amateur cyclist (aged between 50 to 65 years) compared to young amateur cyclist (aged between 19 to 25 years) and Pellicia et al., 2005 where they showed also among 1,777 competitive athletes that in a large population of highly trained athletes, enlarged LA dimension ≥ 40 mm was relatively common, with the upper limits of 45 mm in women and 50 mm in men distinguishing physiologic cardiac remodeling from pathologic cardiac conditions. There had been numerous articles that described thanks to training there is an augmentation of the VO₂max (Ehsani et al., 1991; Giada et al., 1998) and stroke volume that highly correlated with the changes in plasma volume, making this training induced increase one of the most significant training effects (Wilmore et al., 2004) which means that more blood arrives toward the LA, therefore this dilatation can be explained by this

factor. It has been shown also that the strength of atrial contraction, like the ventricle, is a direct function of preload and that atrial emptying is limited by the afterload against which it ejects (Thomas et al., 1991). Thomas et al., 2003 demonstrated that pulsed wave Doppler Tissue Imaging can be used to estimate global atrial contraction and colour Doppler Tissue Imaging can be used to estimate segmental atrial contraction in normal subjects in sinus rhythm into two groups: Group A<50 years and Group B>50 years. The A velocity was noted to increase with age with a significant difference between groups. The peak mitral A wave velocity, mitral A wave velocity time integral, atrial fraction and atrial ejection force significantly increased with age, even though no significant changes were noted in LA size or parameters of pulmonary atrial flow reversal with ageing which might be explained with the fact that they were examining healthy, but non athletic people. This might mean that the total atrial emptying volume remains unchanged, the active emptying volume is increased in compensation for the decreased volume transfer. This possible increase in active atrial emptying volume was reflected by the decrease in peak A velocity through a dilatation of the LA in this study (Toutouzas et al., 1996). Besides, there had been few works which were interested in the physiologic approach of the LA and they were mostly based on the anatomic recordings.

It can be hypothesized that there is a "physiologic continuum" considering the athlete's heart even in this age group which means the dilatation of the atrium to allow a better filling of the left ventricle mostly during exercise and an improvement of the aerobic performance and can be considered as physiologic adaptations to training (Erol et al., 2001; Pellicia et al., 2005; Kasikcioglu et al., 2006). Moreover, increased vagal tone produces a negative inotropic effect in cardiac myocytes, thus the lower Aa might be explained by this fact.

6.1.2 *Resting heart rate*

As expected, resting heart rate was lower in both trained group (MTG and LTG) compared to the control group (NTG) and the hours spent with training seems to influence the best this variable (Nottin et al., 2004; Meyer et al., 2007), while the years spent with training doesn't seem to have a strong effect on resting heart rate.

6.1.3 Hypertrophy of the left ventricle

Cardiac enlargement in response to long term training was first described a century ago and was considered to be a purely physiological response. Much later, the theory was developed that left ventricular hypertrophy is a part of a continuum and that transition from the early (physiological) to late (pathological) forms can occur. Nowadays they suggest that the development of left ventricular hypertrophy is multifactorial, but most authors continue to believe that athletic left ventricular hypertrophy is a purely physiologic condition (Hildick-Smith et al., 2001). Although the effects of training on cardiovascular function are relatively well described in young subjects, little is known regarding the changes that occur with training in middle aged subjects, and it has only been proved not long time ago that even older subjects can adapt to exercise training. The elements that are describing the best the changes of the left ventricle are the IVST, the LVIDD and the PWT.

Moreover, the law of Laplace says that wall tension of a sphere is proportional to the radius of the sphere and the pressure within it. As for the athletic performance, two types of overload exist, one is called pressure overload that is more evident among strength trained athletes and manifest with the increase of septal and free wall thickness to normalize wall stress and volume overload that is more evident among endurance trained athletes and manifest with the increase of LVID with a proportional increase in septal and free wall thickness. The heart generally responds to most athletic disciplines in a manner similar to volume loading: increases cavity size, and wall thickness are appropriate compensatory mechanism (Child et al., 1984; Di Bello et al., 1993).

Among most of the athletes (MTG and LTG group) the IVSD is normal or a little bit higher than the normal values (less than 13 mm). Although, there is some variation in study data, the largest and most comprehensive survey of elite athletes showed that only 2% develop an interventricular septal thickness \geq 13mm (Hildick-Smith et al., 2001). Furthermore, interventricular septum thickness seems to have both age, training intensity effects (Fleg et al., 1986; Pavlik et al., 2001; Nikitin et al., 2006).

The augmentation of the LVIDD is quite frequent among the athletes, particularly among those who are practicing endurance activities (Jaubert-Poignant, 2006). One of the most important studies considering physiologic left ventricular cavity dilatation among athletes was carried out in Italy, where the researchers wanted to evaluate the morphologic characteristics and physiologic limits of left ventricular cavity enlargement associated with intensive, long-term athletic conditioning among 1309 elite Italian athletes, aged between 13 to 59 years. They found that left ventricular end-diastolic cavity dimensions varied widely among the two sexes (so did Sandstede et al., 2000 among men and women healthy volunteers) but was within generally accepted normal limits for most participants (\leq 54 mm) which are well in concordance with the two examined athletic groups in this study (Pellicia et al., 1999).

Most of the athletes has a left ventricular PWT normal or a little thicker (≤ 13 mm) which was highlighted in the study by Spirito et al., 1994 where they showed that among 947 athletes only 16 (so 1.7%) had higher LV wall thickness above normal limit.

The LVM, LVM/BSA showed higher values among the MTG compared to the LTG (Di Bello et al., 1993, Jungblut et al., 2000) which result was described by Giada et al., 1998 where they found that amateur cyclists (aged 50 to 65 years) examined at the end of the competitive season showed a greater value of their EDV and left ventricular mass was proportionally higher in the older than in the young cyclists when compared with their respective sedentary controls.

Even though the above mentioned results has to be interpreted with care because increased PWT was independently associated with increasing age even in this narrow age group, while increased LVIDD and LVIDS were independently associated with the duration of training in years (Gates et al., 2003).

6.1.4 Systolic function

No remarkable difference was observed as to ejection fraction that shows at least during rest, left ventricular systolic function of the examined aged groups is preserved and doesn't depend on training (Fleg, 1986; Giada et al., 1998, Nikitin et al., 2006). At rest end diastolic volume was increased even though it was not significant and stroke volume was non significantly greater by comparing the MTG with LTG and NTG which is similar to the result of the study of Ehsani et al., 1991.

6.2 Doppler measurements

With the advent of pulsed Doppler echocardiography, it is possible to examine more directly the pattern of left ventricular filling. Using this technique, the pattern of blood velocity across the mitral valve recorded in diastole is used to calculate the temporal course of ventricular filling. Several empiric indexes have been derived from the mitral inflow pattern and proposed as markers for ventricular diastolic function, including the peak and integrated velocities of early rapid filling, atrial contraction, and their ratios. The Doppler method has appeal because it provides a beat-by-beat assessment of ventricular filling without hemodynamic impact and is relatively simple to use (Thomas et al., 1991).

With increasing age, prolongation of isovolumic cardiac relaxation and loss of ventricular compliance combine to reduce the efficacy of early diastolic filling and increase the late diastolic filling, therefore there is decrease in the ratio of early to late flow (Spirito et al., 1988; Safar, 1990). Among athletic persons generally a normal or more performant diastolic function can be observed which happened in this study even though the differences were not significant but showed an elevated E peak and a decrease of A peak among the MTG, suggesting that in this age group endurance training doesn't really have an effect primarily on diastolic filling (Giada et al., 1998; Pluim et al., 1999; Galetta et al., 2004; Nottin et al., 2004). Furthermore, the traditionally measured E/A ratio showed no evidence to differ between the examined three groups despite the substantial increase in left ventricular mass of the MTG, even though this ratio was always higher in the trained groups compared to the sedentary group (Pavlik et al., 2001; Owen et al., 2003; Nottin et al., 2004) which was reached through a decrease of the A peak. In this study, a relatively narrow age group was measured (45-55 years) to try to limit the effects of physiologic changes during aging. It seems that training can not really improve the diastolic function even though the runners and cyclists were taken into this study (MTG) were exceptionally well trained with a median of 17 years of training. It must be mentioned that a characteristic feature of pathological LVH is an increase in collagen volume fraction. In physiological LVH no collagen increase occurs. In both forms of hypertrophy the myocytes are hypertrophied (Owen et al., 2003). Therefore it can be suggested that myocyte hypertrophy in itself does not improve or decrease diastolic function, rather the abnormal collagen matrix that can be found in pathological hypertrophy which can

impair the relaxation of the myocytes. Finally, it seems that endurance exercise training at any intensity does not appear to alter normative aging effects on left ventricular diastolic function in this age group (Gates et al., 2003). A normal IVRT were detected in each group, therefore it seems that regular training doesn't influence the age related decline in LV relaxation properties on this variable (Nottin et al., 2005).

6.3 Doppler Tissue Imaging

Doppler Tissue Imaging is a relatively new echocardiographic technique that uses Doppler principles to measure the velocity of myocardial motion. It relies on detection of the shift in frequency of ultrasound signals reflected from moving objects. With this principle, conventional Doppler techniques asses the velocity of blood flow by measuring high-frequency, low-amplitude signals from small, fast-moving blood cells. In DTI, the same Doppler principles are used to quantify the higher amplitude, lower-velocity signals of myocardial tissue motion. Pulsed-wave DTI is used to measure peak myocardial velocities and is particularly well suited to the measurement of long-axis ventricular motion because the longitudinally oriented endocardial fibers are most parallel to the ultrasound beam in the apical views. Because the apex remains relatively stationary throughout the cardiac cycle, mitral annular motion is a good surrogate measure of overall longitudinal left ventricular contraction and relaxation. Pulsed-wave DTI has high temporal resolution but does not permit simultaneous analysis of multiple myocardial segments (Ho et al., 2006).

Peak Ea lateral and septal, peak Aa lateral and septal velocities were measured and it seems because of intrinsic differences in myocardial fiber orientation, septal Ea and Aa velocities in all the three groups were less than on the lateral side (Galiuto et al., 1998; Ho et al., 2006), therefore these DTI diastolic velocities suggest a better relaxation activity in the longitudinal axis at the lateral side of the mitral annulus of the LV. On the contrary with other studies (Zoncu et al., 2002; Galetta et al., 2003; Galetta et al., 2004), the MTG did not show a significant increase on their Ea on both sides but there was a significant decrease compared to NTG considering their Aa on the lateral side (Galetta et al., 2004; Bilkoo et al., 2006) and had a non significantly greater Ea/Aa ratio on both sides compared to LTG and NTG (Galetta et al., 2003; Galetta et al., 2004; Bilkoo et al., 2006). Therefore it seems that training doesn't influence the Ea deterioration but counterbalances the Aa increases from middle age which is implying a compensatory augmentation of atrial function (Nikitin et al., 2003). Furthermore, Ea/Aa ratio is an expression of changes in left atrial to LV pressure gradient as well as of passive diastolic properties of LV walls, this increase can indicate a training-induced improvement in LV myocardial compliance in the MTG.

As for the E/Ea, all the three groups showed normal values (E/Ea<8) which correlates with a normal LV end-diastolic pressure.

6.4 Finite Element Analyzis

A simplified model of the left ventricle (isotrop, homogen; not taking into account the valves and left atrium) was used to show the differences of stress and strain among athletic (MTG) and non-athletic (NTG) people analyzed by Abaqus explicit.

Even with this simplified model, the following physical and physiological statement can be highlighted:

The law of Laplace states that the wall tension of a sphere is proportional to the radius of the sphere and the pressure within it. This law can be loosely extrapolated to the setting of left ventricular hypertrophy that is presented among the examined athletic group and showed a difference considering the measured data (Hildick-Smith et al., 2001).

Furthermore, it can be hypothesized that there is a sort of a transform of the strain from the apex toward the basal lateral side that can explain why the rapid filling is able to cause a large increase of the internal volumes of the left ventricle and might have an influence on the viscoelasticity that can be related to the hypertrophy of the myocardium. Bettendorf et al., 2006 wrote that the rapid filling phase can be seen as the period where the myocardium recoils from its end-systolic configuration. The deformation energy stored during systole becomes effective when the mitral and tricuspid valves open and serves to displace blood into the ventricles. Accordingly, at the beginning of diastole, the myocardium cannot be assumed to be free of substantial stresses and deformation. The analyzes carried out underlines this statement with the augmented strain at the level of the mitral valves on the lateral side of the left ventricle and can explain why there was no difference on the Ea peak considering the two

examined groups (and knowing the fact that the first phase of diastole is a rapid, but passive phase). No article states until now that this accumulation of strain can be beneficial on the second phase in diastole but knowing the echocardiographic findings among the MTG it can be hypothesized.

Knowing the fact, that the human heart is a very complex organ it is planned to have a future research on its global function while including a 3D shape model of the heart (taken from MRI) and fluid dynamics model of blood inside of the left ventricle.



Strain of the LV at t=0.12 msec in the NTG



Strain of the LV at t=0.24 msec in the NTG



Strain of the LV at t=0.12 msec in the MTG



Strain of the LV at t=0.24 msec in the MTG

Figure 38 Summary of strains at different time in the two examined groups

6.5 Study limitations

6.5.1 Ratio of men-women in the non trained group (NTG)

The first limitation concerns the distribution of men-women in the non trained group (7 men, 8 women) and can have influence on the comparison with the T-test for independent samples between the three examined groups. Since women generally have smaller body size compared to men, therefore smaller hearts and smaller left ventricles which is related to their smaller blood volume (Sandstede et al., 2000; Salton et al., 2002; Nikitin et al., 2006) and seems to correspond with this study also.

6.5.2 Limitations to the term 'intensity of training'

In this study, the creation of the two athletic groups depended on the number of hours spent by week. Unfortunately, there was no possibility to carry out vita maxima exercises to measure the intensity of training through VO2max, maximum heart rate (HRmax) and lactate threshold (LT) that would allow following the classification of physical activity intensity, based on physical activity lasting up to 60 minutes written by the American College of Sport Medicine (ACSM) (Pollock et al., 1998), even though it seems that it has to be updated when classifying high level athletes (Lounana et al., 2007).

6.5.3 Limitations to echocardiographic exams

The second limitation concerns diagnostic errors that can be related to the overestimation of wall thickness (failure to recognize right ventricular bands or false tendons). Furthermore, intrinsic to Doppler technic, there is angle dependence and the possible presence of artefacts. However, it seems that the same angle incidence of transmitral Doppler and Doppler Tissue Imaging is good. It is more and more a trend to check the interobserver variabilities, that would have been welcomed in this study but was not carried out because of lack of time (D'Andrea et al., 2006).

6.5.4 Limitations to FE analyzis

It is not clear whether the LV wall is free of substantial stresses and deformation at end-diastole. In this study, a simplified FE model (isotrop, homogen,

and did not include the valves and the left atrium) was used to show differences between the MTG and NTG without taking into account the possible influence of local and individual inhomogenities throughout the LV wall (Bettendorf-Bakman et al., 2006).

6.5.5 Limitations to nutrition

Eating behavior was not studied at all because it was not the principal goal of this study, though lately several studies confirmed the positive effects of caloric restriction. Meyer et al., 2006 even showed in their study that caloric restriction (CR) has cardiac-specific effects that ameliorate aging-associated changes in diastolic function and these beneficial effects on cardiac function might be mediated by the effect of CR on blood pressure, systemic inflammation and myocardial fibrosis.

6.5.6 Limitations to the number of participants

Last, but not least, the number of participants could have been higher to be able to caracterise the generalities on the cardiac variables of the chosen groups.
6.6 Suggestions

Since LA volume appears to be a better indicator of true LA size than M-mode LA dimension, it would be advised to perform these measurements (such as LA passive emptying volume, conduit volume, LA passive emptying fraction, LA active emptying, LA active emptying fraction, LA total emptying and the contribution of passive emptying volume, of conduit volume, and of active emptying volume to LV stroke volume) to have additional information on LA volume changes related to exercise.

Strain and strain rate echocardiography are emerging real time ultrasound techniques that provide a measure of wall motion. They offer an analysis of wall deformation using the rate of deformation of a myocardial segment (strain rate) and its deformation over time (strain). Strain rate and strain are less affected by passive myocardial motion and tend to be uniform throughout the left ventricle in normal subjects. Maybe with the use of this technique the differences showed considering the DTI velocities on the lateral and septal sides can be better understood.

Nevertheless, the previously mentioned study limitations would be favourable to taken into account in the planned future studies.

7. Conclusion – Conclusion

Aging causes many changes in the body. With physiological (healthy) aging, the left ventricle undergoes tonic structural and functional changes that include an increase in wall thickness and chamber diameter, increased mass and reduced diastolic function.

Exercise seems to slow down the aging process.

The present study was designed to characterize the nature of cardiovascular adaptations to exercise spent more or less 5 hours per week among 45-55 years old athletic and non-athletic subjects.

Middle aged men with intensive training shows the typical adaptation to training, such as lower heart rate, larger left atrium, thicker interventricular septum and posterior wall thickness, larger end-diastolic diameter and higher LVM. The only difference found between the sedentary group and the recreationally active group was a decrease in the resting heart rate, as for the other morphologic variables, there were no significant difference between these two groups.

Systolic function seems to be preserved.

Thanks to pulsed Doppler tissue echocardiography, the diastolic function can be measured non-invasively. It seems that regular endurance exercise spent more or less 5 hours/week does not improve diastolic function, even though the MTG showed a slight increase, while the LTG remained the same considering the E-wave, and there was a decrease in the A-wave compared to the sedentary group.

Pulsed-wave DTI was used to assess peak myocardial velocities at septal and lateral mitral annulus. Septal Ea and Aa velocities were less in all the groups compared to the lateral side. There was a decrease in the lateral Aa in the MTG, that can be related to a compensatory augmentation of atrial function. It can be suggested that pulsed DTI is more sensitive to detect small improvements in LV diastolic function, unlike standard echocardiographic techniques in this age group. Moreover, it seems that endurance training can only partially minimize the age-associated changes of diastolic function and tissue Doppler measures.

As for the differentiation of physiologic and pathologic hypertrophy, pulsed Doppler imaging and pulsed Doppler Tissue imaging can be useful methods, since physiologic hypertrophy, that can be related to healthy aging and exercise, was not associated with altered relaxation patterns in this age group.

It can be concluded that under normal conditions the influence of stress on the tissue of the heart should not be disregarded in ventricular mechanics and the finite element analysis can be a useful method for a better understanding of heart mechanics.

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Annexes

Annexe I:

Sahn, D.J., De Maria, A., Kisslo J., & Weyman, A. (1978). For the Committee on Mmode Standardization of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation*, **58**, 1072-1083.

Annexe II:

Schiller, N.B., Shah, P.M. & al. (1989). Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr*, **2**, 358-367.

Annexe III:

Questionnaire used to obtain personal and echocardiographic data
Nom:
Date de naissance:
Height/Taille:
Weight/Poids:
BSA:
Sport:
Depuis quand?
Frequency:
Maladies:
HR/FC:
BP/'PA:
IVSd:
LVIDd:
PWTd:
IVSs:
LVIDs:
PWTs:
Ε
Α
E/A
AOV:
IVRT:
AOD:
LADS:
lateral Ea
lateral Aa
lateral Ea/Aa
septal Aa
septal Ea
septal Ea/Aa
E/Ea

Left ventricular morphologic parameters, diastolic filling, pulsed Doppler Tissue Imaging and stress analyzes among 45-55 years old athletes and highly trained athletes.

Paramètres morphologiques, fonction, Doppler Tissulaire et analyse des contraintes du ventricule gauche chez les sportifs âgés de 45 à 55 ans

KISPETER Zs.

Abstract – Normal aging is associated with the impairment in left ventricular diastolic filling. To test the hypothesis, that endurance training at a recreational level (less than 5 hrs/week) and at a high level (more than 5 hrs/week) among 45-55 years old men, is associated with enhanced ventricular diastolic filling indices, pulsed Doppler, pulsed Doppler Tissue imaging, and FE analyzis were carried out. The physiologic increase of LV which is manifesting in the thickening of IVST, dilatation of left ventricular internal diameter (LVID) and the thickening of posterior wall thickness (PWT), in response to exercise spent more than 5 hours/week among the MTG occurs in parallel with an augmentation of the diameter of the left atrium (LA) and with the decrease in late wave velocity (Aa) on the lateral side of the heart despite of the missing significative differences between standard echocardiographic indexes. Systolic function seems to be preserved among the three groups. Additionally, it seems that that under normal conditions the influence of stress on the tissue of the heart should not be disregarded in ventricular mechanics and the finite element analysis can be a useful method for a better understanding of heart mechanics. This finding underlines the hypothesis that the decline of the LV diastolic function related to aging is due in part of lifestyle, and not only to aging itself and the worsening of the diastolic indexes can be prevented by a well loaded training. Furthermore, DTI may be useful for the screening of middle aged athletes and to distinguish pathological form of hypertrophy from physiologic hypertrophy.

Keywords: LV diastolic filling \cdot aging \cdot Doppler Tissue Imaging \cdot echocardiography \cdot athlete's heart

ANNEXES