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FACULDADE DE DESPORTO
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Functional fitness, cardiovascular risk factors, and health-related quality of life in older adults: interrelations and effects of different exercise types

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Dissertação apresentada às provas para obtenção do grau de Doutor em Actividade Física e Saúde, nos termos do Decreto - Lei nº 216/92 de 13 de Outubro, orientada pela Professora Doutora Maria Joana Mesquita Cruz Barbosa de Carvalho e co-orientada pelo Professor Doutor José Manuel Fernandes de Oliveira.

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thesis and aims to explain the interactions between CVD risk factors, an inactive lifestyle, functional fitness, impairment-disability evolution, and HRQoL in physically independent, community-dwelling older adults with no serious medical conditions.

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$BMI = Weight (kg)/ (height [m])^2$

$HR_{max}= 208 \times 0.7 (age)$

$HR_{Reserve} = HR_{max} – HR$ at rest

Resumo

Objectivo. Esta tese teve como principais objectivos: (i) investigar as possíveis relações entre a performance avaliada mediante testes simples de terreno para avaliação da aptidão física e funcional, factores de risco para doenças cardiovasculares (DCV) e a qualidade de vida relacionada a saúde (QVRS), (ii) determinar e comparar a magnitude dos efeitos de dois tipos de exercício físico sobre os factores de risco cardiovasculares modificáveis, função cardíaca, aptidão funcional e QVRS, em idosos fisicamente independentes e sem condições clínicas severas. **Método.** Para atingir estes objectivos, esta tese foi dividida em cinco estudos. O Estudo I foi o estudo piloto, os Estudos II e III foram estudos descritivos nos quais as relações entre factores de risco cardiovascular (pressão arterial, composição corporal, função autonómica, marcadores bioquímicos e inflamatórios), aptidão física e QVRS foram determinadas. Os Estudos IV e V foram estudos experimentais delineados para verificar os efeitos de oito meses de treino (aeróbio *vs*. resistido), com frequência semanal de três dias sobre as variáveis do estudo. **Resultados.** No *baseline*, 105 indivíduos (68.9±5.4 anos) foram avaliados. No Estudo II, os modelos de regressão linear demonstraram que o teste de seis minutos de caminhada (6MWT) está associado à percentagem de gordura corporal (%BF; p<0.01), pressão arterial sistólica (SBP; p<0.01) e duplo-produto em repouso (RPP_{rest}; p<0.01). No Estudo III, os modelos de regressão logística demonstraram que os indivíduos com melhor performance no 6MWT têm maiores *odds ratio* (OR) de auto-reportarem maiores valores nos domínios de QVRS, função física (PF; OR = 1.87), limitação devido a problemas físicos (RP; OR = 1.95) e vitalidade (VT; OR = 1.79). Os indivíduos com maior força de preensão manual também tiveram maiores *odds ratio* de auto-reportarem menos limitações devido a problemas físicos (OR = 2.37) e maior VT (OR = 1.83). Nos estudos experimentais, 85 indivíduos foram aleatoriamente sorteados para integrarem os grupos de treino aeróbio (AT), treino resistido (RT) ou lista de espera. Após oito meses de treino, foram observadas mudanças significativas (Δ%) na %BF (-5.4±6.3% e -3.3±2.9%), gordura de tronco (8.9±11.3% e -4.8±4.5%), performance nos testes de sentar e levantar cinco vezes (-18.2±10.8% e -21.5±13.9%), subir degraus (-12.8±9.9% e -20.1±11.4%), *8-foot up-and-go* (-8.8±9.7% e -13.3±9.6%) e, domínio saúde geral (16.8±17.0% e 14.4±19.7%) no RT e AT, respectivamente. A força de preensão manual (9.0±8.4%) e a variabilidade da frequência cardíaca total (29.7±40.0%) mudaram significativamente em resposta ao RT; A performance no 6MWT (9.5±6.9%), a pressão arterial sistólica e diastólica em repouso (-9.2±9.8% e -8.5±9.6%), a frequência cardíaca (-4.6±6.5%), a actividade parassimpática (364.0±739.0%), a hs-CRP (-18.6±60.6%), os domínios PF, (4.4±8.1%) e saúde mental (21.9±37.3%) mudaram em resposta ao AT**. Conclusão.** Os resultados sugerem que, em indivíduos idosos, fisicamente independentes, vivendo na comunidade e sem condições clínicas severas: (i) uma baixa aptidão aeróbia está relacionada a um risco cardiovascular acrescido, (ii) uma maior aptidão aeróbia está associada a uma melhor função cardiovascular em repouso, (iii) um maior nível de aptidão física, avaliada pelo 6MWT e pela força de preensão manual, está associada a uma melhor percepção em vários domínios da QVRS, (iv) oito meses de treino, independentemente do tipo de exercício (aeróbio *vs*. resistido), com intensidade de moderada a vigorosa são capazes de melhorar a aptidão física e funcional, reduzir o risco cardiovascular, aumentar a função cardiovascular e, melhorar a QVRS auto-reportada, não havendo diferenças estatisticamente significativas nas mudanças observadas entre os dois tipos de treino.

Palavras-chave: Treino; Qualidade de Vida; Envelhecimento; Aptidão Física; Função Cardiovascular.

Abstract

Purpose. This thesis aimed (i) to investigate the possible relationships between performance on simple functional fitness field tests, cardiovascular disease (CVD) risk factors, and health-related quality of life (HRQoL), (ii) to determine and to compare the magnitude of the effects of two different types of exercise training on modifiable CVD risk factors, cardiovascular function, functional fitness, and HRQoL. **Methods.** This thesis encompassed five studies, Study I, a pilot study; Studies II and III, descriptive, correlational studies in which relationships between subjects' CVD risk profile (blood pressure, body composition, autonomic function, inflammatory and biochemical markers), functional fitness, and HRQoL were explored; and Studies IV and V (randomized controlled trials studies, RCT) which were designed to test the effects of two types of exercise training (resistance *vs.* aerobic) performed during eight months, three days per week, on outcomes. **Results.** A total of 105 subjects (68.9±5.4 years) had outcomes evaluated at baseline. In Study II, the multiple linear regression models demonstrated that 6MWT was associated with percentage of body fat (%BF; $p < 0.01$), systolic blood pressure (SBP; $p<0.01$) and rate-pressure product at rest (RPP_{rest}; $p<0.01$). In Study III, the logistic regression models demonstrated that individuals with superior 6MWT were more likely to score higher on HRQoL, namely on physical function (PF; OR = 1.87), role limitations due to physical problems (RP; OR = 1.95) and vitality (VT; OR = 1.79). Additionally, individuals with superior hand-grip strength were more likely to score higher on RP (OR = 2.37) and VT (OR = 1.83). In the RCT studies, 85 subjects were randomized into, aerobic training (AT), resistance training (RT) or waiting list groups. After eight months of training, it was observed a significant change (Δ%) in %BF (-5.4±6.3% and -3.3±2.9%), central body fat (8.9±11.3% and -4.8±4.5%), performance on the sit-to-stand five times (-18.2±10.8% and -21.5±13.9%), stair ascent (-12.8±9.9% and -20.1±11.4%), 8-foot up-and-go (-8.8±9.7% and -13.3±9.6%) tests, and general health (16.8±17.0% and 14.4±19.7%) in RT and AT groups, respectively; hand-grip strength (9.0±8.4%) and overall heart rate variability (29.7±40.0%), changed significantly in response to RT; 6MWT (9.5±6.9%), resting systolic and diastolic blood pressure (-9.2±9.8% and -8.5±9.6%), heart rate (-4.6±6.5%), vagal activity (364.0±739.0%), hs-CRP (-18.6±60.6%), PF, (4.4±8.1%), and mental health (21.9±37.3%) changed in response to AT**. Conclusion.** Results suggest that, in physically independent, community-dwelling, older adults with no serious clinical condition: (i) a worse cardiovascular profile is related with lower aerobic fitness; (ii) an elevated aerobic fitness level is correlated with a favorable cardiovascular function at rest; (iii) higher levels of physical fitness, as assessed by hand-grip strength and 6MWT, are associated with higher self-reports in several domains of HRQoL; (iv) eight months of moderate to vigorous exercise training is capable to improve physical and functional fitness, decrease CVD risk profile, increase cardiovascular function, and improve subjective HRQoL, and finally, (v) it seems that AT and RT induce changes of similar magnitude on physical and functional fitness, CVD risk profile, and subjective HRQoL.

Key-words: Training; Quality of Life; Aging; Physical Fitness; Cardiovascular Function.

List of Abbreviations

Abs – Antibodies

ACh – Acetylcholine

ACSM – American College of Sports Medicine

AHA – American Heart Association

ANOVA – Analysis of variance

ApoA – Apoliprotein A

ApoB – Apoliprotein B

AT – Aerobic training

BMI – Body mass index

BP – Blood pressure

BP – Bodily pain

CHD – Coronary heart disease

CI – Confidence intervals

CRP – C-reactive protein

CS – Cigarette smoking

CVD – Cardiovascular disease

CRF – Cardiovascular risk factors

CVDRF – Cardiovascular risk factors

DBP – Diastolic blood pressure

DXA – Dual-energy X-ray absorptiometry

eNOS – endothelial nitric oxide synthase

FD – Frequency domain

FRS – Framingham Risk Score

GH – General health

HDL – High density lipoprotein

HDL-C – High density lipoprotein cholesterol

HF – High frequency

HR – Heart rate

$HR_{reserve}$ – Heart rate reserve

HR_{rest} – Heart rate at rest

HRQoL – Health-related quality of life

HRT – Hormone replacement therapy

HRV – Heart rate variability

ICAM-1 – Inter-cellular adhesion molecule-1

ICC – Intra-class correlation

IDL – Intermediate density lipoprotein

IFN-ɣ – Interferon-gamma

IL-1 – Interleukin-1

IL-6 – Interleukin-6

INE – Instituto Nacional de Estatística

LDL – Low density lipoprotein

LDL-C – Low density lipoprotein cholesterol

LF – Low frequency

LM – Lean mass

M – Mean

MCP-1 – Monocyte chemo-attractant protein-1

MCS – Mental component summary

Md – Median

MH – Mental health

NCEP – National Cholesterol Education Program

OR – Odds ratio

PA – Physical activity

PCS – Physical component summary

PF – Physical functioning

PI – Physical inactivity

PP – Pulse pressure

QoL – Quality of life

RCT – Randomized controlled trial

RE – Role limitations due to emotional problems

Reps. – repetitions

ROS – Reactive oxygen species

RP – Role limitations due to physical problems

RPE – Rating of perceived effort

RPP_{rest} – Rate-pressure product at rest

RT – Resistance training

SBP – Systolic blood pressure

SCORE – Systematic Coronary Risk Evaluation

SD – Standard deviation

SDRR – Standard deviation of normal RR intervals

SES – Socioeconomic status

SF – Social functioning

SF-36 – Medical Outcomes Study 36-item Short-Form Health Study Questionnaire

SPSS – Statistical Package for the Social Sciences

SFT – Senior fitness test

TD – Time domain

TG – Triglycerides

TNF-α – Tumor necrosis factor-alpha

USDA – United States Department of Agriculture

VCAM-1 – Vascular cell adhesion molecule-1

VLDL – Very low density lipoprotein

VLF – Very low frequency

VO_{2max} – Maximal oxygen consumption

VT – Vitality

WHO – World Health Organization

WL – Waiting list

%BF – percent of total body fat

R_a% – Adjusted partial Eta squared

$^{\cdot}NO$ – Nitric oxide

1RM – one repetition maximum

6MWD – 6-minute walk distance

6MWT – 6-minute walk test

8FUG – 8-foot up-and-go

List of Publications

Peer-reviewed Scientific Journal Published Articles

Wanderley F A C, Silva G, Marques E, Oliveira J, Mota J, Carvalho J. (2011). Associations between objectively assessed physical activity levels and fitness and self-reported quality of life in community-dwelling older adults. *Quality of Life Research.* 2011. DOI: 10.1007/s11136-011-9875-x.

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Wanderley F A C, Oliveira N L, Marques E, Moreira P, Oliveira J, Carvalho J. Health-related Quality of Life (HRQoL), Body composition and functional fitness of older adults: results from aerobic *vs.* resistance training. Submitted to the Journal of Aging and Physical Activity on the 04th of January, 2011. Current Status: Under review.

Wanderley F, Moreira A, Sokhatska O, Palmares C, Carvalho J. Cardiovascular Function, Body Composition, hs-CRP, and Physical Fitness in Older Adults: Effects of two training regimens. Submitted to the Journal of Aging Research on the 31st of August, 2010.

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Wanderley F, Oliveira J, Marques E, Carvalho J. Time-course of Changes in Body Fat, Blood Pressure, C-reactive Protein, and Physical Function, During 8-month Exercise Training in Older Adults. Chapter contribution to the edited textbook entitled 'Body Fat: Composition Measurements and Reduction Procedures' to be published by NOVA Medical Publishers. Current Status: Page Proofs.

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CHAPTER I

INTRODUCTION AND BACKGROUND

1. INTRODUCTION AND BACKGROUND

1.1. Statistics on Cardiovascular Diseases and Aging

Although cardiovascular-related mortality has been decreasing in Western countries, cardiovascular diseases (CVDs) continue to be the leading cause of death and are an important source of disability in most European populations. The fact that cardiovascular morbidity and mortality increases steeply with advancing age (Versari, Daghini, Virdis, Ghiadoni, & Taddei, 2009), in addition to the rapid increase in older adults worldwide, seems to be contributing in a large part to the maintenance of high levels of CVD incidence and prevalence as well as to the increased healthcare expenses derived from these medical conditions.

In these regards, Portugal is no exception. CVDs accounted for 32.3% of total deaths in 2008 (Instituto Nacional de Estatística [INE], 2008a). The older population is growing both in the number of older people and as a proportion of the total population due to a declining birth rate and increasing longevity. While at the beginning of the 20th century, the proportion of the population over 65 years of age did not exceed 5.0%; currently this segment represents 11.0% of the global population, as estimated by the World Health Organization (WHO, 2010). In Portugal, the group of older adults that in 1960 represented 8.0% of the population had increased to 11.4% by 1981 and to 14.0% by 1991. In 2007, the group 65 and over reached 17.4% (59.4% of them women) in this country (INE, 2008b). This proportion is projected to continue to rise in the 21st century.

The ensuing demographic change will have obvious impacts on society and healthcare systems. Unfortunately, the increased longevity generally represents a longer period of time that older people will suffer from decreased levels of functioning and independence because of chronic diseases such as CVDs. The elevated cost of CVD treatment has increased interest in developing new tests and therapies that would improve screening, prognosis and prevention.

Consequently, a number of risk factors[1] have been identified and other potential factors have been investigated.

1.2. Cardiovascular Diseases Risk Factors

Because CVD etiology is related to multiple risk factors, generally, global risk assessment seems to be more accurate than the investigation of a single risk factor (Greenland, Smith, & Grundy, 2001). Global risk scores, such as the Framingham Risk Score (FRS) or the Systematic Coronary Risk Evaluation (SCORE), incorporate the major traditional CVD risk factors, i.e., age; sex; cigarette smoking; levels of total, high (HDL) and low density lipoproteins (LDL); cholesterol (HDL-C and LDL-C, respectively); diabetes or fasting glycemia; and levels of blood pressure (BP). These factors are combined in predictive models to estimate the risk of fatal and non-fatal cardiovascular events (Greenland, et al., 2010). Though obesity and physical inactivity are not included in these predictive models, they are considered major risk factors by the American Heart Association (AHA) (Grundy, Pasternak, Greenland, Smith, & Fuster, 1999). Other factors associated with increased risk for coronary heart disease (CHD) are classified as: 1) conditional risk factors – those associated with CHD although their causative independent contribution to CHD has been not yet well documented; and 2) predisposing risk factors – those that exacerbate the independent risk factors. Generally, the first category includes a family history of premature CHD, ethnic characteristics, and psychosocial factors. The latter category includes elevated serum triglycerides, small LDL particles, elevated serum homocystein, and elevated serum lipoprotein(a) (Grundy, et al., 1999). In addition to these traditional risk factors, inflammatory (e.g., C-reactive Protein [CRP]), infectious and thrombotic (e.g., fibrinogen) markers have been emerging as CHD risk factors due to their ability to improve risk assessment (Greenland, et al., 2001). The influence and impact of each of the above-mentioned CVD risk factors on health will be briefly discussed in the following paragraphs.

[1] Social, economic or biological status, behaviors or environments which are associated with or cause increased susceptibility to a specific disease, ill health, or injury (WHO, 1998).

1.2.1. Age

The absolute risk for CVD increases with advancing age and reflects, mainly, the cumulative nature of arteriogenesis (Greenland, et al., 2001) and the increased time of exposure to other cardiovascular risk factors (Versari, et al., 2009), which lead to a more advanced stage of atherosclerosis. Older adults generally present higher BP levels (Blacher & Safar, 2002), increased abdominal fat content (Guo, Zeller, Chumlea, & Siervogel, 1999), dyslipidemia[2] (Windler, et al., 2007), low-grade chronic inflammation (Sajadieh, et al., 2004), increased heart rate (Sajadieh, et al., 2004), and reduced heart rate variability (Sajadieh, et al., 2004).

Despite researchers' increased efforts, the role of specific age-associated changes in cardiovascular structure and function in concerning age-CVD interaction continue to be mainly recognized (Lakatta & Levy, 2003).

1.2.2. Sex

Compared to men of a similar age and postmenopausal women, the incidence of CVD is significantly lower in premenopausal women (Roeters van Lennep, Westerveld, Erkelens, & van der Wall, 2002). It was also demonstrated that the overall median age of people experiencing their first acute myocardial infarction is about nine years lower in men than in women in all regions of the world (Yusuf, et al., 2004). To date, the hypothesis that endogenous estrogen is cardioprotective in women is the most widespread, but not exclusively accepted explanation for the gender-related differences in CVD risk (Rossouw, 2002).

Indeed, higher estrogen levels attenuate the development and progression of the atherosclerotic process through a variety of mechanisms such as the lowering of total cholesterol, LDL-C, lipoprotein(a), and homocystein, as well as increasing HDL-C and post-prandial lipid metabolism. Moreover, estrogens

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[2] Dyslipidemia, the imbalance between atherogenic and atheroprotective lipoproteins is one of the most powerful and potentially modifiable risk factors for CVD (Windler, Schöffauer, & Zyriax, 2007), is characterized by low concentrations of HDL-C, elevated triglycerides and a preponderance of small, dense LDL particles that confer increased atherogenicity (Windler, et al., 2007).

have an acute vasodilatory effect and inhibit smooth-muscle cell proliferation, as reported by Roeters van Lennep, et al. (2002) and Vaccarino (2011). Additionally, women tend to have higher parasympathetic activity, and therefore a more favorable autonomic function, whereas men tend to have a higher sympathetic cardiac activity. It is possible that such differences in the autonomic control of heart are modulated by other factors like obesity, hormone levels or inflammation (Vaccarino, et al., 2011).

Despite the lower incidence of CVD in premenopausal women, which has long been attributed to ovarian hormones, there is no evidence of an increase in the year-on-year rate of increase of CHD around the age of menopause. Moreover, there is a constant proportional increase in CHD incidence with age, with no inflection upward at the average age of menopause. This is greater evidence for an age effect than for a gender effect (Rossouw, 2002), even though the specific mechanisms underlying the CVD protection in females until menopause have not been completely elucidated.

1.2.3. Family History of Premature Coronary Heart Disease

A family history of premature CHD, defined most often as occurring in a first-degree male relative <55 years of age or in a first-degree female relative <65 years of age, has long been considered a risk factor for CHD in offspring (Greenland, et al., 2010). More recently, it was suggested that a maternal history of CHD may be more strongly associated with the risk of CHD than a paternal history (Sesso, et al., 2001). Higher CHD risk for maternal versus paternal histories of CHD may reflect mothers' influence on their children's dietary and behavioral patterns retained later in life (Sesso, et al., 2001).

Although family history of CHD is an independent risk factor for CVDs, it was suggested that a large part of the effect of family history might be mediated through known risk factors like hypertension, dyslipidemia, diabetes or obesity, which could be affected by both shared lifestyles and genetic factors, rather than through independent pathways (Greenland, et al., 2010; Yusuf, et al., 2004). Moreover, family history seems to be more important in the young than in older individuals (Sesso, et al., 2001; Yusuf, et al., 2004).

1.2.4. Ethnic Characteristics

Black men and women seem to be more prone to CVD morbidity compared with their caucasian counterparts (Carnethon, et al., 2006). Mensah, Mokdad, Ford, Greenlund, & Croft (2005) reported that the age-adjusted death rates for heart diseases in United States were 30% higher among Black individuals than among Caucasians of both sexes. In the same vein, Thomas et al. (2005) observed that more than four times as many Black men as Caucasian men had elevated risk factor levels. However, the adjustment for age, income, and major risk factor differences explained 35% of the excess mortality among Black men in this study, suggesting that higher overall mortality among Black men can be largely explained by differences in socioeconomic status.

Another study also observed that most traditional risk factors (smoking status, diabetes, body mass index [BMI], age, education, high cholesterol level and hypertension) had similar associations with mortality in Black and Caucasian adults of the same sex (Carnethon, et al., 2006).

It is difficult to prove the independent risk of ethnicity in CVD because evidence demonstrates that a great proportion of ethnic minorities live in unfavorable socioeconomic levels that can mask the real contribution of ethnicity in CVD risk (Thomas, et al., 2005). In addition, a great proportion of studies come from countries with Caucasian majorities and only compare Blacks versus Caucasians and do not include other ethnic groups.

The only well-established difference between Blacks and Caucasians concerning CVD is that the former group has the highest prevalence rates of hypertension (Carnethon, et al., 2006; Mensah, et al., 2005).

1.2.5. Blood Pressure

Beyond a high prevalent CVD, hypertension is also considered a major risk factor for other CVDs like stroke (Wolf-Maier, et al., 2003) or heart failure (Levy, Larson, Vasan, Kannel, & Ho, 1996). The relative importance of the various components of blood pressure (BP) in predicting CVD risk seems to change with increasing age. Initially, diastolic BP (DBP) was thought to be the best measure of risk, but today it is known that in patients <50 years of age DBP is the strongest predictor, between 50 and 59 years of age there is a transition period when DBP, systolic BP (SBP) and pulse-pressure (PP) are comparable predictors, and from 60 years of age on, DBP is negatively associated with CVD, and PP and SBP become superior predictors of risk (Franklin, Larson, et al., 2001).

The prevalence of hypertension increases with age and generally over-reaches the rate of 40% in European older populations (Wolf-Maier, et al., 2003). In Portugal, for example, the 2005/2006 National Health Report reported that 55.9 and 57.2% of men and women between 65 and 74 years older, respectively, had used prescribed medications to low BP (Instituto Nacional de Estatística & Instituto Nacional de Saúde Doutor Ricardo Jorge, 2009). The most prevalent type of hypertension in older adults is isolated systolic hypertension (Franklin, Jacobs, Wong, L'Italien, & Lapuerta, 2001), which is characterized by SBP ≥ 140 mmHg with a DBP < 90 mmHg. This is favored by the average DBP decreases concomitantly with SBP increases that are also observed with advancing age (Shephard, 1994).

Hypertension, as other CVDs, has multiple origins. It is not the aim of this study to discuss all of them in depth, however, considering the great impact that high levels of BP have on older adults' health, it seems important to briefly point out the main aspects involved in creating hypertension in older adults, namely, the increase in PP due to an increase in SBP and a decrease of DBP, the disappearance of PP amplification, early wave reflections, and the increased arterial stiffness, which is generally observed in the central arteries (Blacher & Safar, 2002). Taken together, these changes have deleterious consequences on left ventricular structure and function. The increased SBP induces myocardial hypertrophy, impairs diastolic myocardial function and reduces the left ventricular ejection fraction. In addition, increased SBP and PP accelerate arterial damage, increasing the fatigue of biomaterials, causing degenerative changes and further arterial stiffening (Blacher & Safar, 2002). In summary, vascular and cardiac changes induced by age and prolonged exposure to CVD risk factors make older individuals more prone to ischemia-reperfusion injuries and heart failure.

1.2.6. Obesity

It has been well documented that obesity is associated with increased risk for many chronic conditions including CHD (Tanne, Medalie, & Goldbourt, 2005), stroke (Winter, et al., 2008) and diabetes mellitus (Narayan, Boyle, Thompson, Gregg, & Williamson, 2007), as well as disease risk factors such as hypertension (Sardinha, Teixeira, Guedes, Going, & Lohman, 2000; Williams, Hunter, Kekes-Szabo, Snyder, & Treuth, 1997) and dyslipidemia (Williams, et al., 1997). Indeed, the evidence suggests that a central distribution of body fat (subcutaneous or visceral) is much more closely related with an atherogenic metabolic profile than total body fat (Sardinha, et al., 2000).

Although the etiology of obesity is multifactorial, the root cause is an energy imbalance, i.e., more calories consumed than expended. This energy imbalance leads to the storage of excess energy in adipocytes, which exhibits both hypertrophy and hyperplasia. The increase in the number of increased adipocytes is associated with intracellular abnormalities of adipocyte function, particularly endoplasmatic reticulum and mitocondrial stress (de Ferranti & Mozaffarian, 2008). The resultant intracellular and systemic consequences include adipocyte insulin resistance, cytokine[3] production, free-fat acids, inflammatory mediators, and the promotion of systemic dysfunction (de Ferranti & Mozaffarian, 2008).

In fact, obesity is now increasingly recognized as an inflammatory disorder (Brooks, Blaha, & Blumenthal, 2010). The adipose tissue, particularly the highly metabolically active visceral tissue, is now regarded as a complex organ that

[3] Cytokines are low-molecular-weight proteins that, after binding to specific receptors, affect immune cell differentiation, proliferation and activity (Johnston & Webster, 2009).

not only contributes to the management of energy flux, but also interactes with the inflammatory system and vascular wall (Mathieu, Poirier, Pibarot, Lemieux, & Despres, 2009). At the adipose tissue level, an abundance of triacylglycerol creates large adipocytes that initiate cellular stress responses, leading to the activation of inflammatory pathways. The release of cytokines promotes the recruitment of monocytes, which are then shunted down the inflammatory pathway and become macrophages. When activated, these macrophages will locally produce tumor necrosis factor-alpha (TNF-α) and induce the expression of interleukin-6 (IL-6). The increased levels of circulating cytokines will further induce the hepatic synthesis of acute-phase proteins including fibrinogen, C-reactive protein (CRP) and serum amyloid A (Brooks, et al., 2010; Ribeiro, Alves, Duarte, & Oliveira, 2010). Furthermore, there is evidence that these cytokines play a role in regulating the size of the adipose tissue stores (Mohamed-Ali, et al., 1997). Therefore, an increase in inflammation might lead to an increase in adiposity, initiating a cycle of dysfunction.

Recent evidence (Christou, Parker Jones, Pimentel, & Seals, 2004; Gonzalez-Clemente, et al., 2007; Heffernan, et al., 2009; Jamerson, Julius, Gudbrandsson, Andersson, & Brant, 1993; Shibao, et al., 2007) suggests that there is intricate interplay among adipocytes, inflammation, the sympathetic nervous system, and the rennin-angiotensin system, which can partially explain the close relationship between obesity, hypertension and insulin resistance.

Given that the major cause of obesity in most individuals is an energy imbalance, the optimal approach to restore caloric balance is lifestyle modification. Relatively modest changes in lifestyle seem to powerfully affect multiple pathways related to obesity (de Ferranti & Mozaffarian, 2008).

1.2.7. Total and Low Density Lipoprotein Cholesterol

Cholesterol is a fat-like substance (lipid) that is present in cell membranes and is a precursor of bile acids and steroid hormones. Cholesterol travels in the blood in distinct particles containing both lipids and proteins (lipoproteins). Three major classes of lipoproteins are found in the serum of a fasting individual: LDL, HDL, and very low density lipoproteins (VLDL). Another lipoprotein class, intermediate density lipoprotein (IDL), resides between LDL and VLDL, but in clinical practice, IDL is included in the measurement of LDL (National Cholesterol Education Program [NCEP], 2002).

Many earlier studies measured only total serum cholesterol, although most of the total cholesterol is contained in LDLs. Thus, the robust relationship between total cholesterol and CHD observed in epidemiological studies indicates that an elevated LDL level is a powerful CVD risk factor (NCEP, 2002). For years LDL-C, a measure of the amount of cholesterol present in LDL particles (Kastelein, et al., 2008), has been recognized under treatment guidelines as the primary target of lipid therapy (this is supported by an extensive evidence base) (Windler, et al., 2007).

The link between LDLs and CVD is based on the central role of LDL particles in atherogenesis. Atherosclerotic plaque results from the progressive accumulation of cholesterol and diverse lipids in native and oxidized forms, extracellular matrix material, and inflammatory cells (Kontush & Chapman, 2006). LDL particles, in particular, move into the arterial intima through a gradient-driven process, and the rate of passive diffusion increases when the concentration of circulating LDL particles increases. Once inside the intima, the LDL particles bind to proteoglycans and initiate a process whereby the LDL particles become oxidized or otherwise modified and are taken up by monocytes or macrophages to form foam cells (Contois, et al., 2009). These lipid-laden phagocytes amplify inflammation in the vessel wall by secreting several cytokines (interleukin -1 [IL-1], IL-6 and TNF-α), and hence contribute to leukocyte infiltration and accumulation, smooth muscle cell proliferation, and extracellular matrix remodeling (Ribeiro, et al., 2010). Cholesterol serves as a useful surrogate for estimating LDL-related risk, but the cholesterol molecules contained in the LDL are “passengers”; the intact LDL particles are those which drive the atherosclerotic process. In normal-lipidemic states, LDL-C concentrations reflect a similar risk to LDL particles, but LDL-C concentration can vary widely between individuals with the same LDL particle concentration.

This happens because metabolic reactions involving lipids can alter both lipoprotein size and lipid composition (Contois, et al., 2009). Therefore, as will be discussed later on, other markers have been studied in order to better evaluate lipid-related risk of CVD.

According to the Fourth Joint Task Force of the European Society of Cardiology and the Societies on Cardiovascular Disease Prevention in Clinical Practice (2007), in general, to decrease CVD risk, individuals should have a total plasma cholesterol below 5 mmol/L (190 mg/dL), and an LDL cholesterol below 3 mmol/L (115 mg/dL).

1.2.8. Smaller, Denser Low Density Lipoprotein Particles

The most common dyslipidemia associated with premature vascular disease (hypertriglyceridemic, hyper-ApoB) is characterized by an increased quantity of LDL particles, which are smaller and denser because they contain less cholesterol (Miremadi, Sniderman, & Frohlich, 2002). Attention is given to this kind of particle because it has been demonstrated that smaller and denser LDL is present in higher concentrations in subjects with CHD than in controls with no CVD (Ai, et al., 2010). Additionally, an increased number of smaller and denser LDL particles were also able to predict cardiovascular and cerebro-vascular events in individuals with metabolic disorders (Rizzo, et al., 2009). Because these smaller and denser LDL particles are cholesterol-depleted, measurement of the total and LDL cholesterol levels under such conditions may not accurately reflect their number in plasma (Miremadi, et al., 2002).

1.2.9. High Density Lipoprotein Cholesterol

Low HDL-C is a risk factor for adverse cardiovascular outcomes that is independent of levels of LDL-C. The atheroprotective effect of HDL is due to its biological properties, including 1) its capacity to mediate cellular cholesterol efflux by acting as a primary acceptor, thereby facilitating reverse cholesterol transport from the arterial wall and peripheral tissues to the liver; 2) the protection of LDLs against oxidative stress; 3) anti-inflammatory actions on arterial wall cells; and 4) anti-apoptotic, 5) vasodilatory, 6) anti-thrombotic, and 7) anti-infectious activities (Kontush & Chapman, 2006).

Low levels of HDL-C are commonly found to coexist with insulin resistance, hypertriglyceridemia and a shift in the subclass distribution of LDLs towards smaller, denser, and more atherogenic lipoproteins, especially in patients with type 2 diabetes or the metabolic syndrome[4] (Eric Bruckert, 2006). The prevalence of low HDL-C levels can vary from 20% in the general population to 60% in patients with established CHD (Kontush & Chapman, 2006). It was estimated that the overall prevalence of low HDL-Cs among Europeans under treatment for dyslipidemia is 33% in men and 40% in women (Bruckert, Baccara-Dinet, McCoy, & Chapman, 2005).

The available evidence suggests that as an ever-larger proportion of the population reaches an age at which atherosclerosis becomes a major cause of morbidity and mortality, a low HDL-C level will become a more important therapeutic target for the prevention of atherosclerotic vascular disease in addition to the conventional risk factors (Windler, et al., 2007).

No specific treatment goals are defined for HDL cholesterol, but concentrations of HDL cholesterol <1.0 mmol/L (~40 mg/dL) in men and <1.2 mmol/L (~50 mg/dL) in women, serve as markers of increased cardiovascular risk (Graham, et al., 2007; Kontush & Chapman, 2006).

1.2.10. Serum Apoliproteins, Lipoprotein(a) and Non-HDL Cholesterol

Beyond the standard fasting lipid profile (total cholesterol, LDL-C, HDL-C, and triglycerides), additional measurements of lipid parameters have been proposed to extend the relationship between risk factors and cardiovascular prediction (Greenland, et al., 2010).

Apoliproteins, the protein components of lipoproteins, collectively have three major functions. They are involved in (1) modulating the activity of enzymes that

[4] The term “metabolic syndrome” refers to the combination of several factors that tend to cluster – central obesity, hypertension, low HDL-C, raised triglycerides and raised glycemia – to increase risk of diabetes and CVD (Graham, et al., 2007).

act on lipoproteins, (2) maintaining the structural integrity of the lipoprotein complex, and (3) facilitating the uptake of lipoproteins by acting as ligands for specific cell-surface receptors (Contois, et al., 2009).

Atherogenic lipoproteins including LDL particles, VLDL particles and remnants of triglyceride-rich particles each contain one molecule of apoliprotein B (ApoB). Consequently, the quantity of ApoB gives an accurate estimation of the total number of atherogenic particles (Roeters van Lennep, et al., 2002). The relationship between apoliprotein A (ApoA) and HDL is less direct (Greenland, et al., 2010), probably because HDL has two subclasses: HDL that only contains apoliprotein A-I (ApoAI) and HDL particles that contain both ApoAI and apoliprotein AII (ApoAII). ApoAI is the major apoliprotein of HDL and is considered to be more protective against CHD than ApoAI/AII (Roeters van Lennep, et al., 2002).

Lipoprotein(a) is an LDL subfraction containing ApoA. It is highly homologous with plasminogen and competes with plasminogen for fibrin-binding sites, inhibiting fibrinolysis (Fletcher, et al., 2005). Non-HDL cholesterol, in turn, is the sum of the cholesterol concentration in all pro-atherogenic lipoproteins (VLDL, IDL and LDL particles) and ApoB, the major apoliprotein in these particles (Kastelein, et al., 2008).

Most of the early population and intervention studies measured LDL in terms of its associated cholesterol, but in recent years, as immunoassays for ApoB have improved and become more readily available, researchers have increasingly investigated both ApoB and LDL-C (Contois, et al., 2009). Considerable debate and controversy have developed regarding the relative merits of monitoring LDL in terms of cholesterol content or particle concentration, as measured by ApoB, to assess risk and monitor therapy (Contois, et al., 2009).

In the Framingham Heart Study, little additional risk information was obtained from ApoB or the ApoB/ApoAI ratio compared with the total/HDL-cholesterol ratio (Ingelsson, et al., 2007). Nevertheless, the superiority of non-HDL cholesterol or ApoB compared with LDL-C as a cardiovascular risk predictor was recently demonstrated during a statin treatment, as were the superiority of ApoB/ApoAI compared with other single pro-atherogenic measurements and other pro-atherogenic/anti-atherogenic measurements (Kastelein, et al., 2008).

1.2.11. Triglycerides

The principal cardiovascular significance of an elevated triglyceride (TG) level is that it is a component of atherogenic dyslipidemia, which is commonly found in patients with type 2 diabetes, metabolic syndrome, and excess adiposity. The triad of lipid abnormalities in these conditions consists of an elevated plasma TG level (>150 mg/dL), reduced HDL-C level (<40 mg/dL for men; <50 mg/dL for women), and a relative excess of small, dense LDL particles that accompanies generally normal total LDL-C levels (Fletcher, et al., 2005).

The role of plasma TG as an independent risk factor is still elusive. First, there are methodological difficulties in interpreting TG levels because of high biologic intra- and inter-individual variability. Second, strong interactions exist between TG and other lipid factors (Roeters van Lennep, et al., 2002). For example, elevated triglycerides are often seen with lower HDL levels (Bruckert, et al., 2005).

There are a number of underlying causes of elevated serum TG: being overweight or obese; lacking physical inactivity; cigarette smoking; excessive alcohol consumption; high-carbohydrate diets (>60% of total energy); other diseases such as type 2 diabetes, chronic renal failure, and nephrotic syndrome; and a genetic predisposition (Fletcher, et al., 2005). Similarly to HDL-C, no specific treatment goals are defined for triglycerides, but a concentration of fasting triglycerides >1.7 mmol/L (~150 mg/dL), serve as the marker of increased cardiovascular risk (Graham, et al., 2007).

1.2.12. Diabetes and Fasting Glycemia

Diabetes is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or a combination of both (Rydén, et al., 2007)

Classification of diabetes includes etiological types and different clinical stages of hyperglycemia. Four main etiological categories have been identified: type 1 diabetes, type 2 diabetes, other specific types, and gestational diabetes. Type 2 diabetes is caused by a combination of decreased insulin secretion and decreased insulin sensitivity. This type of diabetes comprises over 90% of adult diabetes and typically develops after middle age. In Portugal, 46.9% of the diagnosed cases of diabetes occur in individuals aged 65 years and over. These patients are often obese and physically inactive (Rydén, et al., 2007).

Atherosclerotic CVD is the major cause of premature mortality in patients with type 2 diabetes (Krentz, 2002). It has been observed that up to 75-80% of diabetic patients die of CVDs, and 75% of those deaths are caused by CHD (Roeters van Lennep, et al., 2002).

The mechanisms underlying the increased risk of CVD in type 2 diabetes remain incompletely delineated, but several possible mechanisms linking type 2 diabetes and atheroma have been suggested: central obesity, vascular endothelial dysfunction,[5] and disordered lipid metabolism (Krentz, 2002). Insulin sensitivity and cardiovascular risk may also be influenced by adipocytokines,[6] excess fatty acids liberated from visceral fat (Krentz, 2002), and inflammatory processes (de Rekeneire, et al., 2006). Finally, disturbances of the neuro-endocrine system, possibly mediated via visceral obesity, have also been identified as possible factors (Krentz, 2002).

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[5] Endothelial dysfunction is a broad term that implies diminished production or availability of nitric oxide and/or an imbalance in the relative contribution of endothelium-derived relaxing and contracting factors, such as endothelin-1 angiotensin, and oxidants (Szmitko, et al., 2003).

[6] Cytokines synthesized and released by the adipose tissue (e.g., leptin and adiponectin).

It is important to refer to results from an epidemiological study (Meigs, Nathan, D'Agostino, & Wilson, 2002) and from a meta-analysis (Levitan, Song, Ford, & Liu, 2004) that demonstrated that subjects with impaired glucose regulation (as assessed by fasting blood glucose or post-challenge glucose levels), have higher CVD risk even before the onset of type 2 diabetes than their peers with normal glucose regulation.

The current European Guidelines on CVD Prevention (Graham, et al., 2007) recommend values of fasting glycemia below 110mg/dL in order to maintain a lower CVD risk.

1.2.13. Homocysteine

Homocysteine is a sulfur-containing amino acid that is rapidly oxidized in plasma to the disulfides homocystine and cysteine-homocysteine. Plasma/serum total homocysteine, also termed homocystine, is the sum of homocysteine in all three components (Malinow, Bostom, & Krauss, 1999). Observations in epidemiological studies (Vollset, et al., 2001) have suggested that beyond the sensitive markers of folate and cobalamin (vitamin B12) deficiencies (Refsum, et al., 2004), increased total plasma homocysteine is an independent risk factor for cardiovascular mortality.

Because variable changes in homocysteine levels have been observed post-prandially, it is customary to obtain measurements in the fasting state. Normal levels of fasting plasma homocysteine are considered to be between 5 and 15 µmol/L. Moderate, intermediate, and severe hyperhomocysteinemia refer to concentrations between 16 µmol/L and 30 µmol/L, between 31 µmol/L and 100 µmol/L, and >100 µmol/L, respectively (Malinow, et al., 1999). However, the cost of homocysteine analysis, coupled with the lack of definitive evidence for the clinical benefits of reducing homocysteine levels (O'Leary, Knuiman, & Divitini, 2004), precludes recommendations for population-wide screening. Thus, some researchers consider that a reasonable approach is to determine levels of fasting homocysteine in “high-risk patients” only (Malinow, et al., 1999).

1.2.14. Inflammatory, Infectious and Thrombotic Markers

Cardiovascular diseases are life course diseases that begin with the evolution of risk factors that in turn contribute to the development of subclinical atherosclerosis (Vasan, 2006). Atherosclerosis is characterized by the accumulation of lipids and fibrous elements in the large arteries, resulting in increased arterial stiffening, decreased blood flow, and consequently, the reduction of oxygen supply to the tissues (Lusis, 2000). This pathology is especially harmful because it evolves silently, without clinical manifestation. The traditional cardiovascular disease risk factors are not sensitive enough for use in evaluating the progression of the atherosclerotic pathology.

In recent years, there has been a growing appreciation that the immune system plays a critical role at every stage of the atherosclerotic process, from lesion initiation to the rupture of atherosclerotic plaque (Kritchevsky, Cesari, & Pahor, 2005). The involvement of the immune system is a key factor in the development and progression of atherosclerosis, which is now viewed as a dynamic and progressive pathology arising from the combination of endothelial dysfunction and inflammation (Szmitko, et al., 2003).

Because inflammation is considered to be of paramount importance in the pathogenesis of atherosclerosis, numerous inflammatory biomarkers have been evaluated as risk factors or risk markers for CVD. The most intensively studied inflammatory biomarker associated with CVD risk is high-sensitivity CRP (hs-CRP) (Greenland, et al., 2010). The intense interest in this acute-phase protein derives from accumulating evidence that CRP is one of the strongest independent predictors of all-cause and cardiovascular death in a number of settings (den Elzen, van Manen, Boeschoten, Krediet, & Dekker, 2006; Willems, Trompet, Blauw, Westendorp, & de Craen, 2010).

High levels of CRP elicit a multitude of effects on endothelial biology that favor a pro-inflammatory and pro-atherosclerotic phenotype. For example, CRP potently down-regulates endothelial nitric oxide synthase (eNOS) transcription in endothelial cells and destabilizes eNOS mRNA, with resultant decreases in vasodilatory responses. Indeed, CRP has been shown to stimulate endothelin-1 and IL-6 release, up-regulate adhesion molecules, and stimulate monocyte chemo-attractant protein-1 (MCP-1), while facilitating macrophage LDL uptake. More recently, CRP has been shown to facilitate endothelial cell apoptosis and inhibit angiogenesis (Szmitko, et al., 2003).

Many other "novel" biomarkers of endothelial dysfunction (vascular cell adhesion molecule-1 [VCAM-1] and intercellular adhesion molecule-1 [ICAM-1]) and vascular inflammation (TNF-α, IL-6, IL-10, and IL-18) have been used as additional tools to assess CVD risk. TNF-α is a primary and potent inflammation mediator. It is primarily synthesized by monocytes/macrophages and T cells. TNF-α plays a critical role in coordinating the inflammatory response and activating mediators distantly in the cytokine cascade; it is also a potent inducer of other pro-inflammatory cytokines, and an activator of coagulation and muscle catabolism (Johnston & Webster, 2009). However, despite its importance, it has not been frequently measured in epidemiologic studies (Kritchevsky, et al., 2005). IL-6 synthesis is induced by TNF-α and IL-1 from many cell types (e.g., lymphocites, fibroblasts and monocytes); its biological effects include neutrophil activation, induction of the hepatic acute-response, and activation of coagulation (Johnston & Webster, 2009). High levels of IL-6 have been associated with higher mortality in older women with CVD (Volpato, et al., 2001). Interferon-gamma (IFN-ɣ) is a pro-inflammatory cytokine secreted by activated T cells that limits the synthesis of new collagen required for fibrous plaque cap preservation (Szmitko, et al., 2003). IL-10 is an anti-inflammatory cytokine that inhibits the production of a variety of pro-inflammatory cytokines such as IL-2, IL-6, TNF-α and IFN-ɣ, and it is strongly associated with better prognosis in patients with acute coronary syndromes (Kritchevsky, et al., 2005).

Additionally, the soluble plasma glycoprotein fibrinogen, which is synthesized in the liver, is also considered a biomarker related to atheroma, since it is involved in the coagulation cascade leading to clot formation as a consequence of the vascular inflammatory process.

1.2.15. Cigarette Smoking

Smoking is the single most important preventable cause of CHD. Cigarette smoking (CS) also predisposes the individual to atherosclerosis and to its related acute clinical syndromes such as angina pectoris, myocardial infarction, stroke, and sudden death (Ambrose & Barua, 2004). As few as one to five cigarettes per day increases an individual's CVD risk (Yusuf, et al., 2004). Indeed, this increased CVD risk seems to be reported in both active and passive smokers (Venn & Britton, 2007).

The mechanisms behind the increased risk of CVD observed in smokers versus non-smokers are not completely understood; however, increases in intima-media thickness (Ambrose & Barua, 2004), endothelial dysfunction (Mazzone, et al., 2001), fibrinogen (Venn & Britton, 2007), homocystein (Venn & Britton, 2007), inflammation as assessed by white blood cell (WBC) count, (Mazzone, et al., 2001), IL-6 (Tappia, Troughton, Langley-Evans, & Grimble, 1995), CRP (Tracy, et al., 1997) and TNF-α (Tappia, et al., 1995), as well as a modification of lipids (Ambrose & Barua, 2004) have been observed in smokers.

Endothelial dysfunction is one of the earliest manifestations of atherosclerotic changes in a vessel. Nitric oxide (˙NO), a free radical, is primarily responsible for the vasodilatory function in the endothelium; it also helps to regulate inflammation, leukocyte adhesion, platelet activation, and thrombosis. Therefore, an alteration in ˙NO availability could have primary and secondary effects on the initiation and progression of atherosclerosis and on thrombotic events (Liu-Ambrose, et al., 2005). Several lines of evidence (Powell, 1998) suggest that smoking impairs the synthesis of ˙NO by the endothelium, increases lipid oxidation and reactive oxygen species (ROS) production, decreases anti-adhesive properties of the endothelium, and triggers vascular inflammation and thrombogenesis.

Despite previous findings (Hatsukami, et al., 2005) relating the improvement in several biomarkers of CVD risk to a reduction in the recurrence of CS, it is not clear whether these changes translate into significant health improvements.

On the other hand, CS cessation can considerably reduce (~24%) the risk of CVD after two to three years of abstinence (Kawachi, et al., 1993). The exceeded risk for total mortality and cardiovascular mortality among former smokers approaches the level of that people who have never smoked after 10 to 14 years of abstinence (Kawachi, et al., 1993).

1.2.16. Physical Inactivity

Physical activity (PA) is believed to improve several CVD risk factors. PA-related benefits include raising HDL-C cholesterol, lowering LDL-C and TG, lowering BP, improving fasting and postprandial glucose insulin homeostasis, inducing and maintaining weight loss, improving psychological well-being, and likely lowering inflammation, improving endothelial function, and facilitating smoking cessation (Mozaffarian, Wilson, & Kannel, 2008). Physical inactivity, (PI) on the other hand, is thought to contribute to an increased risk for all-cause (Martinson, O'Connor, & Pronk, 2001) and CVD mortality (Haapanen-Niemi, et al., 2000).

Physical inactivity is defined differently by different research instruments. The following examples were listed by Oldridge (2008) in order to exemplify the variety of definitions for PI found in the literature: “doing very little or no physical activity,” “no participation plus sitting down for >6 h/week,” “<10% of leisure-time in activities ≤4 metabolic equivalents.” Despite these definitions, consensus is growing that, for health benefits, some, but insufficient, activity is defined as “<2.5 h/week of moderate intensity activity” (Oldridge, 2008).

Independent of the adopted definition, many studies have demonstrated the increased CVD risk in less physically active individuals when compared with their more active peers. In a prospective 16-year follow-up study, compared with the most active subjects, the men and women with no weekly vigorous PA had higher relative risks of 1.6 and 4.7, respectively, for CVD mortality (Haapanen-Niemi, et al., 2000). A similar relationship was observed in individuals with diagnosed chronic conditions. In these individuals, those who were physically inactive had twice the rate of subsequent mortality over a short follow-up (42 months) of the more active individuals (Martinson, et al., 2001). Finally, in a recent meta-analysis that included 33 studies and 883,372 individuals, PA was associated with a risk reduction of 35% for CVD mortality (Nocon, et al., 2008).

The importance of PA in the prevention of CVD is also reflected in healthcare costs. Allender et al. (2007), for example, estimated that in the United Kingdom, the costs associated with CHD directly attributed to physical inactivity amounted to approximately £1.06 billion. Considering the great contribution of PI to mortality and the costs of CVD and other chronic conditions, nowadays, PA is recommended for all age groups (children, young, middle-aged, and older adults) and for a wide range of health conditions including individuals with CVD (ACSM, 2000; ACSM/AHA, 2007; Pescatello, et al., 2004; Pollock, et al., 2000). For the former group, however, a clinical judgment including exercise testing is necessary (Graham, et al., 2007).

Despite knowledge of the benefits of an active lifestyle, a large majority of individuals still maintains a sedentary lifestyle. Actually, it was estimated that the prevalence of PI ranges from 30.0-61.4% depending on age, gender, geographical living site and criteria used to assess PA or PI (Kruger, Ham, & Sanker, 2008; Martins, Assis, Nahas, Gauche, & Moura, 2009). The prevalence data on PI available from the World Health Organization Global InfoBase Online estimates that the mean prevalence of leisure time PI is 35.7% in developed countries (WHO, 2011).

In the elderly population, physiological and mental changes that come with increasing age may contribute to PI (Graham, et al., 2007). In fact, few older adults participate in levels of PA that may benefit their health (Taylor, et al., 2004). However, considering that regular PA may effectively slow down age-related changes, decrease CVD morbidity and mortality, and lower healthcare costs, PA should be promoted in older-aged individuals (Graham, et al., 2007).The net potential benefits on health and savings appear to be greatest in those with greater disabilities and highest costs, which probably refers to the oldest and sickest (Martinson, et al., 2001).

1.2.17. Psychosocial Factors

An association between lower socioeconomic status (SES) and poorer health has been observed for hundreds of years (Kaplan & Keil, 1993). Indeed, the evidence appears to support that SES is an important factor in the etiology, treatment, and progression of CVDs and their risk factors. For example, it was observed that a lower prevalence of high BP, as well as diabetes mellitus and high cholesterol, was associated with higher SES as assessed by income or education (Kanjilal, et al., 2006). Negative associations between SES and risk of CHD were also observed by Andersen, Osler, Petersen, Gronbaek, & Prescott (2003). A reasonable explanation for these relationships is that individuals with lower SES have fewer possibilities for success in terms of quality of housing, access to healthcare, variety in diet, and group-based physical activity (Andersen, et al., 2003).

1.2.18. Autonomic Dysfunction

The rhythm of a healthy heart varies as a result of physical and autonomic nervous system activity, mental stress, body position, respiration, blood pressure regulation, thermoregulation, rennin-angiotensin system activity, and other unknown factors (Kowalewski & Urban, 2004; Pitzalis, et al., 1996). Of these, the two limbs (sympathetic and parasympathetic/vagal) of the autonomic system are the most important in determining changes in heart rate (Pitzalis, et al., 1996). The parasympathetic influence on heart rate is mediated via the release of acetylcholine by the vagus nerve, and the sympathetic influence on heart rate is mediated by release of epinephrine and norepinephrine. Under resting conditions, parasympathetic activity prevails and variations in heart period are largely dependent on vagal modulation (Malik, et al., 1996).

Conversely, autonomic dysfunction reflects reduced parasympathetic and/or increased sympathetic nervous system activity (Kamphuis, et al., 2007). Although autonomic dysfunction is not considered a “traditional” CVD risk factor, it is involved in the pathophysiology of myocardial ischemia, heart failure, diabetes, ventricular tachycardia, ventricular fibrillation, and sudden cardiac death (Kamphuis, et al., 2007). It has also been related to high blood pressure, inflammation, dyslipidemia, and obesity (Christou, et al., 2004; Felber Dietrich, et al., 2006; Sajadieh, et al., 2004). Indicators of heart autonomic dysfunction are elevated resting heart rate, low heart-rate variability (HRV), and prolonged cardiac cycle (Kamphuis, et al., 2007).

Evidence for an association between a predisposition for lethal arrhythmias and signs of either increased sympathetic or reduced vagal activity have encouraged the development of quantitative markers of autonomic activity. HRV, the spontaneous fluctuations around the mean heart rate (Schuit, et al., 1999), represents one of the most promising prognostic markers of cardiovascular mortality and morbidity (Felber Dietrich, et al., 2006; Malik, et al., 1996; Tsuji, et al., 1996). Generally, HRV is assessed by time domain (TD, which includes statistical and geometrical measures) or frequency domain (FD) measures. The Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (Malik, et al., 1996) suggest the use of the FD measures compared to the TD measures when analyzing data from short-term recordings. Three main spectral components are distinguished in a spectrum calculated from short-term recordings of two to five minutes, using very low frequency (VLF), low frequency (LF), and high frequency (HF) components. Efferent vagal activity is considered a major contributor to the HF component. The interpretation of the LF component is more controversial, while some authors consider it as a marker of sympathetic modulation (Pitzalis, et al., 1996; Sinnreich, Kark, Friedlander, Sapoznikov, & Luria, 1998), others refer that it includes both sympathetic and vagal influences (Schuit, et al., 1999). The physiological explanation of the VLF component is much less defined, and the existence of a specific physiological process attributable to these heart period changes might be questionable (Malik, et al., 1996).

It is easy to understand that some CVDs risk factors are non-modifiable, while others are susceptible to lifestyle modification. Since the aging process, similarly with gender and race, is not reversible, the therapeutical approach might focus on the greatest number of modifiable risk factors as possible in order to decrease the global risk.

Several strategies, policies, and drugs have been developed, and many others still being studied, that aim to counteract CVD risk factors and mortality. Generally, CVD risk factor management includes extensive lifestyle counseling by healthcare providers with a variety of expertise (physicians, nurses, dietitians, and exercise specialists), in addition to prescription drug therapies (Fletcher, et al., 2005). In fact, the increase in longevity observed in the past few decades can be mainly attributed to this combined effort. However, morbidity due to CVDs remains high, which means that individuals are living longer, but are usually limited by chronic conditions. Although medications can be prescribed to people who are at great risk of developing dyslipidemia, diabetes or hypertension, providing medications to hundreds millions of adults worldwide is not desirable for many reasons, including cost and potential adverse side effects. Since many more people are living longer today, it is crucial to understand how to prevent disability and increase the quality of life among this aged population.

It was previously suggested that the adoption of healthy lifestyle changes, such as the daily consumption of fruits and vegetables, regular PA, and avoiding smoking, can potentially reduce the risk for CVD by approximately 75% (Yusuf, et al., 2004). In specific case, several studies have demonstrated that low levels of PA are associated with several CVD risk factors such as increased total body and trunk fat (Scott, Blizzard, Fell, & Jones, 2009); higher concentrations of CRP, white blood cells, and fibrinogen (Geffken, et al., 2001); lower HRV (Rennie, et al., 2003); and increased levels of SBP and DBP (Reaven, Barrett-Connor, & Edelstein, 1991).

Equally, or perhaps even most importantly, are the findings suggesting that, beyond reducing individual and global CVD risk, PA levels are positively related with quality of life (QoL) in older adults (Brown, et al., 2004; Leinonen, Heikkinen, & Jylha, 2001).

1.3. Important Definitions

Before a discussion of the interplay between PA, chronic conditions, functional limitation, disability, and QoL, it is necessary to define these terms. PA, in this thesis, refers to any bodily movement produced by contraction of skeletal muscle that substantially increases energy expenditure (Howley, 2001) and exercise (or exercise training) is an assumed subcategory of PA in which planned, structured and repetitive bodily movements are performed to improve or maintain one or more components of physical fitness (Howley, 2001). Physical fitness, in turn, will be defined as a set of attributes that people have or achieve that relate to their ability to perform PA. This is generally sub-classified as performance-related fitness and health-related fitness (Howley, 2001). The former focuses mainly on body composition, cardiorespiratory fitness, muscular strength, endurance, and flexibility (Howley, 2001).

More recently, with increased interest in the study of the older population, another term current in use is functional fitness. Functional fitness describes having the physiologic capacity (all components of health-related fitness plus balance and agility) necessary to maintain independence and the ability to perform the activities of daily living, such as walking, stepping or standing from a seated position, without undue fatigue (Rikli & Jones, 1999).

A chronic condition or a chronic disease is usually characterized by complex causality, multiple risk factors, a long latency period, a prolonged course of illness, functional impairment or disability, and in most cases, the unlikelihood of cure (National Public Health Partnership, 2001). Cardiovascular diseases, cancer, chronic lung diseases and diabetes are examples of such conditions. Functional limitation, as primary used by Nagi and referred by Jette (2006), represents restrictions in a person’s performance. An example of functional limitation that might result from arthritis of the knee could include limited performance in the person's ability to walk or stand from a seated position. Disability is a limitation to performing the socially defined roles and tasks expected of an individual within a socio-cultural and physical environment (Jette, 2006).

QoL is very difficult to define because it has been used to refer to different parameters in a variety of contexts. There is no definitively accepted theoretical framework of QoL, however, classic conceptualizations have included such domains as physical health; social relationships and support; environmental, financial, and material circumstances; and cognitive beliefs (Halvorsrud & Kalfoss, 2007). Each of these domains can also be influenced by several factors. Although each factor has a different impact on different individuals, it is assumed that there are group-specific characteristics in QoL (Netuveli & Blane, 2008). For older adults, family relationships, social contacts and activities, functional ability, health status, and general health seem to be important factors when assessing QoL (Farquhar, 1995).

Although health is not a unique factor influencing QoL in older adults, it is generally considered an important aspect. In this regard, instruments used with this population to assess health-related quality of life (HRQoL) include several aspects of life such as illness, chronic conditions, disability and SES, which affect perceived physical and mental health (Brown, et al., 2004; Halvorsrud & Kalfoss, 2007).

1.4. Theoretical Background on Disability and Health-related Quality of Life

Although several models have been suggested to explain the interactions between active lifestyles and the prevalence of chronic diseases and their impact on functionality and the HRQoL of older adults, until now, these complex interactions were not full elucidated. According to Rikli & Jones (1999), all these factors interact with one another. The clinical manifestation of a chronic disease leads to a decline in functional capacity, which is linked to a tendency to reduce PA. Physical inactivity, in turn, can exacerbate disease and therefore decrease functional capacity. If any other factor interferes in this cycle, great disability would result (Rikli & Jones, 1999).

Chronic illness, disability, and decreased health and QoL usually occur in older adults. In 2005 in Portugal, 45.1% of individuals aged 75 years and over self-reported disability related to health factors (Instituto Nacional de Estatística & Instituto Nacional de Saúde Doutor Ricardo Jorge, 2009) and in 2007, 46.0% of the individuals in this age range rated their health status as bad or very bad (INE, 2008b). Nevertheless, cumulative lifetime disability could be reduced if primary prevention were implemented to postpone the onset of chronic conditions, as demonstrated by Newman, et al. (2003). These researchers observed that the prevention of subclinical vascular disease might increase the quantity and quality of years in later life as assessed by the likelihood of maintaining intact health and function.

With regard to the observed associations between PA with CVDs, loss of functionality and HRQoL among older adults, numerous organizations strongly recommend the dissemination of exercise programs and the adoption of a more active lifestyle as primary and secondary methods of CVD and disability prevention (ACSM/AHA, 2007; Chodzko-Zajko, et al., 2009; Graham, et al., 2007). However, the existing body of evidence is based mainly on epidemiological observations or in experimental setups using isolated endurance exercise training and, less frequently, resistance exercise training programs (Durstine, Grandjean, Cox, & Thompson, 2002). While the effects of endurance training programs on the traditional cardiovascular risk factors are well established (Durstine, et al., 2001), data are often contradictory regarding the role of resistance training, with some authors describing the positive benefits (Fahlman, Boardley, Lambert, & Flynn, 2002) and others not (Vincent, Braith, Feldman, Kallas, & Lowenthal, 2002). Additionally, few studies have directly investigated the effects of exercise training, independent of type, on the "novel" biomarkers of CVDs and on autonomic dysfunction.

Another point to clarify is if the benefits associated with PA are really due to PA, or if they are due to an increase in overall fitness induced by higher levels of PA. Many studies have reported that the associations between fitness and CVD risk factors (Dvorak, et al., 2000; McMurray, Ainsworth, Harrell, Griggs, & Williams, 1998; Suzuki, Yamada, Sugiura, Kawakami, & Shimizu, 1998), or between fitness and CVD mortality (Nocon, et al., 2008), are stronger than those observed between PA and CVD risk factors and mortality. Indeed, the associations between fitness and HRQoL in older adults have not been well explored. The lack of appropriate measures to assess fitness in older populations may make it difficult to clarify the independent associations between PA and fitness with CVD risk factors, as well as to better explore the relationship between fitness and HRQoL.

The most traditional protocols for assessing fitness are, generally, linear adaptations of those that are applied to the youngest portion of the population (Rikli & Jones, 1999). Considering that recent evidence proposed that exercise capacity represents the most powerful predictor of total mortality in a clinical population (Laukkanen, Kurl, Salonen, Rauramaa, & Salonen, 2004), it seems important to have valid, but feasible, instruments for evaluating the physical fitness of older adults. Many studies use aerobic fitness, assessed by maximal oxygen consumption (VO_{2max}) determination tests, to assess general fitness. Tests to determine VO_{2max} are, in general, inadequate for the majority of older adults, and very little is known about the predictive value of functional field tests like the 6-minute walk test (6MWT) on cardiovascular risk factors or HRQoL of this population.

1.5. Questions and Objectives of the Study

Based on the above-described background, three study questions were formulated:

1. Are simple physical/functional fitness field tests capable of identifying, in a group of community-dwelling older adults, those who are at an increased risk of CVD and those with a lower HRQoL?

2. Does exercise training improve the CVD risk profile, cardiovascular function, functional fitness, and HRQoL of community-dwelling older adults?

3. Are there differences in the effects of aerobic versus resistance training on the CVD risk profile, cardiovascular function, functional fitness, and HRQoL of community-dwelling older adults?

Guided by these research questions, the studies included in this thesis had three main objectives:

1. To investigate the possible relationships between performance on simple functional fitness field tests, CVD risk factors, and HRQoL in community-dwelling older adults;

2. To determine the effects of two different types of exercise training on modifiable CVD risk factors, cardiovascular function, functional fitness, and HRQoL in community-dwelling older adults.

3. To observe if the effects of two different types of exercise training (aerobic and resistance) on modifiable CVD risk factors, cardiovascular function, functional fitness, and HRQoL in community-dwelling older adults have the same magnitude.

In order to achieve these objectives, this thesis was divided into nine chapters. Chapter I contains a brief background of the theme and presents the main objectives of the study, as well as its structure. Chapter II describes the adopted methodology. The following five chapters (III to VII) present five original studies, each presented in article format; all of these were submitted to peer-reviewed scientific journals. The titles and specific objectives of each study are presented in Table 1. The final chapters (VIII and IX) report the final remarks and the main conclusions of the thesis.

Table 1. The titles, specific objectives, and status of each study included in the thesis.

Chapter III **Study I**	**Title:** Effects of a Moderate-intensity Walking Program on Blood Pressure, Body Composition and Functional Fitness in Older Women: Results of a pilot study. Flávia A. C. Wanderley, José Oliveira, Jorge Mota, Joana Carvalho **Aim:** To evaluate the effects of a moderate-intensity walking program on the physical fitness, body composition, and resting blood pressure of older women. **Status:** Published in *Arch. Exerc. Health Dis.* (2010)*,*1(2):50-57
Chapter IV **Study II**	**Title:** Six-minute walk distance (6MWD) is associated with body fat, systolic blood pressure and rate-pressure product in community-dwelling elderly subjects Flávia A. C. Wanderley, José Oliveira, Jorge Mota, Maria Joana Carvalho **Aim:** To determine if aerobic fitness assessed by 6MWD is able to predict resting cardiovascular function and cardiovascular disease risk factors. **Status:** Published in *Arch. Gerontol. Geriatr* (2011), 52(2):206-210 DOI: 10.1016/j.archger.2010.03.020
Chapter V **Study III**	**Title:** Associations between Objectively Assessed Physical Activity Levels and Fitness and Self-reported Health-related Quality of Life in Community-dwelling Older Adults Flávia A. C. Wanderley, Gustavo Silva, Elisa Marques, José Oliveira, Jorge Mota, Joana Carvalho **Aim:** To examine the associations between self-reported health-related quality of life (HRQoL) and each of habitual physical activity (PA) and physical fitness in community-dwelling older adults. **Status:** Published on line in *Qual. Life Res*, DOI: 10.1007/s11136-011-9875-x
Chapter VI **Study IV**	**Title:** Effects of training on fatness, inflammation and autonomic function in older adults Flávia A. C. Wanderley; André Moreira; Oksana Sokhatska; Carmo Palmares; Pedro Moreira; José Oliveira; Joana Carvalho **Aim:** To examine the effectiveness of two different training regimens on reducing body fat, improving autonomic dysfunction, and decreasing low-grade inflammation in community-dwelling older adults with no serious medical conditions. **Status:** Submitted to European Journal of Cardiovascular Prevention and Rehabilitation, on 3rd of March, 2011
Chapter VII **Study V**	**Title:** Health-related Quality of Life (HRQoL), Body Composition and Functional Fitness of Older Adults: Results from aerobic *vs.* resistance training. Flávia A. C. Wanderley, Nórton L. Oliveira, Elisa Marques, Pedro Moreira, José Oliveira, Joana Carvalho **Aim:** To investigate the effects of two types of exercise training on subjective Health-related Quality of Life (HRQoL), functional fitness, and body composition of independent community-dwelling older adults with no serious medical conditions. **Status:** Under review - Journal of Aging and Physical Activity

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CHAPTER II

METHODOLOGY

2. METHODOLOGY

2.1. Study Design and Participants

2.1.1. Study Design

This thesis encompasses five studies with three different designs (see Figure 1): Study I was a pilot study with a pre-experimental design in which a unique group of older women was followed for eight months, maintaining their normal nutritional and physical activity habits for the first four months, and engaging in a walking program of moderate intensity for the final four months. Outcomes were assessed in three distinct moments: at baseline, after the four months of normal habits, and after the four-month walking program. This first study was conducted in order to ensure that practical problems in the study design and protocols were identified and solved before the initiating following studies (Peat, 2002).

Studies II and III were descriptive, correlational studies in which older adults' outcomes were evaluated and relationships between these outcomes were explored. Correlations were used to describe whether and to what degree variations in one variable were associated with variations in another variable (Haag, 2004). Although this type of study cannot prove a causal relationship between variables, in detecting the presence or absence of relationships, it may suggest a possible positive outcome of experimental study.

Once causal relationships could be proven in randomized controlled trials (RCT) (Haag, 2004), Studies IV and V were designed to test the effects of the interventions on outcomes. In these studies, older adults that met the inclusion criteria were given informed consent and had outcomes assessed as a baseline and then were entered in randomized groups for aerobic training (AT), resistance training (RT), and a waiting list (WL). After eight months of their respective interventions, the subjects' outcomes were assessed again.

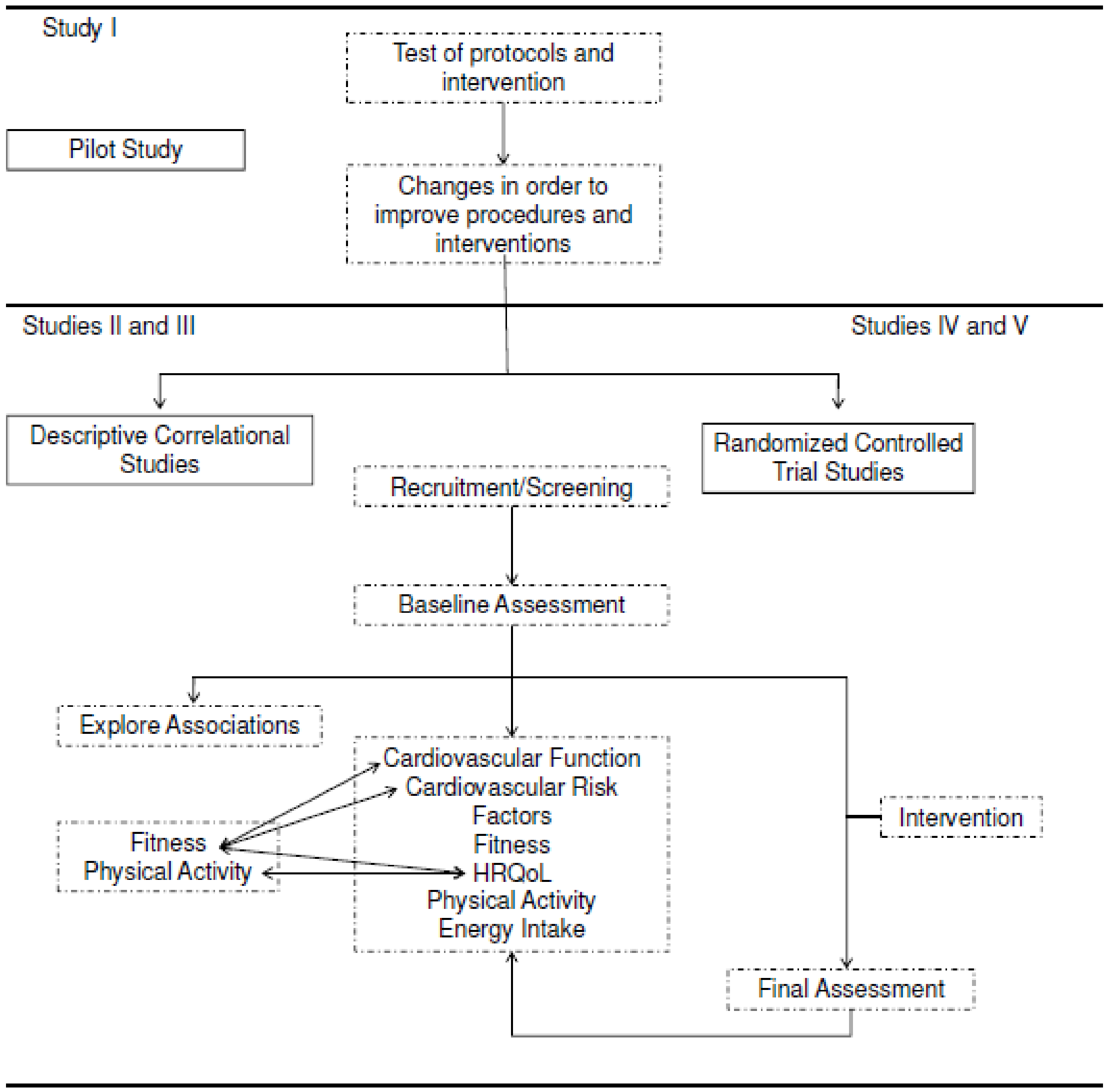

Figure 1. Thesis design.

2.1.2. Participant Selection Criteria

A total of 139 physically independent community-dwelling subjects were recruited in the Porto area (Portugal) through newspaper advertisements. At first, 31 women volunteered to participate in the pilot study; later, 108 men and women volunteered for the descriptive and RCT studies. In order to identify the subjects attending inclusion criteria, at the screening, the health history of the subjects was obtained via individual interviews. Data on the use of medication and the presence of the following chronic conditions were obtained: heart disease, hypertension, stroke, diabetes, dyslipidemia, osteoarthritis, osteoporosis, severe pulmonary disease, liver disease, thyroid disease, and depression. This questionnaire also included information on smoking status and on demographics (education, income, and civil status).

The inclusion criteria of the sample required that the subjects: (i) be older than 60 years, (ii) complete the baseline testing, and (iii) be physically independent. The exclusion criteria were the following: (i) registered blindness, (ii) severe hearing impairment, (iii) uncontrolled hypertension or diabetes, (iv) symptomatic cardiorespiratory disease, (v) severe renal or hepatic disease, (vi) uncontrolled epilepsy, (vii) progressive neurological disease, (viii) chronic disabling arthritis, (ix) present acute or terminal illness, (x) use of walking aids, and (xi) any neurological, skeletal-muscle or joint disturbance that precluded participation in testing. Lastly, (xi) subjects involved in any regular supervised exercise training (performing moderate to vigorous exercise for 20 minutes or more at least twice a week) in the previous six months were excluded from the RCT studies.

In order to increase the statistical power and considering that anthropometrics, body composition, resting BP, resting HR, and 6MWT were assessed in all studies accordingly to the same protocols and by the same investigators, in Study II, the sample from the pilot study was added. The number of individuals recruited and the number of participants included in statistical analysis for each study are presented in Table 1.

The nature, benefits, and risks of the studies were explained to the volunteers, and their written informed consent was obtained before the study, consistent with the Helsinki Declaration. Finally, all methods and procedures were approved by the Institutional Scientific Board.

2.2. Intervention

The aerobic and resistance exercise programs used in this thesis are consistent with the recommendations established by the American College of Sports Medicine and the American Heart Association (ACSM/AHA, 2007; Chodzko-Zajko, et al., 2009).

Table 1. Sample size of each study

	Recruited	Baseline Assessment	Included in Analysis
Study I	31	22 women	19 women
Study II	139 (31 from pilot study and 108 from the original study)	105 (78 women and 27 men)	105 (78 women and 27 men)
Study III	108	85 (64 women and 21 men)	85 (64 women and 21 men)
Study IV	108	85 (64 women and 21 men)	50 (39 women, 11 men)
Study V	108	85 (64 women and 21 men)	50 (39 women, 11 men)

2.2.1. Walking Program (Pilot Study)

The length of the walking program was four months, with exercise sessions three times per week, each lasting approximately 50 minutes. Training workouts consisted of a 10-minute warm-up, thirty minutes of walking at a moderate intensity corresponding to 50-70% $HR_{Reserve}$, and ended with a 10-minute cool-down. Once the walking program was not effective at improving body composition or subjects' resting HR, for the subsequent RCT studies, the intensity of the aerobic training was slightly increased, as was the duration of the program. In addition, a different type of exercise (RT) was included in the study.

2.2.2. Aerobic Training, Resistance Training, and Waiting List (RCT)

In the RCT studies, both AT and RT groups trained three times per week (non-consecutive days) for eight months – each exercise session lasted approximately 50 minutes. Taking into account that previous researchers have suggested a possible dose-response relation between the intensity of training and improvements in functional performance and health (Seynnes, et al., 2004), it was decided for the RCT studies, for both exercise types, to implement an intensity classified as moderate to high (70-80% of $HR_{reserve}$ for AT and 80% of 1RM for RT).

Aerobic training. AT consisted of a 10-minute warm-up, that included walking or cycling, calisthenics and stretching, 30 minutes of aerobic exercises – mainly walking – at an intensity corresponding to 70%-80% $HR_{Reserve}$ or a rating of perceived effort (RPE) of 7 to 8 on a 10-point scale, and ending with a 10-minute cool-down. In order to ensure that the subjects were exercising at the targeted intensity, Polar Heart Rate Monitors (Polar Team System, Finland) were used during exercise sessions and RPEs were registered.

Resistance training. RT consisted of a 10-minute warm-up that included walking or cycling; calisthenics and stretching; nine exercises (leg press, chest press, leg extension, seated row, seated leg curl, abdominal flexion, biceps curl, low-back extension, and triceps extension) for different muscular groups; and finished with a 10-minute cool-down. The load for each exercise was based on the one repetition maximum (1RM) test. Subjects performed two sets of 12-15 repetitions (reps.) at 50-60% of the 1RM, or RPE 4-6, during the first month. After this month, the 1RM was measured again and the load was increased to 80% of the 1RM, or RPE 7-8. At this intensity, subjects performed two sets of 8-12 reps. Every two months, the 1RM was measured in order to keep the training stimulus consistently at 80% of the 1RM, or RPE 7-8.

Waiting list. During the study period, individuals randomized to the WL group were contacted by phone every four months to certify that they were still interested in participating in the study. At these intervals, they were also asked not to change their lifestyle. After the eight-month observation period, they were invited to participate in specific exercise programs designed for seniors by the Faculty of Sport.

2.3. Measurements

2.3.1. Anthropometrics

Body weight was measured to the nearest 0.1kg with an electronic scale (*SECA 708*). Height was measured to the nearest 1 mm with a standard stadiometer. BMI was determined as weight divided by height squared (kg/m^2). Percent of total body fat (%BF), trunk fat (kg), and lean mass (kg) were determined by whole body scan using a dual-energy X-ray absorptiometry (DXA – Hologic QDR-4500, software for Windows XP, version 12.4) with subjects in the supine position. All scans were analyzed by the same investigator.

2.3.2. Biochemical Analysis

Biochemical analysis of the traditional CVD risk factors of plasma glucose, cholesterol (total, LDL-C, and HDL-C), and TG, were measured using standard enzymatic methods. hs-CRP levels were determined by means of particle-enhanced immunonephelometry using a BN™ II nephelometer (Dade Bhering).

2.3.3. Cytokine Measurements

Taking into account that the individuals included in this thesis had no diagnosed CVDs and, therefore, it is less probable that they have advanced atherosclerotic plaques (unstable plaque or plaque rupture), we opted to investigate cytokines that are thought to mark earlier phases of atherosclerosis such as, IL-6, IL-10, IFN-γ, and TNF-α (Vasan, 2006).

In order to assess these cytokines, a human multiplex immunoassay kit from Millipore was used according to the manufacturer's protocol. Briefly, 10 µl of plasma was diluted and assayed for IL-6, IL-10, IFN-γ, and TNF-α using specific antibodies (Abs) conjugated into beads and read on a Luminex 100 instrument

(Luminex). The concentration of each cytokine was determined by preparing a standard curve using standard cytokine concentrations. Results are expressed in picograms per milliliter. The detection levels of these Abs were between 1 and 5 pg/ml with little or no cross-reactivity among the Abs.

2.3.4. Resting Blood Pressure and Heart Rate

Resting BP and heart rate (HR) were measured using an automated blood pressure monitor (Colin, DP 8800). After 15 minutes at rest in a quiet, temperature-controlled room, BP measurements were taken with the subjects seated in an upright position with an arm comfortably placed at heart level. The average of three measures for SBP, DBP, and HR were entered as data. The analyses were conducted between 8:00 am and 11:00 am, by the same investigator.

2.3.5. *Autonomic Function*

Autonomic function was evaluated using HRV analysis. After a 15-minute supine rest, the R-R intervals were recorded over a short period of five minutes with a Polar recorder (Polar NV vantage, Finland). The HF and LF components of FD were chosen to evaluate vagal and vagal/sympathetic activity. Since the standard deviation of normal RR intervals (SDRR), a component of TD, is also recommended in investigative recordings of short duration, it was used to assess the total HRV (Malik, et al., 1996). Data were saved and filtered using an automatic procedure for further analysis of HRV with Polar Precision Performance software version 2.0 (Polar Electro Oy, Kempele, Finland). Data with more than a 5% error were not considered in statistical analyses.

2.3.6. Physical and Functional Fitness Assessment

The Senior Fitness Test (SFT) (Rikli & Jones, 1999) was used to assess physical fitness in the pilot study. This battery consists of six assessment items designed to assess the physiological parameters that support physical functionality and mobility in older adults. The test items include lower body muscular endurance (30-second chair stand), upper body muscular endurance

(30-second arm curl), aerobic endurance (6MWT), lower body flexibility (chair sit-and-reach), upper body flexibility (back to stretch), and dynamic balance and agility (the 8-foot up and go [8FUG]).

Of those above mentioned tests, only the 6MWT and the 8FUG were maintained in the RCT studies for assessment of functional fitness. The 30-second arm curl test was replaced by the hand-grip strength test because it has been widely used as a surrogate measure of total body strength (Herman, et al., 2005), and thus permitting comparisons of results across a greater number of studies. Moreover, among older adults, hand-grip strength has been shown to correlate with a decline in the activities of daily living and cognition (Taekema, Gussekloo, Maier, Westendorp, & de Craen, 2010), markers of frailty (Syddall, Cooper, Martin, Briggs, & Aihie Sayer, 2003), and disability (Al Snih, Markides, Ottenbacher, & Raji, 2004). Since lower-limb power and strength seem to be important contributing factors to perform daily living activities rather than muscular endurance (Bean, et al., 2002), the 30-second chair stand, a test more close related with muscular endurance was replaced by the sit-to-stand five times and the stair ascent tests which have been demonstrated to be more related with lower-limb muscular strength and power (Bean, et al., 2002; Tiedemann, Sherrington, & Lord, 2007; VanSwearingen & Brach, 2001). Finally, taking into account that flexibility was not the priority in the designed exercise training programs, we decided to not assess this fitness component. The descriptions of the tests used to evaluate fitness in the descriptive correlational and RCT studies are described in the specific methods section of each study

2.3.7. Health-related Quality of Life

The HRQoL of older adults was subjectively assessed using the Medical Outcomes Study 36-Item Short-Form Health Study questionnaire (SF-36) adapted and validated for the Portuguese population (Ferreira, 1998), which was applied through personal interview. The SF-36 comprises eight health concepts: physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE), and mental health (MH). These eight concepts can be aggregated into two components, the SF-36 Physical Component Summary (PCS) and Mental Component Summary (MCS). There is also a single separate item that is used to assess any change in health from the previous year.

In Study V, norm-based scores for the SF-36 were calculated using the methods set out by Ware et al. (1993) and Ware and Kosinski (2001). In the norm-based scales and components, a score of 50 represents the mean. Therefore, all scores above or below 50 can be interpreted as above or below normal for the general population (United States population).

2.3.8. Daily Physical Activity

In the pilot study, daily PA levels were assessed using the Baecke (Baecke, Burema, & Frijters, 1982) modified physical activity questionnaire (Voorrips, Ravelli, Dongelmans, Deurenberg, & Van Staveren, 1991). This questionnaire evaluates and generates scores in household activities, sporting activities and other physically active leisure-time activities, which together result in a PA score. Although the Baecke questionnaire has been shown to generate valid and reliable classification scores for activity in older subjects when completed during a personal interview, in the pilot study some older women had difficulty quantifying the time spent on PA. Therefore, we opted to use an objective measure to assess the PA levels of the participants in Studies III, IV and V.

In these studies, daily PA levels were assessed using accelerometers (Actigraph GT1M, Actigraph LLC, Pensacola, FL). The Actigraph accelerometer is a uniaxial monitor that measures the intensity of movement averaged over 1-min sampling intervals called 'epochs.' Data from each monitor was downloaded by the investigator and compared with data from a diary before the average counts/min were calculated. This unit measurement (counts/min) was generated based on the magnitude and frequency of movement (Mark & Janssen, 2008).

2.3.9. *Energy Intake*

The lack of control of energy intake in the pilot study might have induced misinterpretation of the body composition results, thus, this potential confounder was assessed in the other studies using a four-day dietary record (three weekdays and one weekend day) at two points (before and after the intervention). Dietary records were analyzed using an adapted Portuguese version of the software Food Processor Plus® (ESHA Research Inc, Salem, Oregon, USA), a nutritional analysis program that converts food intake into total energy and nutrients based on food composition tables available from the United States Department of Agriculture and national data on typical Portuguese foods.

2.4. Data Analysis

Means and standard deviations (M±SD) were computed for the variables with normal distribution and median with percentiles 25 and 75 (Md, 25th percentile – 75th percentile) computed when normal distribution was not verified. To better describe the subjects, the frequencies and percentages of the main characteristics were also calculated. The normality of distribution was determined by a Kolmogorov-Smirnov or Shapiro-Wilk test.

To assess the relationship between variables, Pearson (*r*) or Spearman's *rho* correlation coefficients were used. To examine the predictive value of the 6MWT, whenever risk factors and resting cardiovascular parameters related with performance on the 6MWT, linear regression analyses were employed. Logistic regression models were used to estimate the odds ratio (OR) of scoring in the highest quartile of each HRQoL domain per quartile increase in each of the PA and physical fitness index scores.

The Mann–Whitney *U* test was used for gender comparisons. Between-group differences in baseline values were determined using one-way analysis of variance (ANOVA). When a significant main effect was detected at a significance level of $P<0.05$, the Bonferonni correction was used for post-hoc comparison. In order to detect changes within groups across time, the paired *t*-

test or the one-way ANOVA for repeated measures was employed. In this case, when a significant main effect was detected at a significance level of $P<0.05$, the Tukey test was used for post-hoc comparisons.

The pre-to-post changes (Δ) for each subject were related to the individual baseline level to define the relative change (%Δ = [(post-test score – pretest score)/ pre-test score] x 100) in all selected variables. General Linear Models were used with relative change as the dependent variable and group as the fixed factor. Afterwards, covariates were inserted into the models. Finally, the Mann-Whitney *U* test was used to observe, in each group, differences between dropouts and compliant subjects.

Analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 16.0 or 17.0 for Windows, Chicago, IL) accepting the 0.05 level of probability as statistically significant. Post-hoc power analyses were performed to verify the effect size *f* on dependent outcomes included in this study, using G Power 3 for Windows (Faul, Erdfelder, Lang, & Buchner, 2007). A summary of the statistical tests used in each study is shown in Table 2.

Table 2. Statistical tests used in each study.

	Pearson (r)	Spearman (rho)	Linear Regression	Logistic Regression	Paired *t*-test	Mann-Witney *U* test	One-way Anova (repeated measures)	One-way Anova	General Linear Models
Study I							X		
Study II	X		X			X			
Study III		X		X		X			
Study IV					X	X		X	X
Study V	X				X	X		X	X

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CHAPTER III

STUDY I

Effects of a Moderate-intensity Walking Program on Blood Pressure, Body Composition and Functional Fitness in Older Women: results of a pilot study

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Effects of a Moderate-intensity Walking Program on Blood Pressure, Body Composition and Functional Fitness in Older Women: results of a pilot study

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Objective: The positive impact of regular physical activity among older adults is well recognized. However, few studies have assessed the effectiveness of walking exercise programs in older women with regard to their impact on physical fitness, body composition and resting blood pressure. Therefore, the aim of this pilot study was to evaluate the effects of a moderate-intensity walking program on the physical fitness body composition and resting blood pressure of older women. ***Design:*** Twenty-two older women (71.4±5.9 years; BMI= 27.7±2.6) not in the habit of regularly exercising volunteered to participate in this study. Subjects were evaluated at three distinct points in time: at baseline, after four months with no exercise, and after participating in a four month walking program. Habitual physical activity, blood pressure, heart rate, body composition (DXA) and physical fitness (Senior Fitness Test) were assessed each time. Training consisted of a 10 minute warm up, 30 minutes of walking at an intensity corresponding to 50-70% $HR_{Reserve}$ and ending with a 10 minute cool-down. ***Results:*** After walking, data demonstrated: i) a mean reduction of 12mmHg ($p = 0.001$) in the women's systolic blood pressure; ii) improvements of 5 repetitions ($p < 0.001$) on the muscular endurance of the lower limbs; iii) however, there were no significant alterations after the walking program on body composition variables. ***Conclusions:*** These findings suggest that a four month's walking program with progressive duration and moderate intensity is able to improve the blood pressure of older women and the muscular endurance of the lower limbs. *Arch Exerc Health Dis 1 (2):50-57*

Key Words: older adults, risk factors, functional fitness, aerobic training

INTRODUCTION

The likelihood of having a cardiovascular disease (CVD) is substantially higher in older individuals compared to younger ones, reflecting the effect of age as a cardiovascular risk factor and the increased prevalence of other antecedents of CVD in this age group (25). Despite the fact that cardio-respiratory fitness is not considered as an independent risk factor for CVD, it has been consistently reported that the risk for CVD is greater for the least fit individuals (6, 11, 15, 26, 30). Moreover, impairments to fitness are responsible for the inability to carry out activities of daily living which can lead to a loss of independence, reinforcing sedentary behaviours (14). Therefore, sustaining older adults' ability to live independently as well as reducing blood pressure (BP) and body weight via healthy lifestyle interventions are very important goals of public health, geriatrics, and gerontology.

To promote general health, guidelines and recommendations (3, 13, 40) for physical activity encourage adults to meet or exceed thirty minutes of moderate-intensity physical activity "most" days of the week. Unfortunately, the majority of older adults do not meet this recommendation. In Women's Health and Aging Studies I and II, just 12.7% of the women, aged 70-79 years, met the recommended guidelines for activity (21). Alarmingly, the Centre for Disease Control and Prevention (12) reported that 39.2% of women aged 70 and older have no leisure time physical activity.

Walking is an accessible form of physical activity and is a means of transportation for the vast majority of people regardless of age, gender and social status (36, 46). Furthermore, habitual walking (20, 31), brisk walking and walking programs (16, 42) seem to be effective in improving overall functional fitness and the profile for cardiovascular risk factors (CRF). However, the duration and intensity of walking needed to achieve optimal health-related benefits has not always been well controlled in the studies using interventional programs aiming to modify health-related outcomes, including cardiovascular risk factors and/or functional fitness

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associated with daily-living activities. In some of these studies, the interventional programs were home-based and lacking close control of walking intensity or duration (31). On the other hand, walking programs conducted in laboratory environment (18-19, 33) may not correspond to a natural walking pattern that could be incorporated in lifestyles of older women.

In this way, while the positive impact of regular physical activity among older adults is well recognized, the effects of supervised exercise programs, based mainly on walking with a progressive duration at a moderate intensity are less well known. Considering all the arguments mentioned above, the aim of this pilot study was to evaluate the effects of a moderate-intensity walking program on older women's physical fitness, body composition and resting BP. We hypothesized that a supervised walking-based exercise program with a progressive duration and moderate-intensity would be effective in improving physical fitness, body composition and resting BP of older women.

DESIGN AND METHODS

Participants and Study Design

The study design is presented in figure 1. Community-dwelling and independent older women were recruited in the Porto area through advertisements in newspapers. At the screening, participants completed a health history questionnaire to record past and present conditions and medications.

The selection criteria of the sample were the following: (i) older than 64 years; (ii) not have participated in regular exercise training in the previous six months, which means not having been involved in supervised exercise of moderate to vigorous intensity for 20 minutes or more at least twice a week; (iii) no present acute or terminal illness; (iv) no severe or uncontrolled hypertension or any cardiovascular and/or respiratory disorder; (v) no neurological, skeletal-muscular or joint disorder or disturbance that precludes participation in exercise; (vi) not be under pharmacological therapies that could compromise safety during exercise or influence the responses of cardiovascular function.

Thirty-one women volunteered to participate in the study. From these, nine subjects were excluded because they didn't fully meet the selection criteria. Thus, only twenty-two women (aged 71.4 ± 5.9 years, BMI= 27.7 ± 2.6) initiated the study protocols. Those included in this longitudinal study acted as their own control by taking part in a four month control period followed by the four month walking program, comprising 48 sessions. An attendance rate of at least 80% of the previewed walking sessions had to be accomplished by the subjects in order to consider the training program complete. Additionally, older women who were absent for eight or more consecutive sessions were also excluded.

Data were collected for all variables at baseline (M1), after the four month control period (M2), and finally, at the end of the four month walking program (M3).

In order to characterise participants' habitual physical activity and to identify possible changes in this potential confounder during the study period, a questionnaire based on the Baecke questionnaire (4) and validated for older populations (45) was applied to all the subjects at three points in time. Participants were instructed not to change their daily physical activity routines or dietary patterns during the course of the study.

According to the Helsinki Declaration, the nature, benefits, and risks of the study were explained to the volunteers, and their written informed consent was obtained. All methods and procedures were approved by the Institutional Review Board.

Training Protocol

The length of the walking program was three times/week for four months, with each exercise session lasting approximately fifty min. Training workouts consisted of a ten minute warm-up, thirty minutes of walking at an intensity corresponding to 50-70% HRreserve, and ending with a ten minute cool-down.

In order to raise the subject's functional fitness so that they were able to sustain thirty minutes of continuous walking at the targeted intensity, the training load was gradually increased during the first four weeks. The walking duration in the first session was fifteen minutes at 50-70% HRreserve, and it was increased by five minutes each week until subjects were able to walk continuously for thirty minutes (week 4). In order to be sure that the subjects were exercising at the targeted intensity, Polar Heart Rate Monitors (Polar Team System, Finland) were used.

Measurements

During assessment, the test administrator and the time of day used for collection remained constant.

Anthropometrics and Body Composition

Body weight was measured to the nearest 0.1kg with an electronic weight scale (SECA 708). Subjects were weighed barefoot wearing light clothing. Height was measured to the nearest 1mm with a standard stadiometer.

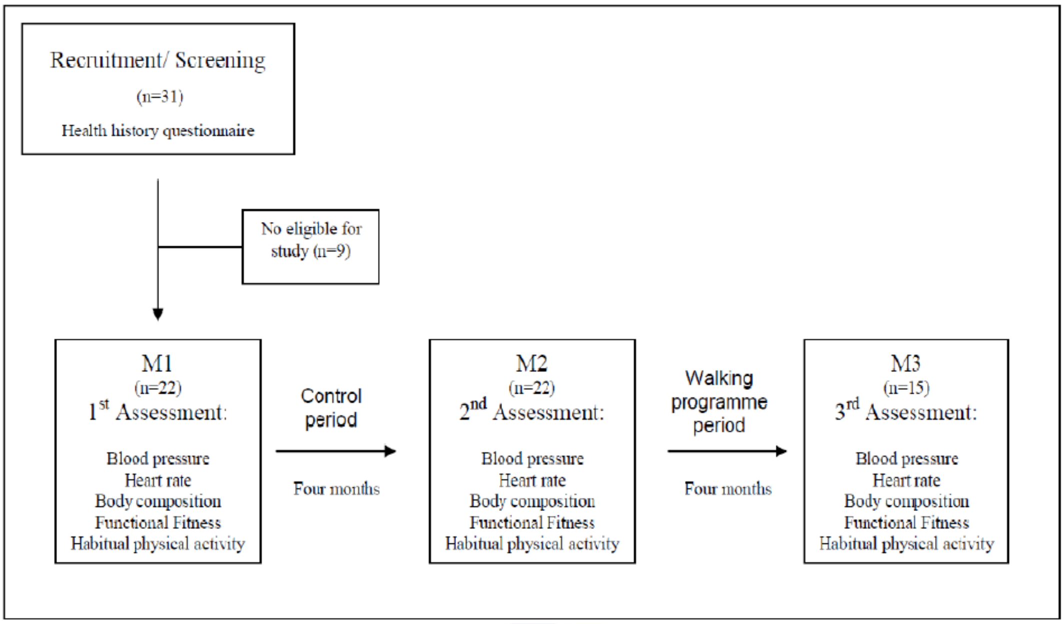

Figure 1. Study Design.

Body Mass Index (BMI) was determined as weight divided by height squared (kg/m2).

Whole body lean mass (LM), percentage of total body fat (%BF) and trunk fat were determined by whole body scan using a Dual-energy X-ray Absorptiometry (DXA – Hologic QDR-4500, software for Windows XP, version 12.4) with subjects in the supine position. All scans were analyzed by the same investigator. The rationale of body composition analysis with DXA is described elsewhere (22).

Blood Pressure and Heart Rate

Resting BP and heart rate (HR) were measured in the right arm with an automated blood pressure monitor (Colin, DP 8800). After being at rest for fifteen minutes in an upright seated position in a quiet, temperature-controlled room, BP measurements were taken with the subjects seated in an upright position with the arm comfortably placed at heart level. The average of three measurements for SBP, DBP, and HR were entered as data. The measurements were performed between 8:00 am and 11:00 am, by the same investigator.

Questionnaire (Habitual Physical Activity)

Daily Physical activity (PA) levels were assessed using the Baecke modified physical activity questionnaire (45), which has been shown to generate valid and reliable classification scores for activity in older subjects. The questionnaire evaluates and generates scores of household activities, sporting activities and other physically active leisure time activities, altogether resulting in a physical activity score. The questionnaires were completed by the same researcher during a personal interview.

Physical Fitness Assessment

The Senior Fitness Test (SFT) (the eight foot up and go to) was used to assess physical fitness (39). This battery consists of 6 assessment items, designed and validated ($0.77 \leq r \leq 0.83$) to assess the physiological parameters that support physical functionality and mobility in older adults (39). The test items include lower body muscular endurance (thirty second chair stand), upper body muscular endurance (thirty second arm curl), aerobic endurance (six minute walk test), lower body flexibility (chair sit-and-reach), and dynamic balance and agility (the eight foot up-and-go to assess) (14). In our laboratory, the test-retest reliability for SFT was established in 15 subjects (68.6 ± 5.8 years; BMI=27.6 ± 3.0 Kg/m2) tested in two sessions separated by 12 days; all tests showed good reliability ($0.92 \leq ICC \leq 0.96$).

All test stations were organized in a circuit, and the same conditions were maintained for each test at all testing periods. On the testing days, subjects first completed an eight to ten minute warm-up led by a

Table 1. Weight, Percent Body Fat (%BF), Trunk Fat, Lean Mass (LM), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Heart Rate (HR): Mean ± SD on different moments (M1, M2, and M3).

Outcomes	M1	M2	M3	Overall *F* values	Overall *p* values
Weight (kg)	66.1 ± 7.4	64.3 ± 6.1	63.4 ± 6.6	0.111	0.895
%BF	38.9 ± 4.1	40.2 ± 3.9	39.5 ± 4.2	0.077	0.926
Trunk Fat (kg)	11.63 + 3.02	13.01 + 3.30	13.06 + 3.23	0.860	0.431
LM (kg)	39.96 ± 3.70	38.86 ± 3.55	39.64 ± 3.78	0.354	0.704
SBP (mmHg)	142.8 ± 11.1	136.1 ± 14.0	124.1 ± 12.4†‡	7.964	0.001
DBP (mmHg)	75.1 ± 4.8	70.5 ± 3.9*	65.3 ± 4.8†‡	8.418	0.001
HR (bpm)	66 ±10	68 ±12	68 ± 9	0.250	0.780

* Significant difference from M1 to M2 ($p<0.05$); †Significant difference from M1 to M3 ($p<0.05$); ‡Significant difference from M2 to M3 ($p<0.05$)

physical education instructor and then completed all the test items.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 16) for Windows. The Shapiro-Wilk test was used to ascertain the normality of data distributions on all variables. One-Way ANOVA for repeated measures was used to compare means across time. The Tukey test was used for Post-hoc comparisons. The 0.05 level of probability was accepted as significant. Post hoc power analyses were performed to verify the effect size f on dependent outcomes included in this study, using G Power 3 for Windows (17).

RESULTS

Of the 22 participants who underwent the initial assessment, two subjects were excluded from the study because they exceeded a 20% rate of absence and one subject failed the post-training assessment. Therefore, compliance was 86.4%, meaning that 19 individuals with a mean age of 71.4 ± 5.9 years completed the program.

Of the 19 women, three have diagnosed osteoporosis, six are hypertensive (controlled by angiotensin-1 converting enzyme inhibitor – n=3, and diuretics – n=3), three have controlled dislipidaemia (under statins), and one is diabetic (controlled). Two are taking medication for depression, and one is undertaking hormone replacement therapy.

At baseline, the women presented 142.8 ± 11.1/ 75.1 ± 4.8mmHg for SBP and DBP, respectively (table1). Considering their mean baseline BMI (27.7 ± 2.9 Kg/cm²) values they are classified as overweight. At the fitness assessment, they had performed at or above normative values (38) in the greater part of the tests (table 2). No significant changes were observed in body weight, %BF, trunk fat, LM or HR across the eight months, but significant decreases in SBP and DBP were detected (table 1). The mean SBP at the end of the program (M3) was significantly lower than the SBP at M1 and M2. A different pattern was observed for the mean DBP, which lowered across the three time points (table 1).

Physical fitness performance was maintained or significantly decreased (upper body muscular endurance) between M1 and M2 (table 2). On the contrary, between M2 and M3, significant improvements were found on lower body muscular endurance.

Physical activity patterns did not change between M1 (2.77 ± 1.59) and M2 (3.23 ± 2.56). As was expected, between M2 and M3 (5.61 ± 1.64) a significant increase (2.38; $p<0.001$) in the total amount of older women's physical activity was observed. However, when we subtracted the walking program score of each participant's total score, the physical activity score differences disappeared, which means that the observed increase in total physical activity corresponds to the addition of the walking program to the women´s routine.

Post hoc power analysis for a sample size of 19 subjects, setting α as 0.05, with a power of 1.0 obtained an effect size f of 1.45; 1.52; 0.41; 0.65; 0.95; 0.85; 1.14; 2.20; 1.31, for SBP, DBP, weight,

Table 2. Physical Fitness: Mean ± SD on different moments (M1, M2, and M3).

Physical Fitness Components	M1	M2	M3	Overall *F* values	Overall *p* values
Lower body muscular endurance (reps)	13.6 ± 2.2	13.9 ± 2.7	18.3 ± 2.3†,‡	16.465	<0.001
Upper body muscular endurance (reps)	21.1 ± 3.8	16.7 ± 1.4*	18.3 ± 2.3	5.929	0.006
Lower body flexibility (cm)	-9.5 ± 9.1	-4.8 ± 11.1	-0.88 ±4.7	2.414	0.103
Upper body flexibility (cm)	-6.32 ± 12.1	-6.4± 12.4	-5.4 ± 8.6	0.036	0.964
Dynamic balance and agility (sec.)	5.76 ±1.0	6.62 ± 1.1	6.3 ± 0.9	0.515	0.602
Aerobic endurance (m)	471.9 ± 51.2	493.2 ± 56.8	485.7 ± 58.1	0.072	0.931

* Significant difference from M1 to M2 (p<0.05); †Significant difference from M1 to M3 (p<0.05); ‡Significant difference from M2 to M3 (p<0.05)

%BF, trunk fat, lean mass, lower-body flexibility, lower-body strength, and upper-body strength, respectively. Adopting α=0.05 with a power of 0.99 agility/balance demonstrated an effect size f of 0.557. Adopting α=0.05 with a power of 0.191, upper-body flexibility demonstrated an effect size f of 0.20. Finally, adopting α=0.05 with a power of 0.54 aerobic fitness obtained an effect size f of 0.24. These results from the post hoc power analysis demonstrate that this sample size of 19 subjects (adopting α=0.05) was large enough to detect medium to large effects in almost all outcomes (with the exception of Upper-body flexibility and Aerobic fitness).

DISCUSSION

The main findings of this pilot study are that a simple and feasible moderate-intensity walking program has beneficial and significant effects on older women's lower body muscular endurance and blood pressure (SBP and DBP). Walking is a popular form of moderate-intensity physical activity that has been linked with many health benefits (34). Despite the epidemiologically strong evidence, only a few experimental studies have observed the effects of moderate-intensity walking on older women's functional fitness, body composition and resting blood pressure.

Similar to other investigations (42), the present study demonstrated that thirty minutes of moderate-intensity walking, three times/week was able to improve important components of physical fitness, namely, muscular endurance in the lower limbs. This is of importance since greater age-related declines in muscle strength of the lower extremities compared to the upper extremities have been described in previous studies (9, 27). Moreover, deficits in lower limb strength, muscular endurance and power are closely related to functional limitations (10), such as impairments to the ability to walk (5), getting in and out of a chair, the speed of climbing steps, and the number of falls in older adults (10). Besides this important fitness improvement, no statistically significant differences were found in the other physical fitness components evaluated.

Many studies have demonstrated that endurance training is effective in improving fitness (19, 34, 37, 47). However, these studies differ from the present one in many aspects such as the subjects' age (34, 47) and gender (41), volume and/or intensity of training (19, 34, 37) and the type of exercise (47). In this way, the lack of significant improvements in those functional fitness components after walking training could be due to different reasons: (i) lack of specificity of the stimulus for these components and (ii) the relatively high conditioning of the sample before the start of the training period. Moreover, concerning aerobic fitness, Kervio et al. (23) observed a learning effect (increase of ~21m) between the first and second six minute walk test trials. These authors highlighted the necessity of a familiarization to the six minute walk test, intending to limit the skill effect in healthy elderly subjects. The American Thoracic Society also suggested in its Institutional Guidelines for the six minute walk test an extra trial to minimize intraday variability (2). The authors strongly believe that this was the main reason besides the improvement (non significant) in the six minute walk test between M1 and M2 and the lack of significant improvement between M2 and M3. Unfortunately, extra trials were not performed in this pilot study. But, authors strongly recommend that next researchers adopt at least an extra trial before the real six minute walk test has

been conducted.
Results show a gradual decrease in SBP and DBP across the eight months. The not expected (and non significant) differences observed in blood pressure between M1 and M2 could be attributed to the "White coat effect". This term refers to an alert reaction which increases basal blood pressure in some individuals (43). The white coat hypertension is a common finding in the population at large (35) but the difference between clinic and ambulatory blood pressure seems to be more pronounced in older patients (1). Generally, the white coat effect occurs in clinical settings but it also happens in response to the environment of the measurement (35). Once, since the subjects did not know the place and the evaluators at baseline, it is not uncommon to observe some kind of nervous and anxiety. Finally, we want to reinforce that the difference in SBP between M2 and M3 was about -12mmHg, almost twice the difference observed between M1 and M2 (7mmHg). The authors do not believe that such a decrease in blood pressure (12mmHg) would happen if no interventions (i.e., exercise, diet or medication change) were implemented. Subjects did not refer any change in medication during the eight months and they attested that they did not alter their nutritional habits. Thus, their changes in exercising habits seem to be the plausible mechanism to lower blood pressure levels between M2 and M3. In agreement with this idea, previous studies (21, 42) described a decrease in SBP and DBP after training. Increased SBP and decreased DBP are characteristic of an aging population (8). On the other hand, as observed in our study, exercise seems to counter-act these age-related alterations, especially on SBP (32-33). Although the mechanisms underlying the lowering effect of exercise on SBP are not fully understood, neuro-hormonal (7, 36), structural (vascular remodelling and angiogenesis) and functional vascular adaptations were recently proposed as possible mechanisms (36). As functional adaptations, it was suggested that aerobic training may possibly: (i) reduce sympathetic nervous activity and the subsequent release of norepinephrine (7), (ii) lower endothelin-1 levels (28), and (iii) increase nitric oxide production (38, 40), together, therefore, reducing vasoconstriction and peripheral vascular resistance (7, 29).
However, despite the fact that the depressor effect of exercise on BP has been attributed to factors such as body composition, many studies (32-33), such as the present study, suggest that, independent of body weight and/or adiposity changes, exercise is effective in lowering BP. Nevertheless, some studies have found significant weight or body fat reductions (19, 41); the majority of them found, as in the present study, minimal (18, 37) or no changes at all (24, 33). These studies, which reported significant changes in body composition, had a greater training volume (≥3 hours/week) and duration (28-52-weeks) than ours. Furthermore, although subjects were instructed to maintain their normal dietary routines throughout the protocol period, this was not strictly controlled. So, it is possible that the participants in our study increased their energy intake in response to the energy demands of exercise training. Although the walking program could not improve body composition, upper body muscular endurance, aerobic endurance, upper and lower body flexibility, dynamic balance and agility in a statistical way, the fact that it could potentially attenuate the decrease in fitness and the increase in body fat mass observed in normal aging merits attention.
The major limitations of this pilot study are: (i) the lack of extra trials before the "true" six minute walk test; (ii) the lack of concurrent measures of dietary habits and food consumption; (iii) self-reported physical activity is a subjective measure that may have been influenced by cognitive status and perceived mastery (44); (iv) our study population was small and limited to healthy old women and thus cannot be considered representative of a normal aging population; and finally (v) there was no separate or randomized control group. Hence the change in the outcomes cannot be fully attributed to the walking intervention.
Considering the above-mentioned limitations, the findings of this pilot study lead us to conclude that a moderate-intensity walking program can improve lower limb muscular endurance and can lower blood pressure. However, for future research, we recommend a larger sample, the use of different intensities and duration protocols, and an investigation of other outcomes related to CVD risk factors in order to make a stronger relationship between exercise and more favourable cardiovascular health in community-dwelling older women possible.

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CHAPTER IV

STUDY II

Six-minute walk distance (6MWD) is associated with body fat, systolic blood pressure, and rate-pressure product in community-dwelling elderly subjects

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ABSTRACT

This study aimed to determine if aerobic fitness assessed by 6MWD is able to predict resting cardiovascular function and cardiovascular disease risk factors (CVDRF). One hundred and five old individuals were analyzed: aerobic fitness (6MWD), body composition (DXA), blood pressure (BP), resting heart rate (HR_{rest}) and rate-pressure product (RPP_{rest}) were evaluated. Pearson correlation analysis was used to assess the relationship between 6MWD, resting cardiovascular function and CVDRF. To examine the shared variance between 6MWD, cardiac function, and CVDRF, linear regression analyses were employed. Inverse associations were observed between 6MWD and age ($r = -0.405$; $p < 0.001$), percent body fat (%BF) ($r = -0.472$; $p < 0.001$), trunk fat ($r = -0.234$; $p = 0.020$), systolic blood pressure (SBP) ($r = -0.307$; $p = 0.002$), HR_{rest} ($r = -0.248$; $p = 0.013$), and RPP_{rest} ($r = -0.400$; $p < 0.001$). In simple linear regressions, except the diastolic blood pressure (DBP), the 6MWD correlated ($0.001 \geq p \leq 0.020$) with all investigated parameters. When models were adjusted (for age and sex), the 6MWD remained associated with %BF ($p < 0.001$), SBP ($0.002 \geq p \leq 0.009$) and RPP_{rest} ($0.001 \geq p \leq 0.002$). Our study reinforces the idea that a worse cardiovascular profile is related with lower fitness. Furthermore, it supports the potential of 6MWD to identify adverse outcomes such as %BF, increased SBP and higher RPP_{rest} in older adults.

1. Introduction

Cardiovascular disease (CVD) and its related comorbidities remain a significant and growing public health problem, especially in older individuals (Pilote et al., 2007). Recent emphasis has been placed on the understanding of risk factors role for CVD progression and in predicting CVD morbidity and mortality (Christou et al., 2005). Several prospective studies have found an interaction of many factors associated with aging that may contribute to the high prevalence of CVD observed in older adults. These factors include increased general and central adiposity, decreased physical activity, and progressive arterial stiffening (Going et al., 1994; Guo et al., 1999; Luuk and Pihl, 2003; Pescatello et al., 2004). Since an increased number of older adults are becoming inactive and unfit, this knowledge is paramount for the implementation of effective public health policy, prevention strategies, and patient management.

Aging and/or inactivity leads to increased arterial stiffness that could explain increase in blood pressure (BP) levels and high prevalence of hypertension in old individuals. Hypertension is associated with an increased incidence of all-cause and CVD mortality and morbidity such as, stroke, coronary heart disease, and renal failure (Rosamond et al., 2007). In addition, it is well established that fatness is closely related to other metabolic risk factors and contribute largely to CVD prevalence in elderly subjects (Going et al., 1994; Williams et al., 1997; Sardinha et al., 2000).

Although many studies have examined the association between aerobic fitness with blood pressure, and adiposity, only few have specifically targeted older subjects (Reaven et al., 1991; Dvorak et al., 2000; Krause et al., 2007). Therefore, a clear need exists to determine whether aerobic fitness contributes to CVDRF in older adults.

Age-related increases on SBP and heart rate at rest (HR_{rest}) are expected to impair cardiovascular function. This impairment could be observed as an increase on resting myocardial oxygen demand (Czernin et al., 1993). It has been observed that rate-pressure product at rest (RPP_{rest}), considered as the best indirect method to measure myocardial oxygen consumption (May and Nagle, 1984), increases with age. However, this increase in RPP_{rest} was suggested to be ascribed to a more sedentary lifestyle observed in the older population (Czernin et al., 1995) and it is not a merely result of aging per se. Therefore, it is possible that fitter older individuals have a decreased myocardial oxygen demand at rest when compared with their less fit peers.

The available data reporting the importance of aerobic fitness in elderly subjects to specific CVDRF and resting cardiovascular

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function are equivocal (Christou et al., 2005). Among others, these conflicting results are likely to be attributable to the different methodologies used to evaluate older population. In fact, the great majority of epidemiological studies had used less accurate anthropometric estimates such as, skin folds, body mass index (BMI) and bioimpedance, to assess fatness, underestimating, therefore, body fat content (Bemben et al., 1998) and confounding the true relationship between fatness and aerobic fitness. Furthermore, although VO_{2max} protocols are widely used to access aerobic fitness as an important predictor for CVD-mortality (Laukkanen et al., 2004), it was observed that one in five older adults is unable to perform the classical laboratory tests (Bautmans et al., 2004). On the other hand, the 6MWD-test is a simple, safe, low-cost valid and reliable (ICC = 0.93, test–retest reliability = $-0.71 < r > 0.82$) alternative tool (Rikli and Jones, 1998; Kervio et al., 2003; Bautmans et al., 2004) to evaluate fitness at levels corresponding to the efforts commonly performed in daily-life activities by elderly (Bautmans et al., 2004). Accordingly, the purpose of the present study was to verify if aerobic fitness assessed by this simple functional test is able to predict cardiovascular function at rest and CVD risk factors.

2. Subjects and methods

2.1. Subjects

One hundred and five independent community-dwelling subjects in the age range of 61–85 years were recruited in the Porto area through advertisements in newspapers. At the screening, participants completed a health history questionnaire to record past and present conditions. The exclusion criteria were the following: registered blindness, severe hearing impairment, uncontrolled hypertension or diabetes, symptomatic cardiorespiratory disease, severe renal or hepatic disease, uncontrolled epilepsy, progressive neurological disease, chronic disabling arthritis. The nature, benefits, and risks of the study were explained to the volunteers, and their written informed consent was obtained before the study, consistent with the Helsinki Declaration and all methods and procedures were approved by the Institutional Scientific Board.

2.2. Weight, height, and body composition

Body weight was measured to the nearest 0.1 kg with an electronic weight scale (SECA 708). Subjects were weighed barefoot wearing light clothing. Height was measured to the nearest 1 mm with a standard stadiometer. Body composition was determined using a Dual-energy X-ray Absorptiometry (DXA, Hologic QDR-4500, software for windows XP, version 12.4) with subjects in the supine position. All total body scans were analyzed by the same investigator and provided measures of %BF and trunk fat (kg). The principles behind body composition analyses with DXA are explained elsewhere (Kelly et al., 1998).

2.3. Resting BP and heart rate (HR_{rest})

Resting BP and HR were measured by an automated blood pressure monitor (Colin, DP 8800). After being 15 min at supine rest in a quiet, temperature-controlled room, BP measurements were taken with the subjects seated in an upright position with the arm comfortably placed at heart level. Average of three measures for SBP, DBP, and HR entered as data. The analyses were conducted between 8:00 and 11:00 am, by the same investigator. Rate-pressure product (RPP = HR × SBP, arbitrary units), a good predictor of myocardial oxygen demand (Overend et al., 2000) was also calculated.

2.4. Assessment of aerobic fitness

Aerobic fitness was assessed using the 6MWD-test which is a commonly used physical performance measure in research (Lord and Menz, 2002) specially to obtain valid measures of submaximal (80% VO_{2max}) physical endurance in older adults (Rikli and Jones, 1998; Kervio et al., 2003). This test measures the distance covered when subjects are instructed to walk as quickly as they can for 6 min. Walks were conducted in a flat 50-m rectangular course, marked off in 5-m segments. If necessary, subjects were allowed to stop and rest.

2.5. Statistical analysis

Descriptive statistics (mean ± S.D.) were computed for the following variables: age, weight, height, %BF, trunk fat, HR_{rest}, RPP_{rest}, SBP, DBP, and cardiovascular fitness. The Kolmogorov–Smirnov test of normality was used to determine that the distribution of the sample data was parametric. For gender comparisons the Mann–Whitney U-test was used. To assess the relationship between performance in 6MWD-test and CVD risk factors (measures of body composition, SBP, DBP) and resting cardiovascular function (HR, RPP) the Pearson correlation coefficients were used. To examine the predictive value of the 6MWD, wherever risk factors and resting cardiovascular parameters related with performance on the 6MWD-test, simple linear regression analyses, and multiple regression analyses adjusting for age, gender, and age plus gender were employed. In these analyses, the performance in the 6MWD-test, measures of %BF, trunk fat, SBP, DBP, HR_{rest}, and RPP_{rest} were entered as continuous data.

All analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 17) for Windows. The $p < 0.05$ level of probability was accepted as statistical significant for all analyses.

3. Results

A total of 105 Caucasian old-aged subjects, 78 women (68.9 ± 5.5 years) and 27 men (69.1 ± 5.1 years), volunteered to participate in this study. On this sample, both men (27.9 ± 5.1%) and women (38.7 ± 3.6%) had high body fat content, their mean blood pressure was 137.6 ± 15.7 mmHg for SBP and 74.0 ± 8.1 mmHg for DBP, classified as borderline hypertensive subjects. As expected, men were taller ($p < 0.001$), heavier ($p < 0.001$) and fitter ($p = 0.001$) than women, and on the other hand, women were fatter ($p < 0.001$) than men. No gender differences were observed on BP neither on HR_{rest}. Characteristics of study sample and gender-specific mean ± S.D. for age, weight, height, body composition variables, blood pressure, HR_{rest}, RPP_{rest}, and cardiovascular fitness are summarized in Table 1.

Older individuals showed poor performance in the 6MWD-test since aerobic fitness was significantly and inversely associated

Table 1
Descriptive characteristics of study sample, mean ± S.D.

Parameters	Older adults	Female	Male
Number	105	78	27
Age (years)	68.9 ± 5.4	68.9 ± 5.6	69.1 ± 5.1
Weight (kg)	69.6 ± 13.1	66.2 ± 9.5*	79.6 ± 16.7*
Height (m)	1.57 ± 0.8	1.53 ± 0.06*	1.68 ± 0.05*
%BF	35.9 ± 6.9	38.7 ± 3.6*	27.9 ± 5.1*
Trunk fat (kg)	11.71 ± 3.7	12.1 ± 3.6*	10.3 ± 3.9*
Resting SBP (mmHg)	137.6 ± 15.7	138.7 ± 16.4	134.5 ± 13.1
Resting DBP (mmHg)	74.0 ± 8.1	73.8 ± 8.9	74.8 ± 5.8
HR_{rest} (bpm)	66.7 ± 9.8	67.5 ± 9.5	64.6 ± 10.4
RPP_{rest} (arbitrary units)	91713 ± 1612.7	9341.5 ± 1613.7	8685.8 ± 1536.5
6MWD (m)	537.8 ± 78.9	521.7 ± 71.5*	584.2 ± 82.6*

* Significant differences between genders ($p < 0.05$).

Table 2
Percentual amount of variance (R_a%) in risk factors explained by the models: unadjusted and adjusted for age and sex.

Variables dependent	Model A independent	Model B independent	Model C independent	Model D independent
%BF	6MWD*: 21.4*	6MWD*: 31.0* Age*	6MWD*: 51.4* Sex*	6MWD*: 53.5* Age* Sex*
Trunk fat (kg)	6MWD*: 4.5*	6MWD*: 10.0* Age*	6MWD: 5.3* Sex	6MWD*: 9.2* Age* Sex
SBP (mmHg)	6MWD*: 8.5*	6MWD*: 7.6* Age	6MWD*: 7.6* Sex	6MWD*: 6.6* Age Sex
DBP (mmHg)	6MWD: 4.0	6MWD: 8.6* Age	6MWD: 9.0 Sex	6MWD*: 9.9* Age* Sex
HR_{rest} (bpm)	6MWD: 5.2*	6MWD: 5.9 Age	6MWD: 4.5* Sex	6MWD: 4.0 Age Sex
RPP_{rest}	6MWD*: 15.1*	6MWD*: 14.2* Age	6MWD*: 14.5* Sex	6MWD*: 14.0* Age Sex

* Significant differences at $p < 0.05$.

with age ($r = -0.405$; $p < 0.001$). Inverse associations were also observed between 6MWD and %BF ($r = -0.472$; $p < 0.001$), trunk fat ($r = -0.234$; $p = 0.020$), SBP ($r = -0.307$; $p = 0.002$), HR_{rest} ($r = -0.248$; $p = 0.013$), and RPP_{rest} ($r = -0.400$; $p < 0.001$), meaning that fitter individuals have lower CVD risk profile as well as lower resting cardiovascular function. No association was found between 6MWD and weight ($r = -0.071$; $p = 0.481$) neither between 6MWD and DBP ($r = -0.062$; $p = 0.541$). Data from simple linear regression showed that 6MWD was significantly ($0.001 \geq p \leq 0.020$) associated with cardiovascular function at rest and all cardiovascular risk factors included in this study, with the exception of the DBP ($p = 0.541$). Additionally, multiple linear regression models showed that even when adjusted for age, sex, as well as age and sex together, the 6MWD remained significantly associated with %BF ($p < 0.001$), SBP ($0.002 \geq r \leq 0.009$), RPP_{rest} ($0.001 \geq r \leq 0.002$). The 6MWD alone explained 21.4% ($p < 0.001$), 4.5% ($p = 0.02$), 8.5% ($p = 0.002$), 5.2% ($p = 0.013$) and 15.1% ($p < 0.001$) of %BF, trunk fat, SBP, HR_{rest} and RPP_{rest} variance, respectively. Inserting age and sex in models increased to 53.5% ($p < 0.001$) the %BF variance explained by the model and to 9.2% ($p = 0.007$) the trunk fat variance. On the other hand, their inclusion diminished the total SBP (6.6%; $p = 0.023$) and RPP_{rest} (14.0%; $p = 0.001$) variance explained by the models. The total amount of variance explained by the models is shown in Table 2.

4. Discussion

In this study, it was demonstrated that in community-dwelling older adults, (1) 6MWD is associated with age, %BF, trunk fat, SBP, HR_{rest}, and RPP_{rest}; (2) 6MWD is able to identify individuals with high %BF, SBP, and RPP_{rest}, even after adjusting for age and sex.

Our results confirm the hypothesis that aerobic fitness is associated with several important cardiovascular risk factors and function. This kind of associations is generally investigated in middle-aged adults (Tulppo et al., 2003; Christou et al., 2005; Rankinen et al., 2007). For example, on HYPGENE cohort (Rankinen et al., 2007), aerobic fitness showed the strongest association with hypertension risk, each increment in fitness level was associated with 19% reductions on SBP. In another study (Carnethon et al., 2005), SBP was higher in subjects in the lowest fitness category, additionally it was also demonstrated consistent inverse associations between fitness, BMI and waist circumference. In middle age group associations between predicted VO_{2max} and %BF ($-0.390 \leq r \geq -0.590$), SBP ($-0.360 \leq r \geq -0.640$), HR ($-0.380 \leq r \geq -0.600$), and RPP ($-0.320 \leq r \geq -0.640$) were observed (Suzuki et al., 1998). Despite differences in age groups, the magnitude of these associations is very close to ours.

In agreement with our results, it was previously demonstrated that changes in aerobic fitness are positively associated with changes in cardiovascular function (Stewart et al., 2006). One possible explanation for this relationship is that an imbalance in the autonomic nervous system in favor of the sympathetic system, increases myocardial contractility, leading to a higher HR (Sajadieh et al., 2004), BP (Cook et al., 2006) and to an increased cardiac work load. Conversely, aerobic exercise training seems to increase parasympathetic tone and the withdrawal of sympathetic activity (Czernin et al., 1995), which is translated by a decrease in resting HR and BP (Iwasaki et al., 2003) and RPP_{rest} (May and Nagle, 1984). Recently (Kokkinos et al., 2007), it was observed that even moderate improvements in aerobic fitness achieved by moderate intensity physical activity can improve hemodynamic and cardiac performance and reduce the work of the left ventricle. To the best of our knowledge, only one study (Dvorak et al., 2000) targeting the associations between cardiovascular fitness and risk factors on older adults, demonstrated that older individuals with higher aerobic fitness were younger ($p < 0.001$), had lower %BF ($p < 0.001$), and trunk fat mass ($p < 0.001$) which is in agreement with our findings (Dvorak et al., 2000). Considering that aging is accompanied by increases in body fat content and taking into account the close relationship between body fat, in special, central fatness, with other metabolic CVD risk factors (Williams et al., 1997; Krause et al., 2007), this study support evidence on the importance of develop aerobic fitness in old populations.

Many studies have also attributed predictive value to aerobic fitness for CVD risk factors. For example, it was demonstrated (Laukkanen et al., 2004) that a given 1 MET increment in the VO_{2peak} reduces the risk of non-fatal coronary events and coronary deaths. It was also observed (McMurray et al., 1998) that individuals with low VO_{2max} increased their relative risk ratios (RR = 0.078; confidence interval = CI = 0.057–0.106) to be obese and hypertensive (RR = 0.119; CI = 0.065–0.220) when compared with fit individuals. However, besides middle-age sampling, the assessment of aerobic fitness in these cases used VO_{2max} as outcome, during maximal exercise testing. This procedure is expensive and time consuming, and, in many times, not feasible to apply in older adults (Bautmans et al., 2004). On the other hand, the 6MWD-test has been suggested as an alternative to cardiopulmonary exercise testing (Rostagno et al., 2003).

The 6MWD-test was firstly used in clinical settings to evaluate cardiopulmonary capacity and function in chronic diseases such as heart failure (Rostagno et al., 2003), chronic obstructive pulmonary disease (COPD) (Pinto-Plata et al., 2004), and pulmonary hypertension (Miyamoto et al., 2000). Previous studies (Miyamoto et al., 2000; Rostagno et al., 2003; Pinto-Plata et al., 2004) consistently demonstrated that 6MWD is a useful prognostic marker of mortality in CVD and COPD patients. Gradually, due to be considered a simple, safe, inexpensive (Rostagno et al., 2003) and valid test, it became popular in other settings. Nowadays, it is widely used to assess functionality in older "healthy" adults. Despite its popularity, until now, little information was available regarding its value in predicting risk factors on older community-dwelling adults.

Our study reinforces the idea that a worse cardiovascular profile, namely a higher %BF, trunk fat, SBP, is related with lower aerobic fitness in older adults. Moreover, it suggests that in older adults, elevated aerobic fitness levels are also correlated with a favorable cardiovascular function at rest. Therefore, supporting current guidelines, our results underline the need for the maintenance or improvement of aerobic fitness as a critical element for the overall strategy for reducing CVD risk. Thus, sedentary older individuals should be encouraged to enlarge their physical activity and improve their aerobic fitness, regardless of their age and sex.

Furthermore, our findings support the potential of 6MWD to identity adverse outcomes such as %BF, increased SBP and higher RPP_{rest} in community-dwelling older adults.

4.1. Study limitations

Some caution is warranted when interpreting the results of this study. First, the sample was comprised by volunteers and thus could not represent a randomized sample. In addition, considering that this is a cross-sectional study, it is not possible to provide evidences for causality from our results. Despite being an independent predictor for %BF, SBP and RPP_{rest}, the total variance explained for the 6MWD was modest. Finally, it is possible that 6MWD could better explain variability of other cardiovascular risk factors, not under investigation in the present study. So, although the key results provide some clue into the useful of 6MWD as CVD risk factor predictor in community-dwelling older subjects, additional evidence is needed to validate and build upon, along with other quantitative measures to address other outcomes related to CVD risk factors.

4.2. Strengths of the study

In spite of these criticisms, this study has several strengths including the investigation of a population in great risk for CVD, the valid and objective %BF assessment, and the use of an instrument which is, at the same time, practical and able to evaluate fitness at levels corresponding to efforts commonly performed by older individuals.

Conflict of interest statement

None.

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CHAPTER V

STUDY III

Associations between Objectively Assessed Physical Activity Levels and Fitness and Self-reported Health-related Quality of Life in Community-dwelling Older Adults

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Associations between objectively assessed physical activity levels and fitness and self-reported health-related quality of life in community-dwelling older adults

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Abstract

Background Previous studies investigated the associations between health-related quality of life (HRQoL) and self-reported physical activity (PA) and/or self-reported physical fitness which are not the most reliable methods to assess PA and fitness. Therefore, this study aimed to examine the associations between HRQoL and each of objectively assessed habitual PA and physical fitness.

Methods Eighty-five community-dwelling older adults (60–83 years) completed assessments for PA (counts/min and steps/day using accelerometers), physical fitness (six-minute walk test [6MWT] and hand-grip strength), and self-reported HRQoL (using the eight subscales of the SF-36). In adjusted logistic regression models, the upper quartile was compared against the lower three quartiles of scores on each HRQoL subscale. Results report the odds ratios that were significant in the adjusted models at $P < 0.05$.

Results Individuals with higher PA levels assessed by counts/min were more likely to score higher on physical functioning (PF) subscale (OR = 1.90). Individuals with superior 6MWT performance were more likely to score higher on PF (OR = 1.87), role limitations due to physical problems (RP) (OR = 1.95), and vitality (VT) (OR = 1.79). Individuals with superior hand-grip strength were more likely to score higher on RP (OR = 2.37) and VT (OR = 1.83).

Conclusions Objectively assessed PA and physical fitness measures were positively associated with physical health HRQoL subscales as reported by community-dwelling older adults.

Keywords Older adults · Physical fitness · Perceived health · Quality of life

Abbreviations

BMI	Body mass index
BP	Bodily pain
GH	General health
HRQoL	Health-related quality of life
M	Mean
MH	Mental health
OR	Odds ratio
PA	Physical activity
PF	Physical functioning
QoL	Quality of life
RE	Role limitations due to emotional problems
RP	Role limitations due to physical problems
SD	Standard deviation
SF	Social functioning
SF-36	Medical outcomes study 36-item short-form health study
VO_{2max}	Maximum oxygen consumption
VT	Vitality
6MWT	Six-minute walk test

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Introduction

Patterns of health and disease have changed dramatically in Western countries. With the benefits of modern technology and therapeutics, the importance of communicable diseases has declined and longevity has increased, accompanied by

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an increase in the prevalence of so-called diseases of civilization and disability [1, 2].

Therefore, improving health and quality of life (QoL) and reducing disability are identified as major priorities for geriatric medical services. One of the barriers to advancing knowledge in the field of QoL is the lack of precision in the definition of this construct. In this study, we opted to use the term health-related quality of life (HRQoL), which includes several aspects of life that affect perceived physical and mental health [3]. Measures of HRQoL have been increasing in popularity because they have been shown to be positively associated with objective health outcomes (e.g., body mass index [BMI] and number of chronic conditions) and mortality [2, 4, 5]. For example, it was observed that men who reported poor health had an eightfold increase in total mortality as compared with those reporting excellent health [5].

Nowadays, researchers intend to better understand which factors are determinant in the subjective perception of HRQoL. Identifying these factors seems to be paramount to developing effective interventions in improving the HRQoL of individuals. Personal habits, such as smoking and sedentarism, seem to play a major role in the etiology of the diseases of civilization. On the other hand, it is believed that promotion of physical activity (PA) is a viable pathway of public health intervention, which includes increasing or maintaining HRQoL [6, 7]. In accordance with this idea, Lorraine et al. [8] have suggested that PA is associated with self-rated health, one indicator of HRQoL. Despite a representative sample in this study, data on PA were obtained by self-report, which is not the most reliable method to assess PA in older adults [9]. Objective PA measures have been increasingly used to overcome the limitations of self-reporting measures. Accelerometry, in particular, provides information on the amount, frequency, duration, and intensity of PA [10].

Simple objective measures of physical fitness were demonstrated as highly predictive of subsequent disability among older people [11]. Considering that disability and autonomy have been shown to be important factors when older adults assess their health [7, 12, 13], we sought to investigate whether objective measures of physical fitness are associated with HRQoL in older adults.

Although some previous studies investigated the associations between HRQoL and self-reported PA and physical fitness, to date the present study is unique in that we investigated the associations between HRQoL and objective measures of PA and physical fitness in the same sample of community-dwelling older adults. Therefore, following the description of previous studies and their limitations, the purpose of this study was to examine the associations between self-reported health-related quality of life (HRQoL) and each of habitual physical activity (PA) and physical fitness in community-dwelling older adults.

Materials and methods

Study design and participants

One hundred and five independent community-dwelling older subjects in the age range from 60 to 83 years were recruited in the Porto area through newspaper advertisements. After the recruitment period, volunteers were invited to a preliminary meeting in which they were informed about the nature, benefits, and risks of the study. Those who agreed to participate in this study provided written informed consent, consistent with the Helsinki Declaration and completed a health history questionnaire.

A second meeting was scheduled to administer the Medical Outcomes Study 36-Item Short-Form Health Study questionnaire (SF-36) and to measure aerobic fitness and hand-grip strength of the participants, in this order. At this meeting, each individual received an accelerometer and was instructed in how to use it. The last meeting was scheduled 8 days after the second. At this time, participants were instructed to bring the accelerometers to the laboratory to be analyzed. All methods and procedures referred to above were approved by the Institutional Scientific Board.

The inclusion criteria of the sample required that the participants: (1) be older than 60 years, (2) complete the baseline testing, and (3) be physically independent. The participants were excluded from the sample if they had: (1) registered blindness, (2) severe hearing impairment, (3) uncontrolled hypertension or diabetes, (4) symptomatic cardiorespiratory disease, (5) severe renal or hepatic disease, (6) uncontrolled epilepsy, (7) progressive neurological disease, (8) chronic disabling arthritis, (9) present acute or terminal illness, (10) use of walking aids, and (11) any neurological, skeletal muscle, or joint disturbance that precluded participation in testing.

Measurements

Habitual physical activity

Habitual PA levels were assessed using accelerometers (Actigraph GT1M, Actigraph LLC, Pensacola, FL) as an objective measure of daily PA. The Actigraph accelerometer is a uniaxial monitor that measures the intensity of movement averaged over 1-min sampling intervals called 'epochs' [14]. Monitors were programmed to start recording at midday of the second meeting and recorded activity for the following 7 days.

Participants were instructed to wear the accelerometer over their right hip [15], for a 7-day period (5 week days and 2 weekend days). Exceptions included time spent sleeping, showering, and participating in water-based activities. Participants were asked to maintain their usual activities and record them in a diary. Data from each monitor were downloaded by the investigators and compared with data from the diary before the average counts per minute were calculated. This unit of measurement (counts/min) is generated based on magnitude and frequency of movement [14].

To the best of our knowledge, there are no appropriate counts/min cut-points that represent meaningful intensity categories (sedentary, moderate, and vigorous) in older adults. Therefore, in the current study, PA levels were expressed as the average counts/min and average number of steps per day (obtained from the Actigraph monitor) over the 7 days.

Fitness assessment

Aerobic fitness and grip strength were used to assess fitness. Aerobic fitness was evaluated using the six-minute walk test (6MWT), which is a physical performance test widely used in research [16], especially to obtain valid measures of submaximal aerobic endurance in older adults [17, 18]. This test measures the distance covered when subjects are instructed to walk as quickly as they can for 6 min. Walks were conducted on a flat 50-m rectangular course, marked off in five-meter segments. If necessary, subjects were allowed to stop and rest. Hand-grip strength was isometrically measured using an electronic hand-grip dynamometer (Takei, TKK 5101 Grip-D) as suggested elsewhere [19]. The subject held the dynamometer in the dominant hand hanging down by his or her side and was asked to squeeze using maximum force. The best score obtained in three trials, with approximately a 2-min rest between trials, was recorded for each subject.

Subjective health-related quality of life

Older adults' perceptions of their HRQoL were assessed using the SF-36 [20], adapted and validated for the Portuguese population [21]. This instrument is a relatively simple and brief questionnaire developed to measure generic health status and HRQoL [22]. It was demonstrated that this questionnaire is suitable for community-dwelling older adults when administered by personal interview [23, 24]. The SF-36 comprises eight health scales: physical functioning (PF; ten items), role limitations due to physical problems (RP; four items), bodily pain (BP; two items), general health (GH; five items), vitality (VT; four items), social functioning (SF; two items), role limitations due to emotional problems (RE; three items), and mental health (MH; five items). There is also a single separate item that is used to assess any change in health from the previous year [22]. The SF-36 was administered by interview, and scores were calculated using the methods set out by Ware et al. [25]. The scores range from 0 to 100, with higher scores indicating better functional health and well-being.

Anthropometrics

Body weight was measured to the nearest 0.1 kg with an electronic weight scale (*SECA 708*). Subjects were weighed barefoot wearing light clothing. Height was measured to the nearest 1 mm with a standard stadiometer. Body mass index (BMI) was determined as weight divided by height squared (kg/m^2).

Health history questionnaire

The participant's health history was obtained individually during an interview and data on the use of medication and the presence of the following chronic conditions were obtained: heart disease, hypertension, stroke, diabetes, dyslipidemia, osteoarthritis, osteoporosis, severe pulmonary disease, liver disease, thyroid disease, and depression. This questionnaire also included information on smoking status (never, former, smoker) and on education (years of formal schooling).

Statistical analysis

Means and standard deviations ($M \pm$ SD) were computed for the following variables: age, BMI, PA levels, 6MWT, hand-grip strength, and HRQoL domains. Frequencies and percentages of the number of diagnosed chronic conditions of individuals classified as overweight and obese, of smoking status categories, and number of school years were calculated. Normality of distribution was determined for all continuous variables by a Kolmogorov–Smirnov test. HRQoL domains and hand-grip strength did not have normal distribution; all of them were negatively skewed. Thus, the Mann–Whitney *U* test was used for sex comparisons, and the Spearman's rho coefficient was used to assess the correlation between PA levels, fitness, and HRQoL.

Self-reported HRQoL subscale scores were dichotomized into lower (first, second, and third quartiles) and higher HRQoL (the fourth quartile) score categories. The lower self-reported HRQoL category for each SF-36 domain was set as the reference category. Physical activity (counts/min and steps/day) and physical fitness levels (6MWT and hand-grip strength) were divided into quartiles and inserted in regression models as a continuous variable.

Table 1 Summary characteristics of study participants and the differences observed between men and women

	Men ($n = 21$)	Women ($n = 64$) M ± SD	Total ($n = 85$)
Age	68.6 ± 5.5	67.8 ± 5.5	68.0 ± 5.5
BMI (kg/m^2)	29.9 ± 5.9	27.7 ± 3.9	28.3 ± 4.5
Physical activity			
Counts/min	355.0 ± 112.7	341.3 ± 127.8	344.8 ± 123.5
N° steps/day	7 493.6 ± 1 704.1	8 390.1 ± 2 954.5	8 166.0 ± 2 713.1
Fitness			
6-min walk test (m)	600.0 ± 89.5	532.8 ± 81.5*	549.6 ± 87.9
Hand-grip strength (kg)	40.8 ± 7.3	23.9 ± 3.9*	28.2 ± 8.8
HRQoL domains			
PF	82.1 ± 19.5	74.8 ± 20.5*	76.6 ± 20.4
RP	89.7 ± 29.4	80.9 ± 32.6	83.1 ± 31.9
BP	69.1 ± 26.2	65.7 ± 24.7	66.5 ± 24.9
GH	65.4 ± 15.6	60.4 ± 16.5*	61.7 ± 16.3
VT	71.8 ± 16.9	63.2 ± 21.1*	65.4 ± 20.4
SF	90.4 ± 15.0	88.5 ± 16.7	89.0 ± 16.2
RE	80.4 ± 31.3	79.1 ± 32.6	79.4 ± 32.1
MH	78.9 ± 15.2	65.8 ± 22.0*	69.1 ± 21.2
		n (%)	
Smoking status			
Never	9 (42.9)	63 (98.4)	72 (84.7)
Former	11 (52.3)	1 (1.6)	12 (14.1)
Smoker	1 (4.8)	0	1 (1.2)
Education (years)			
Lower (0–4)	8 (38.1)	26 (40.6)	34 (40.0)
Medium (5–12)	11 (52.4)	27 (42.2)	38 (44.7)
Higher (>12)	2 (9.5)	11 (17.2)	13 (15.3)
Number of chronic conditions			
0	5 (20.8)	6 (9.8)	11 (12.9)
1	7 (29.2)	18 (29.5)	25 (29.4)
2	8 (33.3)	27 (44.3)	35 (41.2)
3	4 (16.7)	7 (11.5)	11 (12.9)
4	0	3 (4.9)	3 (3.5)

PF physical functioning, *RP* role limitations due to physical problems, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role limitations due to emotional problems, *MH* mental health

* Significant differences between men and women ($P < 0.05$)

Physical fitness and PA were analyzed in this way because it was previously suggested [26] that small improvements in functional status can be statistically significant but sometimes they are below the threshold which individuals notice differences in themselves relative to others. Redelmeier et al. [26] referred that, in chronic obstructive pulmonary disease patients, the distance in 6MWT needs to differ by 54 m for the average patient change his or her self-report of HRQoL. Therefore, we hypothesize that increases of few meters or few counts/min (if these variables were inserted as continuous variables) would not be as sensitive as an improvement equivalent to pass from a lower to a higher quartile in PA or physical fitness. Moreover, when performance in the 6MWT was divided into quartiles, it was observed that the differences across the quartiles were more or less (P 25th = 487,5 m; P 50th = 546,6 m; P 75th = 602.5 m; P 90th = 653,0 m) the 54 m suggested by Redelmeier et al. [26].

For each HRQoL domain, eight logistic regression models were calculated (64 models in total). First, unadjusted logistic regression models were used to estimate the odds ratio (OR) of scoring in the highest quartile of each HRQoL domain per quartile increase in each of the PA and physical fitness index scores (which means the higher quartile compared to the one below it, e.g., 2nd quartile versus 1st quartile; 3rd quartile versus 2nd quartile; 4th quartile versus 3rd quartile). Afterward, the first models were adjusted for BMI, number of diagnosed chronic conditions, and education. BMI and number of diagnosed chronic conditions were inserted as continuous variables.

Education was categorized for analysis into lower (0–4 years), medium (5–12), and higher (>12). All analyses were performed using Statistical Package for the Social Sciences for Windows (SPSS, Inc. Chicago, IL, USA), software version 17. The 0.05 level of probability was accepted as statistically significant for all analyses.

Results

Based on the inclusion/exclusion criteria, 20 individuals out of the 105 recruited were not eligible to be in the study. Thus, results presented are from the 21 men and 64 women who met all research inclusion criteria.

Table 1 shows the main characteristics of the study population and the differences observed between men and women. The participants' ages ranged from 60 to 83 years. Overall, the majority of subjects (almost 71%) had one or two diagnosed chronic conditions. Twenty-three participants were classified as obese (BMI > 30 kg/m^2) and thirty-seven as overweight (25 < BMI < 30 kg/m^2). In this sample, only one individual smoked and more than 50% of older adults did not complete secondary school (which means fewer than 9 years of formal education). Men were fitter ($P \leq 0.01$) than women, even though both genders scored above the norm for 6MWT (570 m for men and 521 m for women) [27] and hand-grip strength (30 kg for men and 20 kg for women) [28]. Men had reported better HRQoL than women on four domains: PF ($P = 0.02$), GH ($P = 0.03$), VT ($P = 0.03$), and MH ($P < 0.01$).

Simple correlation coefficients between each HRQoL domains and each of the PA and physical fitness variables indicated that PA and physical fitness levels were significantly positively correlated with several domains of HRQoL (Table 2). Unadjusted and adjusted ORs obtained for each HRQoL domain with respective 95% confidence intervals (CI) and *P* values are shown in Table 3. In the unadjusted logistic regression models, subjects with higher levels of PA were significantly more likely to score higher on PF (when PA assessed by counts/min) and RP (when PA assessed by steps/day) when compared with individuals with lower PA levels. Unadjusted analyses also demonstrated that fitter individuals had a greater chance of scoring higher on PF, RP, VT, and MH domains. Individuals were more likely to score higher on RP, VT, and MH with each unit increase in hand-grip strength. Similarly, individuals were more likely to score higher on PF, RP, and VT with each unit increase in 6MWT. However, none of the PA or physical fitness variables showed significant associations with BP, GH, RE, and SF domains.

With the exception of the associations between RP and steps/day and between MH and hand-grip strength, the ORs of the adjusted models (adjustment for BMI, number of chronic conditions, and education) were very similar to those obtained in the unadjusted models (Table 3).

Table 2 Spearman's rho correlation coefficients between each self-reported HRQoL domain and each physical activity (PA) or physical fitness variable

	Counts/min	Step/day	6MWT	Hand-grip strength
PF	0.190	0.128	0.359*	0.268*
RP	0.113	0.248*	0.351*	0.284*
BP	0.258*	0.257*	0.205	0.237*
GH	0.040	−0.105	0.050	0.274*
VT	0.105	0.128	0.357*	0.279*
SF	0.116	0.120	0.217	0.115
RE	0.273*	0.245*	0.184	0.077
MH	0.158	0.187	0.156	0.367*

PF physical functioning, *RP* role limitations due to physical problems, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role limitations due to emotional problems, *MH* mental health

* $P \leq 0.05$

Discussion

The main findings of this study show that the way an older physically independent individual reports some aspects of his or her HRQoL is related to both PA levels and physical fitness. In general, the most active and fit older adults have approximately twice as much chance of scoring higher on PF, RP, and VT domains than their less fit and less active peers. Moreover, the observed positive associations between aerobic fitness and PF, RP and VT seem to be independent of BMI, the number of chronic conditions, and education. Similarly, the odds of scoring higher on PF per quartile increase in PA, evaluated by counts/min, and the odds of scoring higher on RP and VT per quartile increase in hand-grip strength, were not affected by adjustment for BMI, the number of chronic conditions, or education.

In support of these results, it was previously demonstrated [7] a positive association between PA and self-reported HRQoL among older adults. Over a 5-year period, Leinonen, Heikkinen, and Jylhä [7] observed that decreases in PA levels were related with decline in self-assessment of health. Rejeski and Mihalko [6], in a review of PA and QoL in older adults, concluded that PA could lead to improved perception of PF and MH in older adults. According to these authors, PA may provide a global indicator of health and functioning through which deterioration in health and functional performance can be perceived and reflected in everyday life.

While some studies have shown associations between PA and perceived HRQoL, associations between fitness

Table 3 Odds ratios (ORs) and 95% confidence intervals (CI) for scoring in highest quartile on each self-reported HRQoL domain per quartile increase in each physical activity and physical fitness variables

Dependent variable	Independent variable	Unadjusted model OR (95% CI)	*P*	Adjusted model[a] OR (95% CI)	*P*
PF	Aerobic fitness	2.03 (1.16–3.57)	0.01	1.87 (1.03–3.38)	0.04
	Hand grip	1.48 (0.91–2.40)	0.12	1.37 (0.82–2.29)	0.22
	Counts/min	1.88 (1.07–3.31)	0.03	1.90 (1.05–3.44)	0.04
	Steps/day	1.30 (0.78–2.17)	0.32	1.32 (0.75–2.33)	0.34
RP	Aerobic fitness	2.12 (2.25–3.59)	0.01	1.95 (1.12–3.39)	0.02
	Hand grip	1.89 (1.17–3.05)	0.01	2.37 (1.33–4.24)	<0.01
	Counts/min	1.43 (0.88–2.32)	0.15	1.35 (0.81–2.27)	0.25
	Steps/day	1.73 (1.04–2.87)	0.03	1.53 (0.89–2.63)	0.13
BP	Aerobic fitness	1.53 (0.92–2.54)	0.10	1.41 (0.82–2.41)	0.22
	Hand grip	1.42 (0.90–2.22)	0.13	1.34 (0.82–2.19)	0.25
	Counts/min	1.63 (0.96–2.77)	0.07	1.61 (0.92–2.82)	0.10
	Steps/day	1.33 (0.80–2.20)	0.28	1.18 (0.69–2.01)	0.54
GH	Aerobic fitness	1.10 (0.66–1.84)	0.72	0.96 (0.53–1.72)	0.89
	Hand grip	1.53 (0.92–2.55)	0.11	1.41 (0.83–2.41)	0.21
	Counts/min	1.24 (0.72–2.11)	0.44	1.26 (0.70–2.26)	0.45
	Steps/day	1.33 (0.78–2.30)	0.30	1.66 (0.85–3.26)	0.14
VT	Aerobic fitness	1.81 (1.12–2.92)	0.02	1.79 (1.08–2.97)	0.03
	Hand grip	1.71 (1.10–2.67)	0.02	1.83 (1.13–2.98)	0.01
	Counts/min	1.33 (0.84–2.11)	0.22	1.45 (0.89–2.38)	0.14
	Steps/day	1.41 (0.88–2.24)	0.15	1.49 (0.89–2.50)	0.13
SF	Aerobic fitness	1.47 (0.95–2.27)	0.08	1.37 (0.86–2.19)	0.18
	Hand grip	1.28 (0.85–1.92)	0.24	1.15 (0.74–1.78)	0.55
	Counts/min	1.20 (0.78–1.85)	0.42	1.18 (0.75–1.87)	0.84
	Steps/day	1.20 (0.78–1.85)	0.42	1.28 (0.80–2.06)	0.31
RE	Aerobic fitness	1.35 (0.87–2.11)	0.18	1.22 (0.76–1.97)	0.41
	Hand grip	1.06 (0.71–1.60)	0.77	1.01 (0.64–1.59)	0.97
	Counts/min	1.58 (0.99–2.51)	0.06	1.62 (0.98–2.67)	0.06
	Steps/day	1.41 (0.90–2.23)	0.14	1.50 (0.91–2.49)	0.11
MH	Aerobic fitness	0.96 (0.59–1.57)	0.88	0.92 (0.53–1.57)	0.75
	Hand grip	1.62 (1.00–2.61)	0.05	1.30 (0.78–2.17)	0.32
	Counts/min	1.47 (0.86–2.52)	0.16	1.72 (0.95–3.11)	0.07
	Steps/day	1.27 (0.75–2.14)	0.38	1.67 (0.88–3.19)	0.12

PF physical functioning, *RP* role limitations due to physical problems, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role limitations due to emotional problems, *MH* mental health

[a] Adjusted for BMI, chronic conditions, and education

and perceived HRQoL have been less well studied. In agreement with the present findings, one of the few studies in this field [29] observed a positive association between hand-grip strength and HRQoL (GH and PF domains) in community-dwelling men and women (59–73 years old).

More recently, it was demonstrated that high BMI [8], low education [8], and an increased number of comorbidities are associated with poor HRQoL. Thus, these covariates were inserted in the logistic regression models to explore the independent associations of each of the PA and physical fitness variables with each of the perceived HRQoL domains. Although some studies have also referred to smoking [7], race, and gender [30] as possible confounders when assessing HRQoL, these covariates were not taken into account in the regression models of this study. Given the sample was comprised only of Caucasian older adults, mainly women, and that only one of the men was actually a smoker, it did not seem that these parameters would affect the observed associations. Results from this study indicated that adjustment for BMI, the number of diagnosed chronic conditions, and education explained only the associations between RP and steps/day and between MH and hand-grip strength. However, in this sample of apparently healthy and autonomous older adults, levels of PA and fitness were associated with self-reported PF, RP, and VT, regardless of BMI, number of chronic conditions, and education.

No significant associations were observed between BP, GH, SF, and RE domains and either PA or physical fitness. In fact, it was previously suggested [6] that the associations of PA on HRQoL are less dramatic in areas where an older individual is functioning at or above the norm. In this sense, with the exception of RE and MH, the mean values of HRQoL domains obtained by the participants of this study are quite similar to the normative values presented by Bowling, Bond et al. [9] when compared to similar mean age groups. These normative values were obtained from a national random sample from the British survey, in which almost 500 older adults were interviewed face-to-face in their own homes.

Moreover, the relationship between PA and health is complex, and there is no single study or instrument able to simultaneously elucidate the mechanisms for all the core dimensions that have been identified as being associated with health and functioning (e.g., living arrangements, financial situation, family life, life styles) [6]. Thus, it is possible that other unmeasured variables can explain the association between PA and HRQoL.

The major limitations of this study are as follows: (1) the cross-sectional design; (2) the small non-population-based sample (leading to selection bias); (3) the lack of control of potential confounders of HRQoL that was not measured, (4) given the sample encompasses only Caucasian older adults and that only one subject was identified as smoker, the findings might not apply identically to non-Caucasians or smokers, and finally, (5) it is important to take into account that in general, study participants performed the selected fitness tests above the norms and they did not have severe diseases, which means that results cannot be generalized to unfit or frail populations.

In spite of these limitations, this study has several strengths, including the use of accelerometers to objectively assess PA and the use of performance-based tests to objectively evaluate fitness.

Considering the possible limitations and the strengths mentioned above, this research demonstrated through objective measurements of PA and fitness that among relatively healthy community-dwelling older individuals, higher PA levels and better physical fitness were associated with higher self-reports of several domains of HRQoL as measured by the SF-36. Indeed, it seems reasonable to propose that implementation and promotion of PA programs for community-dwelling older adults, aimed at improving and maintaining physical fitness, could also positively affect the HRQoL of this population.

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CHAPTER VI
STUDY IV

Effects of training on fatness, inflammation and autonomic function in older adults

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Title page

Effects of training on fatness, inflammation and autonomic function in older adults

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Word-count: 7 324

Abstract

Background: Older adults normally present increased body fat, autonomic dysfunction and low-grade chronic inflammation, increasing susceptibility to develop chronic conditions. Therefore, this study aimed to assess the effectiveness of different training protocols on reducing body fat, improving autonomic function and decreasing low-grade systemic inflammation in community-dwelling older adults.

Design: randomized controlled study.

Methods: Fifty participants (68±5.5 years) were randomly allocated into resistance training (RT), aerobic training (AT) or waiting list (WL) groups. Their body composition (assessed by DXA), inflammatory biomarkers (high-sensitivity C-reactive protein, tumor necrosis-alpha, interferon-gamma, interleukins -6 and -10), lipoproteic profile, fasting glycemia, blood pressure, heart rate variability (HRV; frequency and time domains) and aerobic fitness (assessed by six-minute walk distance) were evaluated at baseline and after the 8-month intervention period. A paired t-test was used to detect changes (%Δ) within groups, while between groups differences were analyzed using the one-way ANOVA or General linear models.

Results: It was observed a significant change both in total (-5.4±6.3% and -3.3 ± 2.9%) and central body fat (8.9±11.3% and -4.8 ± 4.5%) in RT and AT groups, respectively; overall HRV (29.7 ± 40.0%) changed significantly in response to RT; resting systolic and diastolic blood pressure (-9.2±9.8% and -8.5±9.6%), heart rate (-4.6±6.5%), vagal activity (364.0 ± 739.0%), high sensitive C-reactive protein (-18.6 ± 60.6%), and six-minute walk distance (9.5±6.9%) changed in response to AT**.**

Conclusions: Present study supports recommendations that both aerobic and resistance training are effective interventions for health promotion and disease prevention in community-dwelling older adults.

Keywords

Inflammatory biomarkers, heart-rate variability, exercise, elderly

Abstract word-count: 246

Introduction

Increased body fat, autonomic dysfunction and low-grade chronic inflammation have been shown to be interrelated[1-2] and implicated in the aetiology of several chronic diseases such as diabetes[3], hypertension[4], atherosclerosis and other cardiovascular diseases (CVD) [5]. Taking into account that older adults normally present diminished heart-rate variability (HRV), a non-invasive indicator of the autonomic nervous system function, and higher circulating levels of inflammatory biomarkers it is not surprising that a higher CVD morbidity and mortality is normally observed in this population[6-7]. Indeed, it was demonstrated that high circulating levels of inflammatory biomarkers are associated with poorer physical function in older adults[7], and consequently with a reduced quality of life.

Recent findings[1-2] suggest that the parasympathetic nervous system, by discharging acetylcholine (ACh), suppresses the synthesis and release of pro-inflammatory cytokines from activated immune cells and thus inhibits inflammation. These observations may have important implications for developing novel therapeutic strategies against subclinical chronic inflammation and its related morbidity. Examples of such interventions are direct vagal nerve electrical stimulation, acupuncture techniques, relaxation therapy, and the administration of nicotinic ACh receptor agonists[1, 8]. Previous investigations suggest that regular exercise training might also induce positive adaptations in the HRV[9], in body composition[10], and fitness[9], as well as in low grade chronic inflammation[11], collectively decreasing the CVD risk for mortality and morbidity[12]. Therefore, it could be hypothesized that regular exercise training is a complementary or alternative strategy to the above-mentioned interventions.

Exercise training is actually recommended for health promotion and disease prevention in older adults[6]. However, there is conflicting evidence regarding the extent to which training could counteract the increased visceral fat depot, reduced HRV and low-grade chronic inflammation. Explanations for the discrepancy between studies may be related to the use of outcomes measurements derived from less-accurate methods, i.e. use of anthropometrics instead of dual-energy X-ray absorptiometry (DXA) to measure body composition; or by cross-sectional studies including heterogeneous populations of younger or older-diseased populations. Other limitations that could be pointed out in several previous studies are: (i) only a few experimental studies have used alternative types of exercise training instead of aerobic training to diminish inflammatory biomarkers and increase HRV, (ii) the lack of control for habitual daily physical activity and dietary intake, and finally, (iii) most studies use just one or two biomarkers to assess low-grade chronic inflammation.

Thus, the purpose of this study was to examine the effectiveness of two different training programs on reducing body fat, improving autonomic dysfunction and decreasing low-grade inflammation in community-dwelling older adults with no serious medical conditions.

Methods

Participants and Study Design

In this randomized, controlled study, one hundred and eight community-dwelling and independent older adults were recruited in the Porto area (Portugal) throughout advertisement in newspapers. The study design is presented in Figure 1.

Subjects were asked to come to the Faculty of Sport (University of Porto) on four different days. On the first day, one hundred and five volunteers (78 women and 27 men) completed a health history questionnaire to record past and present conditions and medications. According to the Helsinki Declaration, the nature, benefits, and risks of the study were explained to the volunteers, and their written informed consent was obtained. All subjects that were able to participate in the study were included if they were older than 60 years and were not involved in supervised regular exercise training (performing moderate to vigorous exercise for 20 minutes or more at least twice a week) in the previous six months. Subjects who suffered from acute or terminal illness, severe or uncontrolled hypertension or any cardiovascular and/or respiratory disorder, any neurological, skeletal-muscle or joint disorders or disturbances that precluded participation in exercise, or who were undergoing pharmacological therapies that could reduce safety during exercise or influence the responses of cardiovascular function were excluded.

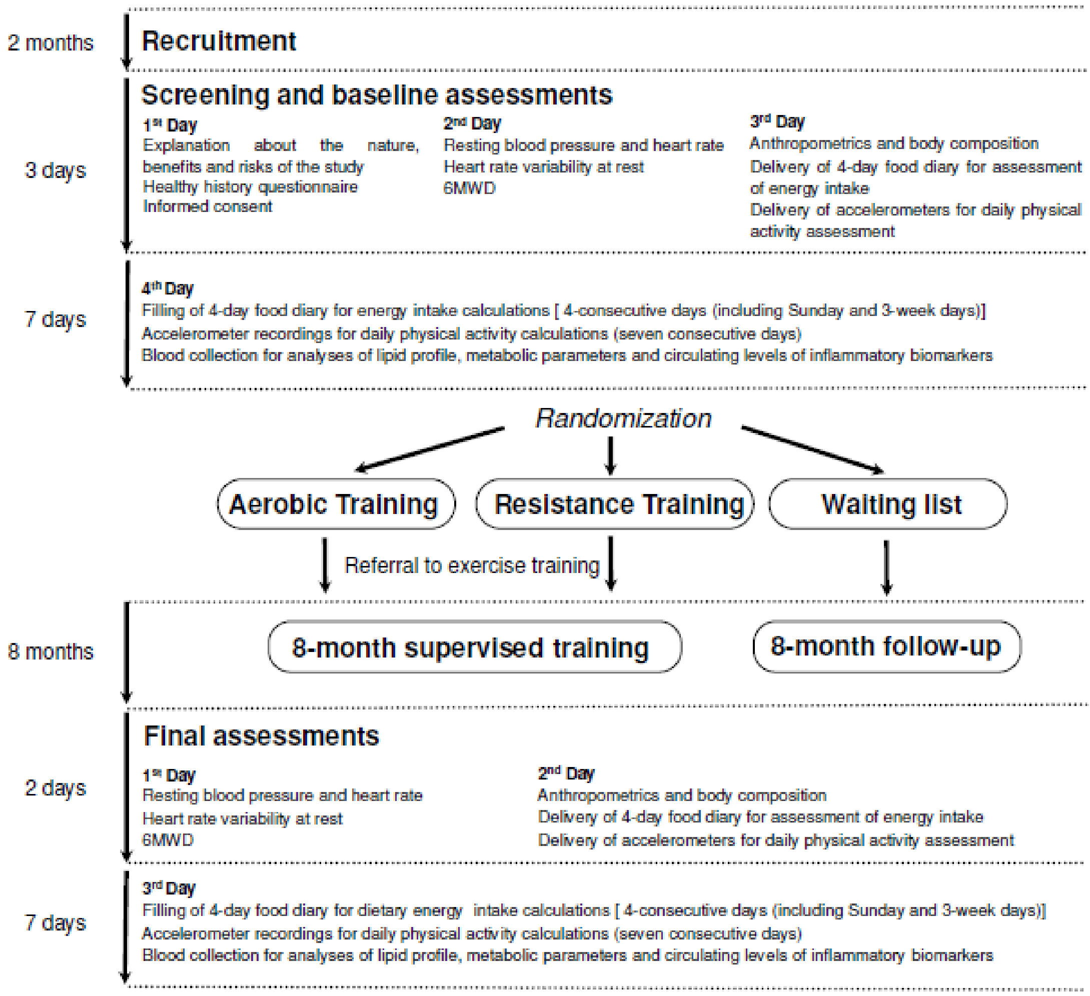

Figure 1. Flowchart depicting the study design

On the second day, subjects underwent several evaluations in the following order: HRV at rest, resting blood pressure and heart rate and 6-minute walk distance (6MWD). On the third day, subjects underwent anthropometrics and body composition measurements. At this time they were also instructed in using accelerometers and in recording the 4-day food diary for assessment of habitual physical activity and dietary intake, respectively. Finally, on the fourth day (at least seven days after the third visit) subjects were asked to return the completed 4-day food diary and the accelerometer recordings, and blood was collected for further biochemical determination of lipid profile, glycemia and circulating levels of inflammatory biomarkers.

After screening and baseline assessments, the eighty-five older adults who achieve inclusion and exclusion criteria were randomly allocated, according to computer generated block randomization, into aerobic training (AT), resistance training (RT) or waiting list (WL) for eight months. Completion of the training program was defined by an attendance rate of at least 80% of the scheduled sessions. Additionally, older adults who were absent from more than seven consecutive sessions were also excluded from the analysis. Participants were instructed not to change the physical activity already included in their daily living routines or dietary patterns during the course of the study. The Institutional Review Board approved all methods and procedures.

Intervention

For both training protocols, older adults trained three times per week (non-consecutive days) for eight months and each exercise session lasted approximately 50 minutes.

Aerobic training (AT) consisted of a 10-minute warm-up and 30 minutes of aerobic exercise, mainly walking at an intensity corresponding to 50%-80% $HR_{Reserve}$ and ending with a 10-minute cool-down. In order to raise the subject's functional fitness so that they were able to sustain 30 minutes of continuous walking at the targeted intensity, the training load was gradually increased during the first four weeks. The walking duration in the first session was 15 minutes at 50 to 60% of the $HR_{Reserve}$ or Rating of Perceived Exertion (RPE) 4-6, and it was increased by five minutes each week until subjects were able to walk continuously for 30 minutes (week 4). Afterwards, intensity was gradually increased to 70-80% of the $HR_{Reserve}$ or RPE 7-8. In order to ensure that the subjects were exercising at the targeted intensity, Polar Heart Rate Monitors (Polar Team System, Finland) were used and RPE were registered.

Resistance training (RT) consisted of a ten-minute warm-up that included stretching; eight exercises (leg press, chest press, leg extension, seated row, seated leg curl, abdominal flexion, biceps curl, low-back extension, and triceps extension) for different muscular groups; and a ten-minute cool-down. During the first week of RT, the subjects were familiarized with the devices by performing one set of 12-15 repetitions (reps) without load. Subjects were taught proper lifting techniques and safety precautions. To minimize excessive BP responses, individuals were told to avoid extended breath-holding (Valsalva manoeuvre), during their reps[13]. Then, a baseline one repetition maximum (1RM) for each exercise was undertaken. Afterwards, older adults performed two sets of 12-15 reps at 50-60% of the 1RM or RPE 4-6, for one month. After this month, the 1RM was measured again and the load was increased to 80% of the 1RM or RPE 7-8. At this intensity, older adults performed two sets of 8-12 reps. Every two months the 1RM was measured in order to keep the training stimulus consistently at 80% of the 1RM or RPE 7-8. Concentric and eccentric movements were performed at a rate of three seconds[10]. A 2-minute rest between each set of reps was provided. All sessions were performed under the supervision of a physical education teacher.

During the study period, individuals randomized to the *Waiting List (WL)* group were contacted by phone every four months to certify that they were still interested in participating in the program. At these moments, they were also asked not to change their lifestyle. After the 8-month observation period, they were invited to participate in specific exercise programs designed for seniors at the Faculty of Sport.

Assessments

The test administrator and the time of day used for collection remained constant.

Anthropometrics and Body Composition: Body weight was measured to the nearest 0.1kg with an electronic weight scale (*SECA 708*). Subjects were weighed barefoot wearing light clothing. Height was measured to the nearest 1mm with a standard stadiometer. Body mass index (BMI) was determined as weight divided by height squared (kg/m^2). Percent of total body fat (%BF), trunk fat (kg) and lean mass (kg) were determined using DXA (Hologic QDR-4500, software for windows XP, version 12.4) with subjects in the supine position.

Biochemical analysis of plasma glucose, cholesterol (total cholesterol, HDL, LDL) and triglycerides were measured using standard enzymatic methods. High sensitivity C-reactive protein (hs-CRP) levels were determined by means of particle-enhanced immunonephelometry using a BN™ II nephelometer (Dade Bhering).

Cytokine measurements were performed using a human multiplex immunoassay kit from Millipore according to the manufacturer's protocol. Briefly, 10 µl of plasma was diluted and assayed for interleukins -6 and -10 (IL-6, IL-10), interferon-gamma (IFN-γ), and tumor necrosis factor-alpha (TNF-α) using specific antibodies conjugated to beads and read on a Luminex 100 instrument (Luminex). The concentration of each cytokine was determined by preparation of a standard curve using standard cytokine concentrations. Results are expressed in picograms per milliliter. The detection levels of these Abs were between 1 and 5 pg/ml with little or no cross-reactivity among the Abs.

Resting Blood Pressure and Heart rate were measured by an automated blood pressure monitor (Colin, DP 8800). After 15 minutes at rest in a quiet, temperature-controlled room, measurements were taken with the subjects seated in an upright position, with the arm comfortably placed at heart level.

The average of the three measurements for systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were entered as data.

Autonomic function was evaluated by HRV analysis. Before HRV recordings, subjects were instructed to 1) not consume coffee, cola beverages, tea, or chocolate for 12h; 3) not drink alcoholic beverages for 24h; and 4) avoid exercise and strenuous physical loads for 24h before the measure. After a 15-minute supine rest, the R-R intervals were recorded over a period of five minutes with a Polar recorder (Polar NV vantage, Finland). Data were saved and filtered using an automatic procedure for further analysis of HRV with Polar Precision Performance software version 2.0 (Polar Electro Oy, Kempele, Finland)[9]**.** Data with more than 5% error were not considered in statistical analyses. The standard deviation of normal RR intervals (SDRR) was used as time-domain (TD) measure of overall HRV. The low frequency power (LF, power in the 0.03 – 0.15 Hz band) and high frequency power (HF, power in the 0.15 – 0.40 Hz band) were calculated to reflect frequency domain (FD). While the efferent vagal activity is considered a major contributor to the HF component, the interpretation of the LF component is more controversial[14]. But in the present study, it is used as a parameter that includes both sympathetic and vagal influences. The TD and FD indexes are expressed as absolute values (ms/Hz and ms^2/Hz, respectively). The breathing frequency was not controlled.

Aerobic Fitness was assessed using the 6MWD, a physical performance measure commonly used in research specifically to obtain valid measures of submaximal aerobic endurance in older adults[15]. This test measures the distance covered when subjects are instructed to walk as quickly as they can for six minutes. Walks are conducted on a flat, indoor 50-meter rectangular course, marked off in 5-meter segments. If necessary, subjects are allowed to stop and rest.

Physical Activity levels were assessed using accelerometers (Actigraph GT1M, Actigraph LLC, Pensacola, FL) as an objective measure of daily physical activity. The Actigraph accelerometer is a uniaxial monitor that measures the intensity of movement averaged over 1-minute sampling intervals called 'epochs'[16]. Monitors were programmed to start recording at midday of the second meeting and recorded activity for the following seven days. Participants were instructed to wear the accelerometer around their waist over their right leg, for a 7-day period (five weekdays and two weekend days). Exceptions included time spent sleeping, showering and during water-based activities. Participants were asked to maintain their usual activities and record them in a diary. Data from each monitor were downloaded by the investigators and compared with data from a diary before the average counts/min had been calculated. This unit measurement (counts/min) is generated based on magnitude and frequency of movement[16]. To the best of our knowledge, there are no appropriate counts/min cut-points that represent meaningful intensity categories (sedentary, moderate and vigorous) in older adults. Therefore, in the current study, physical activity levels were expressed as the average counts per minute (obtained from the Actigraph monitor) over the seven days.

Dietary intake was assessed by a 4-day dietary record (three weekdays and one weekend day) at two points (before and after the intervention). Participants were invited to record and weigh all foods and drinks consumed on each recording day, trying to not change their eating habits while keeping the record, and then to bring the completed records to the research team. Trained researchers reviewed these forms, and when necessary, the subjects were asked to add extra information for the following visit. To ensure standardization in the recording, a nutritionist individually instructed the subjects how to fill out the dietary records correctly. Trained nutritionists in the research centre supervised the coding of records and data in accordance with uniform procedures. Dietary records were analyzed using an adapted Portuguese version of the software Food Processor Plus® (ESHA Research Inc, Salem, Oregon, USA), a nutritional analysis software that converts food intake into total energy and nutrients, based on food composition tables available from the USDA (United States Department of Agriculture) and national data from typical Portuguese foods.

Statistical Analysis

Measures of IFN-γ, hs-CRP, IL-6, IL-10, r-MSSD, TP, LF, and HF, were log normal transformed before analysis to better approximate normal distributions. Between-group differences in baseline values were determined with one-way analysis of variance (ANOVA). When a significant main effect was detected at a significance level of $P<0.05$, the Bonferonni's correction was used for post-hoc multiple comparison. In order to detect changes within groups (before vs. after) the paired t-test was employed. The pre-to-post changes (Δ) for each subject were related to the individual baseline level to define the relative change (%Δ = [(post-test score – pretest score)/ pre-test score] x 100) in all selected variables. General Linear Models (univariate) with relative change as the dependent variable and group as the fixed factor were used. Whenever baseline differences between groups were identified, the baseline value was inserted as a covariate. Afterwards, gender, %BF and medication were inserted as covariates to verify if they were able to interfere in results. When a significant main effect was detected at a significance level of $P<0.05$, the Bonferonni's correction was used for post-hoc multiple comparison. To attest that missing data did not occur in a non-random pattern, the baseline differences in outcome values in the groups with and without missing data were tested using the Mann-Whitney U test. Results are shown as mean with standard deviations (M ± SD) or as median with percentiles 25 and 75 (Md, 25th percentile – 75th percentile). All analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 17.0 for Windows, Chicago, IL).

Results

After randomization, 11 individuals (8 RT, 3 AT) out of the 85 left the study due to incompatibility with the training timetable. Therefore, only 74 older adults began the protocol. During the eight months, another 24 (32.4%) subjects dropped out of the study (8 RT, 4 AT, 12 WL) for different reasons: low back pain and arthrosis (3 RT); knee surgery (1 RT, 1 WL); cerebral stroke (1 AT, 1 WL); medical advice (2 RT, 1 AT); loss of motivation and moved out of the city

(2RT, 1 AT) and 11 (1 AT, 10 WL) were lost because they did not complete the final assessment. The flow of subjects during the study is presented in Figure 2.

Therefore, the final sample was comprised of 50 community-dwelling older adults (68.0 ± 5.5 years), mainly women (n = 39, 78%). Fifty-six percent were controlled hypertensive, 42% had dislipidemia, and 18% had controlled diabetes. According to BMI, 21% were classified as overweight (25 < BMI < 30) and 28% as obese (BMI > 30). None of the participants were currently smokers. Finally, four (10.3%) out of 39 women were on hormone replacement therapy (HRT).

At baseline, no differences between groups were observed for age, body composition parameters, BP, HRV, biomarkers of inflammation, glycemia, lipoproteic profile, or habitual physical activity. However, WL demonstrated a higher HR than RT (*P* = 0.02), and RT showed better performance on the 6MWD than WL (*P* < 0.01). Finally, WL had a higher energy intake than AT (*P* = 0.01). Table 1 presents the main characteristics of the participants for each group at baseline.

After training, a significant decrease in both total (RT, *P* = 0.02; AT, *P* <0.01) and central body fat (RT, *P* = 0.04; AT, *P* < 0.01) was observed in RT and AT groups. In contrast, after the eight months, WL had a higher %BF (*P* = 0.02) and trunk fat (*P* < 0.01). Lean mass remained constant in the three groups across the eight months.

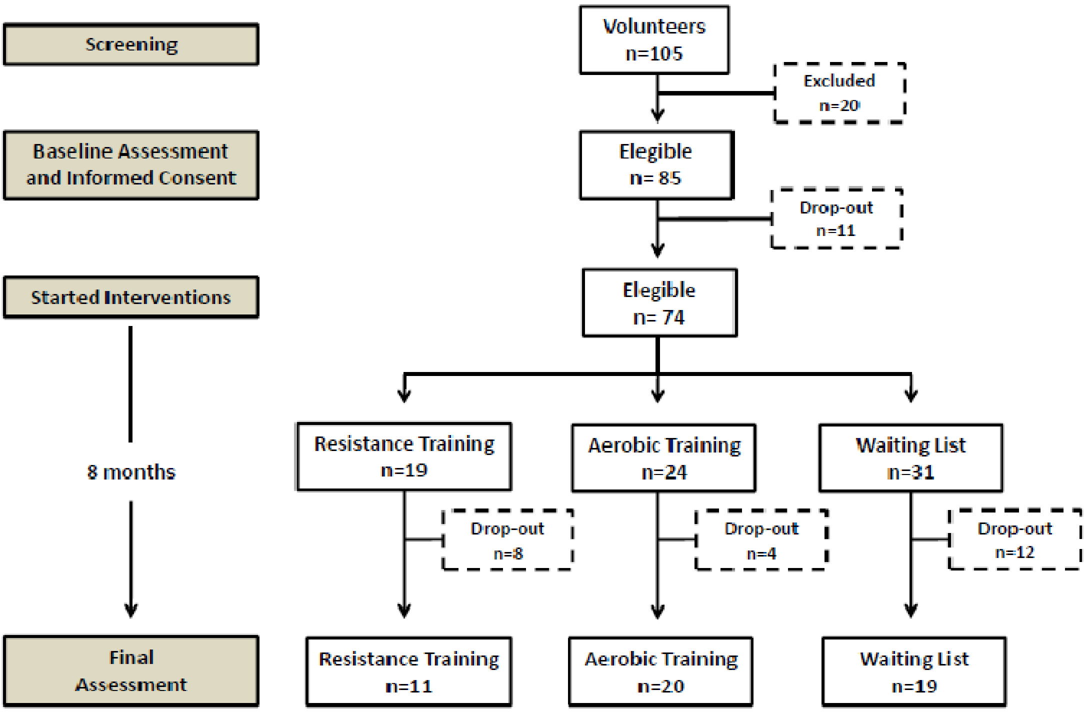

Figure 2. Flowchart describing retention of participants.

Excepting a decrease in HDL cholesterol for AT (*P* < 0.01) and WL (*P* < 0.01), no differences were observed in either the lipoproteic profile or glycemia of the older adults. Nevertheless, AT demonstrated lower levels of hs-CRP (*P* = 0.02) after training and WL increased TNF-*α* levels (*P* = 0.02) after the observation period. At baseline, 36% and 35% of the subjects in RT and AT, respectively, were in the high-risk category for hs-CRP levels (above 3.0mg/dL). Following training, there was a 50% and 85.7% reduction in the number of subjects in the high-risk category for RT and AT respectively. A sub-analysis of the individuals classified in the high-risk category for hs-CRP at baseline demonstrated that when compared with those individuals in the lower-risk category, the high-risk individuals also had higher levels of IL-6 (P < 0.01). Interestingly, the high-risk individuals in AT, beyond the reduction in hs-CRP, also significantly decreased IL-6 levels (-43.5 ± 32.0%; P = 0.04) after training (see Table 2).

Table 1. Baseline characteristics of the participants

	Resistance Training n=11	Aerobic Training n=20	Waiting List n=19
Gender	4 men, 7 women	3 men, 17 women	4 men, 15 women
Age (years)	67.3±4.9	69.9±5.7	67.8±5.5
BMI (kg/m^2)	29.5 ± 5.0	28.1 ± 4.1	27.2 ± 3.5
Controlled hypertension, n (%)	6 (54%)	9 (45%)	13 (68%)
Controlled dislipidemia, n (%)	4 (36%)	10 (50%)	7 (37%)
Controlled diabetes, n (%)	1 (9%)	2 (10%)	6 (32%)
Individuals with hs-CRP>3.0 mg/L, n (%)	4 (36%)	7 (35%)	8 (42%)
Smoking status			
Never, n (%)	9 (82%)	18 (90%)	17 (89%)
Former, n (%)	2 (18%)	2 (10%)	2 (11%)
Smoker, n (%)	0	0	0
HRT, n (%)	1 (9%)	3 (15%)	0

BMI, body mass index; hs-CRP, high sensitive C-reactive protein; HRT, hormone replacement therapy.

The greatest improvements in resting BP were observed in the AT group, which, after intervention, demonstrated significant decreases in SBP (P < 0.01) and DBP (P < 0.01). Additionally, decreases in HR_{rest} were verified in this group (P < 0.01), and interestingly in WL as well (P < 0.05). Despite the fact that no significant differences were found in RT, it is important to refer to the reduction in about eight and four mmHg in the SBP and DBP means of this group, respectively, which was almost two-fold the reduction observed in WL.

Table 2. Changes in body composition, lipoproteic profile, fasting glycemia, and inflammatory biomarkers before and after training. Values normally distributed are represented by means with standard deviations and values not normally distributed are represented by medians with percentiles between 25 and 75 (25th – 75th percentiles).

Outcomes	Resistance Training			Aerobic Training			Waiting List		
	Before	After	Δ%	Before	After	Δ%	Before	After	Δ%
Body composition									
BMI (kg/m²)	29.5 ± 5.0	28.1 ± 4.0	-2.4 ± 4.4	28.1 ± 4.1	27.9 ± 3.8	-0.6 ± 1.5	27.2 ± 3.5	27.6 ± 3.0	2.0 ± 4.6
%BF	34.5 ± 7.1	32.9 ± 8.3*	-5.4 ± 6.3	38.4 ± 5.3	37.2 ± 5.6*	-3.3 ± 2.9	34.5 ± 5.9	35.2 ± 6.0*	2.1 ± 3.5
Trunk fat (kg)	11.6 ± 4.5	10.6 ± 4.4*	-8.9 ± 11.3	12.4 ± 3.5	11.9 ± 3.4*	-4.8 ± 4.5	11.0 ± 3.0	11.6 ± 3.2*	4.9 ± 7.2
Lean mass (kg)	43.7 ± 9.8	43.8 ± 9.8	0.4 ± 4.8	37.2 ± 5.5	37.0 ± 4.5	0.1 ± 5.5	42.9 ± 10.2	42.5 ± 9.7	-0.6 ± 2.5
Biochemical Analysis									
Cholesterol total (mg/dL)	223.2 ± 29.3	221.7 ± 27.3	0.1 ± 12.3	211.2 ± 33.3	200.8 ± 31.6	-3.4 ± 18.0	238.2 ± 33.7	230.3 ± 33.3	-3.1 ± 8.7
LDL (mg/dL)	163.9 ± 37.4	162.5 ± 29.2	1.0 ± 13.3	156.2 ± 37.6	149.2 ± 30.0	0.2 ± 32.7	176.6 ± 39.6	172.6 ± 43.6	-2.0 ± 12.2
HDL (mg/dL)	59.2 ± 17.6	59.1 ± 20.1	-0.9 ± 11.7	54.7 ± 13.8	51.4 ± 11.7*	-5.4 ± 8.5	61.4 ± 17.3	57.3 ± 17.0*	-6.5 ± 8.8
Triglycerides (mg/dL)	76.4 ± 32.3	77.4 ± 28.8	5.0 ± 26.3	111.1 ± 62.3	108.5 ± 58.0	1.4 ± 25.5	108.2 ± 70.7	156.9 ± 229.3	19.0 ± 53.2
Glycemia (mg/dL)	87.9 ± 13.4	88.8 ± 21.6	0.3 ± 11.9	94.6 ± 18.5	93.4 ± 18.8	-1.1 ± 7.3	103.3 ± 30.9	108.0 ± 31.4	5.9 ± 16.1
hs-CRP (mg/dL)	0.2	0.1	93.8 ± 266.3	0.2	0.1*	-18.6 ± 60.6	0.2	0.2	212.2 ± 889.7
	0.1 – 0.5	0.1 – 0.3		0.1 – 0.4	0.1 – 0.2		0.1 – 0.6	0.1 – 0.5	
TNF-α (pg/mL)	8.0 ± 5.6	9.8 ± 6.6	22.5 ± 42.5	11.2 ± 4.1	12.4 ± 5.3	11.1 ± 26.4	10.2 ± 4.8	12.3 ± 4.6*	23.8 ± 39.8
IL-6 (pg/mL)	7.0	6.4	49.8 ± 259.4	10.8	5.2	-4.4 ± 65.4	6.2	7.8	21.0 ± 92.4
	4.0 – 15.6	3.3 – 10.6		3.6 – 17.1	3.3 – 8.4		2.8 – 27.2	4.5 – 16.6	
IL-10 (pg/mL)	10.1	6.7	-29.8 ± 40.3	7.9	5.5	-10.2 ± 41.3	16.4	8.2	-18.0 ± 39.1
	5.58 – 47.7	3.34 – 25.25		5.50 – 15.56	3.52 – 15.5		7.4 – 21.1	6.2 – 18.2	
IFN-γ (pg/mL)	2.0	0.6	29.5 ± 231.3	0.7	0.6	-7.6 ± 100.2	0.6	0.6	-4.8 ± 20.2
	0.6 – 7.5	0.6 – 4.4		0.6 – 2.9	0.6 – 0.6		0.6 – 0.9	0.6 – 0.6	

BMI, body mass index; %BF, percentage of body fat; LDL, low density lipoprotein; HDL, high density lipoprotein; hs-CRP, high sensitive C-reactive protein; TNF-α, tumor necrosis factor-alpha; IL-6, interleukin-6; IL-10, Interleukin-10; IFN-γ, interferon-gamma.

*Differences within groups, $p<0.05$.

HRV indexes were also enhanced after training. Regardless of the fact that both RT and AT showed improved HRV, the improvement was observed in different parameters for each group. The RT presented a higher total variability, translating into a greater SDRR (*P* = 0.04), and AT presented a higher vagal tonus represented by an increased HF (*P* = 0.03). As expected, AT demonstrated better performance in 6MWD (*P* < 0.01) after training. No differences were observed in the habitual daily living physical activity levels or energy intake of older adults across the interventions/observation (see Table 3).

General linear models (see table 4) demonstrated significant differences in relative changes between groups for BMI, %BF, trunk fat, and 6MWD. Post-hoc multiple comparisons demonstrated that relative changes in BMI were more pronounced in RT than in WL (*P* = 0.03). Greater differences were also identified in RT and AT than in WL for %BF (*P* < 0.01) and trunk fat (*P* ≤ 0.01). Finally, older adults in AT demonstrated greater improvements in 6MWD (*P* < 0.01) than those in WL. Further adjustments for %BF, energy intake, gender and medication use did not significantly change the overall results (not presented).

When individuals who completed all tests were compared with individuals who had missing data and who belonged to the same group, minimal differences were observed. In RT, the dropout group had lower 6MWD than the group that had completed the intervention and tests (*P* = 0.04). The opposite was observed in the AT: the remaining individuals had a worse performance at baseline on 6MWD than the individuals who dropped out (*P* = 0.03) as well a greater lean mass (*P* = 0.03) and higher serum level of IL-6 (*P* = 0.04). Volunteers who attended all tests in WL had higher serum levels of IL-10 than volunteers who gave up along the study period (*P* < 0.01). These analyses demonstrated that despite the high withdrawal rate, individuals who gave up presented, for the majority of outcomes, similar characteristics to those of remaining participants. Thus, it seems that the elevated dropout rate did not bias the final results.

Table 3. Changes in blood pressure, heart rate variability and aerobic fitness before and after training. Values are represented by means with standard deviations.

Outcomes	Resistance Training			Aerobic Training			Waiting List		
	Before	After	Δ%	Before	After	Δ%	Before	After	Δ%
Resting Blood Pressure and Heart-rate									
SBP (mmHg)	131.0 ± 11.6	123.3 ± 14.2	-5.4 ± 12.6	137.5 ± 21.8	124.0 ± 19.3*	-9.2 ± 9.8	141.3 ± 16.6	136.2 ± 18.7	-3.1 ± 9.4
DBP (mmHg)	71.3 ± 7.0	67.4 ± 8.2	-5.0 ± 12.7	72.8 ± 9.3	66.5 ± 9.4*	-8.5 ± 9.6	75.9 ± 11.7	73.8 ± 10.0	-2.0 ± 9.6
HR (bpm) †	62.2 ± 10.3	60.3 ± 8.4	-2.5 ± 7.1	67.5 ± 7.8	64.1 ± 6.5*	-4.6 ± 6.5	68.4 ± 8.0	65.5 ± 8.0*	-4.0 ± 8.7
Resting Heart-rate Variability									
SDRR (ms)	34.5 ± 13.6	44.4 ± 16.8*	29.7 ± 40.9	32.0 ± 13.1	34.7 ± 13.5	15.9 ± 42.4	38.7 ± 20.3	32.1 ± 14.3	-5.3 ± 42.2
TP (ms^2)	9 574.2 4 079.8 – 14 297.9	13 875.1 4 377.5 – 24 123.7	33.9 ± 71.2	8 511.9 3 482.4 – 15 370.9	8 421.6 5 481.9 – 13 044.1	49.8 ± 102.2	8 833.3 5 794.5 – 13 337.8	12 166.5 6 752.9 – 15 151.0	41.4 ± 164.0
LF (ms^2)	145.2 111.1 – 446.5	399.6 127.8 – 883.2	83.3 ± 134.5	222.9 93.5 – 361.0	280.2 153.4 – 445.5	68.0 ± 169.0	150.6 102.8 – 332.4	167.6 103.1 – 296.9	-9.4 ± 86.0
HF (ms^2)	274.0 110.0 – 480.3	544.8 173.5 – 1 026.6	110.5 ± 133.8	110.0 41.9 – 269.0	174.0* 89.2 – 361.0	363.9 ± 793.0	82.7 32.3 – 220.7	145.8 46.4 – 280.9	23.9 ± 111.9
Aerobic fitness									
6MWD (m) †	630.5 ± 57.0	659.1 ±73.5	4.6 ±7.4	541.8 ± 70.4	592.4 ± 76.9*	9.5 ± 6.9	524.5 ±97.0	533.2 ± 82.7	-0. 4 ± 9.7
Physical Activity levels (Count/min)	368.9 ± 106.8	438.9 ± 185.1	17.1 ± 26.3	318.4 ± 82.3	334.8 ± 74.3	9.1 ± 25.7	354.9 ± 156.0	361.0 ± 139.3	8.9 ± 40.0
Energy Intake (kcal/day) †	1 554.8 ± 376.8	1 678.8 ± 647.4	9.9 ± 44.3	1 445.2 ± 268.5	1 421.2 ± 308.4	-0.1 ± 24.8	1 845.9 ± 453.7	1 798.7 ± 260.9	0.5 ± 27.3

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; SDRR, standard deviation of normal RR intervals; TP, total power; LF, low frequency; HF, high frequency; 6MWD, six-minute walk distance.

*Differences within groups, $p<0.05$. † Variables show differences between groups at baseline, $p<0.05$.

Table 4. General Linear Models: relative amount of variance explained by models.

Outcomes	*F*	*P*	Partial Eta Squared (%)
Body composition			
BMI	4.00	0.03	14.5
%BF	17.70	<0.01	42.9
Trunk fat	14.47	<0.01	38.1
Lean mass	0.21	0.81	0.9
Biochemical Analysis			
Cholesterol total	0.24	0.79	1.0
LDL	0.07	0.93	0.3
HDL	1.19	0.31	4.9
Triglycerides	1.04	0.36	4.3
Glycemia	1.65	0.20	6.7
hs-CRP	0.76	0.47	3.3
TNF-α	0.67	0.52	2.9
IL-6	0.67	0.52	3.1
IL-10	0.78	0.47	3.8
IFN-γ	0.50	0.61	2.2
Resting Blood Pressure (BP) and Heart-rate (HR)			
SBP	1.60	0.21	6.4
DBP	1.93	0.16	7.6
HR [a]	0.12	0.89	0.5
Resting Heart-rate Variability			
SDRR	1.88	0.17	9.7
TP	0.05	0.95	0.3
LF	1.44	0.25	7.8
HF	1.56	0.22	8.2
Aerobic Fitness			
6MWD [a]	6.86	<0.01	23.8

BMI, body mass index; %BF, percentage of body fat; LDL, low density lipoprotein; HDL, high density lipoprotein; hs-CRP, high sensitive C-reactive protein; TNF-α , tumor necrosis factor-alpha; IL-6, interleukin-6; IL-10, Interleukin-10; IFN-γ, interferon-gamma; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; SDRR, standard deviation of normal RR intervals; TP, total power; LF, low frequency; HF, high frequency; 6MWD, six-minute walk distance.

[a] adjusted for baseline values.

Discussion

The present study showed: (i) that regular training decreases total and central body fat; (ii) RT is able to increase overall HRV; (iii) AT is able to decrease resting blood pressure and resting HR, increase efferent vagal activity, decrease low-grade systemic inflammation, and improve aerobic fitness in community-dwelling older adults; (iv) the magnitudes of changes to all variables investigated were similar for aerobic and strength training. Altogether, these results support current recommendations that both AT and RT are effective interventions for health promotion and disease prevention in community-dwelling old-aged populations with no serious medical conditions.

Studies addressing the impact of training on body composition have provided conflicting results. Reinforcing our observations previous researchers have demonstrated RT[17] and AT[18] as valuable to reduce body fat. Nevertheless, others failed to report any significant change in body composition after interventions[5, 19-20]. These discrepancies can be partly reconciled by differences in the duration[5, 19-20] and intensity[20] of the training programs, by the different age of subjects[5] as well as by different methodologies used to assess body composition.

Although some research indicates that AT and RT may induce positive alterations in the lipoprotein profiles of young[21], middle-aged[18, 22] and older adults[7, 23] the present study failed to observe positive effects of training on the lipid-lipoprotein profile. Concerning the specific case of HDL cholesterol, it is possible that our subjects had such high baseline HDL levels that little room was left for improvement.

A significant mean decrease in hs-CRP, the best overall marker of underlying chronic inflammation, was observed in subjects who underwent AT. This finding is of paramount importance because, more than a biomarker of inflammation, high levels of hs-CRP are closer associated with increased risk for coronary heart disease, stroke and myocardial infarction[24]. In this sense the 85.7% and 50% decrease in the number of subjects classified as having high risk to develop CVD after AT and RT, respectively, might be considered clinically relevant. Finally, the findings from the subanalysis of the subjects with hs-CRP levels above 3.0mg/dL demonstrated that AT also reduced IL-6 levels in this subgroup. This suggests that those high-risk individuals benefit more from AT than those with lower risk.

It is estimated that adipose tissue contributes up to one-third of circulating IL-6 at rest[25]. Increased level of IL-6, in its turn, leads to the secretion of acute phase proteins like CRP by the liver[24-25]. In addition, fat free acids released by adipocytes promote the production of TNF-*α*. Therefore, it is suggested that the exercise-induced loss of body fat may lead to a reduced serum IL-6, TNF-*α*, and, as consequence, reduced CRP[4]. Interestingly, in our study, both total and central body fat loss induced by AT were followed by decreased hs-CRP levels and IL-6 (only for individuals previously classified as high-risk) while the similar total and central body fat decreases induced by RT were not followed by a similar reduction in any of the biomarkers under investigation. These findings suggest that other training-induced mechanisms beyond body fat decrease are necessary to decrease inflammation. It is possible that changes induced by aerobic training in anti-oxidant status[26] or endothelial function[27] are related with the benefits observed in the inflammatory status of AT.

It was also surprising that despite the reduction in body fat, no changes in TNF-*α* were observed after both training protocols. Individuals in WL, on the opposite, demonstrated increased levels of TNF-*α* after the 8-month observation period. Therefore, it is possible to suggest that if exercise training is not able to decrease TNF-*α* levels in older adults with no serious medical conditions, it is at least able to avoid its increase.

Despite its important anti-inflammatory role in a number of inflammatory conditions, the effect of training on IL-10 serum levels it is not frequently assessed[24]. Petersen and Pedersen[11] in their review suggested that the process of muscular contraction during exercise could stimulate the transcription of IL-6 mRNA, with consequent activation of the cascade of antiinflammtory cytokines such as IL-10. Evidence supporting this hypothesis comes mainly from animal models[28], acute effects of exercise[29] or diseased populations[30-31]. Nunes et al.[28] showed that regular physical training improves the anti-inflammatory response by increasing plasmatic levels of IL-10 in a rat model of chronic heart failure. In humans, single bouts of exercise have demonstrated both significant increases in intracellular anti-inflammatory markers such as IL-4, IL-10 and growth hormone[29] and that acute moderate-intensity exercise has neither an anti- or pro-inflammatory effect over seven days following exercise[32]. The chronic effect of exercise in IL-10 is limited to patients with chronic conditions like diabetes [31] and coronary artery disease[30]. In these subjects aerobic training induced increase in circulating IL-10, however, it is important to take into account that individuals diagnosed with such diseases generally present high levels of pro-inflammatory and low levels of anti-inflammatory biomarkers, which theoretically permit greater exercise-induced improvements when compared to apparently healthy individuals. Additional work is clearly needed to better understand the impact of training on IL-10 in older adults free of clinical conditions.

It has been recently suggested that exercise training-related improvements in HRV may also play a role mediating the inhibition of inflammatory response observed in trained individuals[33]. The latest findings showed increased vagal activity to be associated with decreased peripheral inflammatory responses, measured by TNF-*α*, IL-6 and hs-CRP, which may reduce the risk of inflammatory diseases[5]. This immune-modulatory function of the vagus nerve, whereby activation of efferent arm results in regulation of cytokine production, was termed the ´Cholinergic anti-inflammatory pathway´[8]. The improvement in parasympathetic activity followed by reduced hs-CRP levels that were observed after AT seems to reinforce the idea of a cholinergic anti-inflammatory pathway, and at the same time give insight into the role of regular AT in prevention of diseases linked with low-grade inflammation. Although increased vagal activity was not observed following resistance training, this group showed an increase in overall HRV, which is an important finding once decreased HRV has been shown to be a major predictor for subsequent cardiac events in individuals free of clinical heart disease[34].

Concerning BP, although others[35-36] have reported decreases in BP following RT, in the current study only the AT group demonstrated lower levels of SBP and DBP after intervention. Once hypertension is closely related with autonomic dysfunction[4], it is possible that the increased parasympathetic activity observed in AT can, at least, partially explain the BP reduction in AT. Likewise, AT was a unique intervention to improve the aerobic fitness of older adults. The aerobic exercise-induced improvements in BP and aerobic fitness have been systematically verified by other investigators[17-18, 25, 37-38].

Although the AT group demonstrated a greater number of positive changes to the CVD risk profile than the RT group, the comparison of relative changes between groups suggest that the relative mean changes observed over the eight months were not significantly different between these groups. Therefore, we might assume that both training protocols induce changes of similar magnitude in the variables under investigation.

The current study has some limitations. Breathing frequency was not controlled when analyzing HRV; however, it was demonstrated that measures of HRV using a metronome had a similar consistency with time[39] and a similar reproducibility[40] to free breathing conditions. The high dropout rate observed in the resistance-training group might be considered a limitation. Nevertheless, previous studies[22] with long-duration exercise programs like that in the present study have reported a similar withdrawal rate.

In spite of these limitations, this study has important strengths. A key strength is that to our knowledge, this is the first study aimed at assessing training effects on both autonomic function and inflammation in community-dwelling older adults free of clinical heart disease. Additionally, the study is based on well-validated methods for assessing body composition, as well for controlling physical activity and energy intake. Thus it is our belief that the methodology used in the present study may offer more reliable information and provide insight beyond any possible confounders. Lastly, the assessment of several inflammatory biomarkers led us to a broader and deeper evaluation of the effects of exercise in the studied groups.

In conclusion, the present findings provide further evidence for the benefits, by different mechanisms, of AT and RT on reducing body fat, improving autonomic function and decreasing low-grade inflammation in community-dwelling older adults. Although there are a limited number of investigations aimed at assessing the effects of training beyond AT on inflammation and autonomic function of older adults, our results emphasize the need to promote and prescribe RT as a therapeutic strategy against increased body fat and reduced HRV as well as their related increase in CVD risk.

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Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

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CHAPTER VII

STUDY V

Health-related Quality of Life (HRQoL), Body Composition and Functional Fitness of Older Adults: Results from Aerobic *vs.* Resistance Training.

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Health-related Quality of Life (HRQoL), Body Composition and Functional Fitness of Older Adults: Results from Aerobic *vs.* Resistance Training.

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Running head: Training improves HRQoL and fitness in elders

Abstract

This study aimed to investigate the effects of exercise training on body composition, functional fitness, and health-related quality of life (HRQoL) of community-dwelling older adults. Subjects (n=50, 68.0±5.5 years) were randomized into aerobic training (AT), resistance training (RT) or waiting list (WL). Data on body composition, physical function, and HRQoL were assessed. After eight months of training, AT ($p \leq 0.01$) and RT ($p=0.02$) reduced body fat, increased performance on the sit-to-stand five times ($p \leq 0.01$), stair ascent ($p \leq 0.01$) and 8-foot up-and-go (RT, $p=0.02$; AT, $p \leq 0.01$) tests. AT improved 6-minute walk distance ($p \leq 0.01$), scored higher on physical functioning, ($p=0.04$), general health (GH, $p \leq 0.01$), and mental health (MH, $p=0.03$). RT improved hand-grip strength ($p \leq 0.01$) and scored higher on GH ($p=0.04$). WL increased body fat ($p=0.02$) and scored less on GH ($p=0.04$) and MH ($p=0.04$). AT and RT were effective interventions for decreasing body fat, and improving physical function and HRQoL in older adults.

Key Words: older people; physical performance; quality of life, exercise training.

Introduction

Advancing age is generally accompanied by several metabolic and physical alterations that increase susceptibility to many chronic conditions, disability, and reduced quality of life (QoL). In the specific case of xxxxx, The National Institute of Statistics (INE) recently observed that 41.4% and 19.5% of individuals over 65 years of age self-reported their health and QoL respectively, as bad or very bad (INE, 2009). In addition, it was also reported that older adults accounted for 46.9% of the national prevalence of disability (INE, 2009). On the basis of this data, it appears important to develop health policy strategies to prevent disability and reduced QoL in old age.

One of the barriers to advancing knowledge in the field of QoL is the lack of precision in its definition. Despite the lack of agreement regarding the definition of QoL, it is widely accepted that it refers to a multidimensional construct (Halvorsrud & Kalfoss, 2007) that includes physical, emotional, and social domains. Each of these domains can also be influenced by several factors. Although each factor impacts individuals differently it is assumed that there are group-specific characteristics in QoL (Netuveli & Blane, 2008). For older adults, family relationships, social contacts and activities, functional ability, health status, and general health seem to be important factors when assessing QoL (Farquhar, 1995).

Health does not uniquely influencing QoL in older adults, but it is generally considered an important aspect. In this regard, health-related quality of life (HRQoL) includes several aspects of life such as illness, chronic conditions, disability, and socioeconomic status (SES) that affect perceived physical and mental health (Brown, 2004; Halvorsrud & Kalfoss, 2007). This construct is widely used in clinical practice and in research. It is positively associated with objective health outcomes (e.g. body mass index [BMI] and the number of chronic conditions) and mortality (Kroenke, Kubzansky, Adler, & Kawachi, 2008; Mossey & Shapiro 1982; Wannamethee & Shaper 1991).

An earlier disability model (Jette, 2006) suggested that diseases and chronic conditions lead to impairment, which leads to functional limitation, and then, finally, to disability. Rikli & Jones (1999) proposed that physical inactivity could be as responsible for the decline in functionality as diseases. Furthermore, the interactions between physical inactivity and disease increase disability, thereby, influencing perceptions of HRQoL of older adults.

Conversely, several studies demonstrated health benefits related to increased habitual physical activity. Among such benefits are reduced risk of developing cardiovascular diseases (Barengo, et al., 2004) and type II Diabetes (Krause, et al., 2007), reduced body fat (Bouchard, Beliaeff, Dionne, & Brochu, 2007), maintenance of autonomy (Balzi, et al., 2010), and reduced risk of falling (Chang, et al., 2004).

Beyond the observed associations between physical activity and fitness with objective measures of health outcomes, cross-sectional studies have also demonstrated a positive relationship between physical activity and measures of subjective HRQoL (Brown, 2004; Kruger, Bowles, Jones, Ainsworth, & Kohl, 2007). Therefore, it is likely that physical activity has an impact on both objective health outcomes and subjective HRQoL (Leinonen, Heikkinen, & Jylha, 2001).

The accumulating evidence regarding the benefits of physical activity has motivated prominent organizations like the American College of Sports Medicine and the American Heart Association to recommend physical activity in order to improve functionality and prevent disability in older adults (ACSM/AHA, 2007). However, it is still a matter of discussion to whether changes in physical function due to exercise training positively influence perceptions of HRQoL in older adults.

Despite the fact that many cross-sectional and epidemiological studies (Brown, et al., 2004; Leinonen, Heikkinen, & Jylha, 2001; Lorraine, Hammock, & Blanton, 2005) have found a positive association between physical activity and HRQoL, the available data from randomized controlled intervention trials in independent community-dwelling older adults fails to consistently find a strong effect of exercise training on subjective HRQoL (Martins, Assis, Nahas, Gauche, & Moura, 2009). Moreover, the impact of the type of exercise on training-induced improvements in the self-reporting of HRQoL has not been well studied. Therefore, this study aimed (i) to investigate the effects of two types of exercise training based on the recommendations of current guidelines for physical activity in older adults on subjective HRQoL, functional fitness, and body composition and (ii) to determine the relationship between the changes in functionality and body composition and the changes in HRQoL of independent community-dwelling older adults with no serious medical conditions.

Design and Method

Subjects and Study Design

In this randomized, controlled study, one hundred and eight community-dwelling and independent older adults were recruited from the xxxxx area (xxxxx) by means of advertisements placed in newspapers. The study design is presented in Figure 1.

Subjects were asked to come to the Faculty of Sport on four different days. On the first day, 105 volunteers (78 women and 27 men) completed a health history questionnaire to record past and present conditions and medications. The nature, benefits, and risks of the study were explained to the volunteers, and their written informed consent was obtained. Subjects older than 60 years of age who were community-dwelling and physically independent, i.e., those able to perform the basic and instrumental activities of daily living were included. The exclusion criteria included: (i) acute or terminal illness; (ii) severe or uncontrolled hypertension; (iii) severe or uncontrolled diabetes; (iv) cardiovascular and/or respiratory disorders; (v) any neurological, skeletal-muscle or joint disorder or disturbance that precluded the participation in exercise and testing; (vi) being under the influence of pharmacological therapies that could reduce safety during exercise; and (vii) being involved in regular, supervised exercise training (performing moderate to vigorous exercise for 20 minutes or more at least twice a week) in the previous six months.

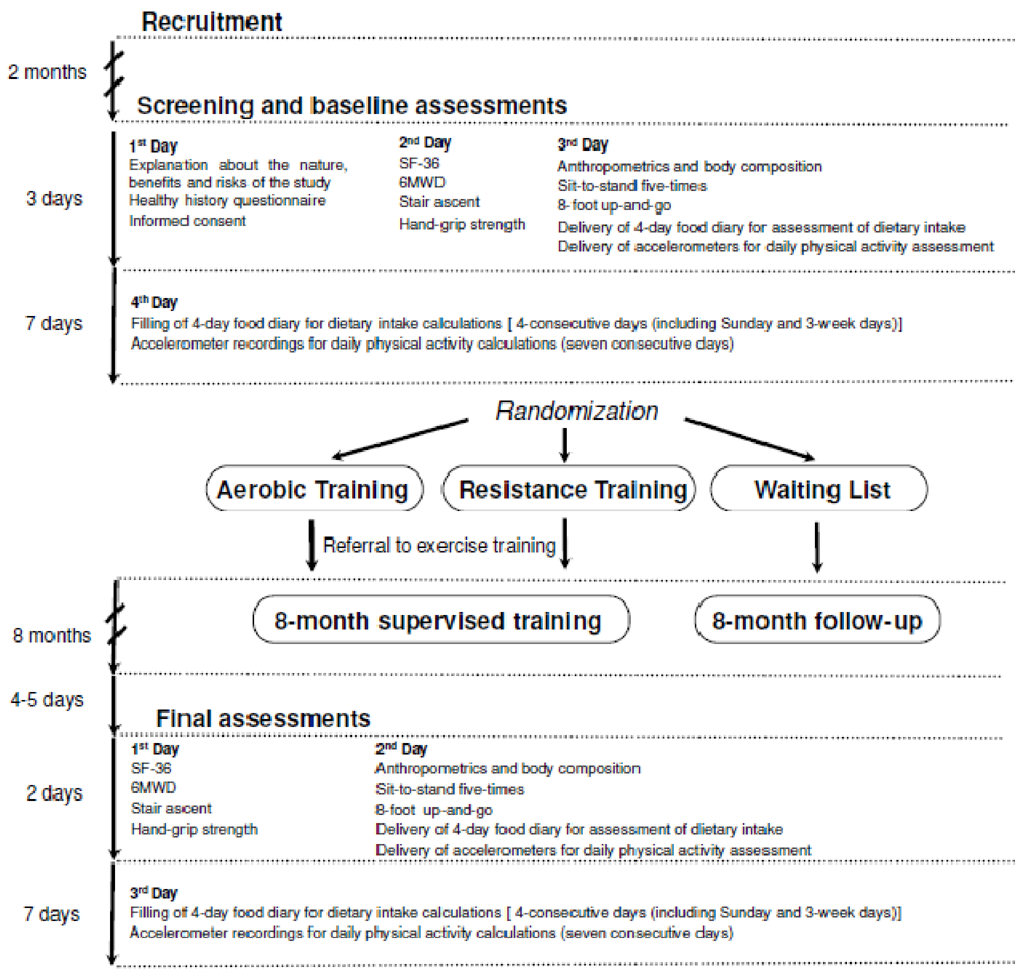

Figure 1. Flowchart depicting the study design.

A second visit was scheduled with each participant to administer the Medical Outcomes Study 36-Item Short-Form Health Study questionnaire (SF-36), and to measure aerobic fitness, stair ascent, and hand-grip strength. On the third day, subjects underwent anthropometric body composition, dual energy X-ray absorptiometry (DXA), and measurements in the 8-foot up-and-go (8FUG) test and, the sit-to-stand five times test. At this time they were also instructed on how to use accelerometers and how to record the 4-day food diary for assessment of habitual physical activity and dietary intake. Finally, on the fourth visit (at least seven days after the third visit) subjects were asked to return the completed 4-day food diary and the accelerometer recordings.

After screening, three individuals were excluded due to cardiovascular diseases (two had had strokes and one had had a cerebrovascular event) and another 17 subjects had given-up and without completing the baseline assessments. Thus, only 85 older adults were randomly allocated, according to computer generated block randomization, into the AT, RT, or Waiting List (WL) groups for eight months. Completion of the training program was defined by an attendance rate of at least 80% of the scheduled sessions. Additionally, older adults who were absent for more than seven consecutive sessions were excluded from the analysis. All subjects were instructed not to change their usual physical activity routines or dietary patterns during the course of the study. Subjects were also asked to inform researchers whenever it was necessary to change medication (type and/or dosage). All methods and procedures were approved by the Institutional Review Board.

Training Protocol

For both exercise training types (AT and RT), older adults trained three times per week (non-consecutive days) for eight months, and each exercise session lasted approximately 50 minutes. Training sessions were generally conducted in indoor facilities.

*Aerobic training.*Training workouts consisted of a 10-minute warm-up that included stretching and callisthenics, thirty minutes of aerobic exercise that mainly consisted of walking, and a 10-minute cool-down. In the first month, the intensity of the AT was gradually increased from 50-60% to 70-80% of the $HR_{Reserve}$ ($HR_{Reserve}$ = HR_{max} – HR at rest), where a subject´s maximum heart rate was calculated as suggested by Tanaka, Monahan, & Seals (2001) (HR_{max}= 208 x 0.7 [age]) or from a rating of perceived exertion (RPE) of 4-6 to 7-8. In order to make sure that the subjects were exercising at the targeted intensity, Polar Heart Rate Monitors (Polar Team System, Finland) was used as primary criteria. All subjects had their RPE registered, but it was only used as primary criteria for five individuals who were on medication known to interfere with HR control (beta-blockers, calcium channel blockers, and vasodilators).

*Resistance training.*The RT protocol consisted of a 10-minute warm-up that included stretching and callisthenics, nine exercises (leg press, chest press, leg extension, seated row, seated leg curl, abdominal flexion, biceps curl, low-back extension, and triceps extension) for different muscle groups, and a 10-minute cool-down. During the first week of RT, the subjects were familiarized with the devices by performing one set of 12-15 repetitions (reps) with no load. Subjects were taught proper lifting techniques and safety precautions. To minimize excessive blood pressure responses, individuals were told to avoid extended breath-holding (Valsalva manoeuvre), during their reps.Then, a baseline one repetition maximum (1RM) for each exercise was undertaken. Afterwards, older adults performed two sets of 12-15 reps at 50-60% 1RM, or a RPE 4-6, for the first month. At the end of the first month, the 1RM was measured again and the load was increased to 80% 1RM or RPE 7-8. At this intensity, older adults performed two sets of 8-12 reps. Every two months, the 1RM was measured in order to keep the training stimulus consistently at 80% 1RM, or a RPE of 7-8. When an individual RPE was under the rating of 7 for two consecutive sessions, the subject was instructed to increase the load so that he/she could perform two sets of 8-12 reps at an appropriate RPE. Concentric and eccentric movements were performed at a rate of three seconds. A 2-minute rest between each set was provided.

Waiting list. During the study period, individuals randomized to this group were contacted by phone in 4-month intervals to attest they were still interested in participating in the program. At these moments, they were reminded to try to not change their lifestyle (physical activity, diet, or medication). After the 8-

month observation period, they were invited to participate in specific exercise programs (their choice of resistance or gymnastics) designed for seniors.

Measures

Throughout all the assessments, the test administrator and the time of day used for testing remained constant.

Anthropometrics and body composition. Body weight was measured to the nearest 0.1kg with an electronic weight scale (*SECA 708*). Subjects were weighed barefoot wearing light clothing. Height was measured to the nearest 1mm with a standard stadiometer. Body Mass Index (BMI) was determined. Whole body lean mass (LM) and percent of total body fat (%BF) were determined using a DXA (Hologic QDR-4500, software for windows XP, version 12.4) with subjects in the supine position.

Functional fitness assessment. All tests were chosen because they are valid and reliable instruments that can be used to obtain measurements in a variety of settings, with minimal equipment costs and without special set-up to obtain the measurements (VanSwearingen & Brach, 2001). Test-retest reliability using the intra-class correlation coefficient (ICC) two-way mixed model for the selected physical fitness tests was determined on a randomly selected subset of 15 subjects (which represents approximately 20% of the sample), five subjects from each group. Subjects completed two sessions of tests separated by 12 days. The ICC values for the 6-minute walk test (6MWT), hand-grip, sit-to-stand five times, stair ascent and 8FUG tests were 0.91 ($p \leq 0.01$), 0.98 ($p \leq 0.01$), 0.93 ($p \leq 0.01$), 0.95 ($p \leq 0.01$), and 0.95 ($p \leq 0.01$), respectively. In all timed tests, the individual's performance was registered with a standard stopwatch to the nearest tenth of a second.

Aerobic fitness. Aerobic fitness was assessed using the 6MWT, which is a commonly test used to assess physical performance in older people (Lord & Menz, 2002), particularly to obtain valid measures of submaximal aerobic capacity and exercise endurance (American Thoracic Society [ATS] 2002;

Kervio, Carre, & Ville, 2003; Rikli & Jones, 1998). This test measured the distance in meters covered when subjects were instructed to walk as quickly as they could for six minutes. Walks were conducted on a flat fifty meter rectangular course, marked off in five meter segments. If necessary, subjects were allowed to stop and rest.

Hand-grip strength. Hand-grip strength has been widely used as a surrogate measure of total body strength (Herman, et al., 2005). Amongst older adults, it has been shown to correlate with a decline in the activities of daily living and cognition (Taekema, Gussekloo, Maier, Westendorp, & de Craen, 2010), markers of frailty (Syddall, Cooper, Martin, Briggs, & Aihie Sayer, 2003), and disability (Al Snih, Markides, Ottenbacher, & Raji, 2004). Moreover it was demonstrated to be a predictor of all-cause mortality in the older population (Ling, et al., 2010; Syddall, et al., 2003). In the present study, hand-grip strength was isometrically measured using an electronic hand-grip dynamometer (Takei, TKK 5101 Grip-D). The subject held the dynamometer in the dominant hand with his or her arm by his or her side and had to squeeze using maximum force. The best score obtained in three trials, with an approximate two-minute rest between trials, was recorded.

Sit-to-stand five times. One of the most common activities of daily living is rising from a seated to a standing position. The ability to perform this movement is important to maintaining physical independence (McCarthy, Horvat, Holtsberg, & Wisenbaker, 2004). In community-dwelling older adults, the sit-to-stand five times test influenced by multiple sensorimotor, balance, and psychological processes; this test represents a particular transfer skill (Lord, Murray, Chapman, Munro, & Tiedemann, 2002) and is a proxy measure of muscle strength (VanSwearingen & Brach, 2001) and power (Bean, et al., 2002). The tests were conducted as suggested by Whitney et al. (2005) and consisted of timing an individual stood five times from an armless standard chair (45cm high).

Stair ascent. Difficulty in stair negotiation (ascent and descent) has been shown to be an indicator of disability closely related with lower limb strength (Tiedemann, Sherrington, & Lord, 2007). Therefore, the time required to ascend a ten-stair (17cm high, 30cm deep) prop was recorded to evaluate older adults' stair negotiation skills.

8-foot up-and-go (8FUG). The 8FUG is a modified version of the 3m timed up-and-go test. Both tests have been widely used to monitor functional mobility and have been found to be good predictors of recurrent falling (Whitney, Lord, & Close, 2005). The test consisted of timing an individual as he or she stood from a standard chair, walked eight feet (2.44m), turned around a cone, returned to the chair, and sat down.

Health-related quality of life (HRQoL). Older adults' perceptions of their HRQoL were subjectively assessed using the SF-36 (Ware & Sherbourne, 1992), which was adapted and validated for the population under investigation (Ferreira, 1998). The SF-36 is a relatively simple and brief questionnaire that was originally developed to assess generic health status (Ware & Sherbourne, 1992). However, it has become a widely used indirect measurement of HRQoL (Hopman, et al., 2000) since important correlations were reported between its scales and several specific dimensions of HRQoL, including living arrangements, financial situation, disability, and family life (Anderson, Laubscher, & Burns, 1996; Ware, Snow, Kosinski, & Gandek, 1993). Moreover, the SF-36 was validated in a variety of countries (Ferreira, 1998; Hopman et al., 2000) and sub-population groups, including stroke patients (Anderson, Laubscher, & Burns, 1996) and relatively healthy older adults (Lyons, Perry, & Littlepage, 1994; Parker, Peet, Jagger, Farhan, & Castleden, 1998). The SF-36 is comprised of eight health concepts: physical functioning (PF; 10 items), role-physical (RP; 4 items), bodily pain (BP; 2 items), general health (GH; 5 items), vitality (VT; 4 items), social functioning (SF; 2 items), role-emotional (RE; 3 items), and mental health (MH; 5 items) (Anderson, Laubscher, & Burns, 1996). These eight scales can be aggregated into two components, the SF-36 Physical Component Summary (PCS) and Mental Component Summary (MCS). There is also a single separate item that is used to assess any change in health from one year before.

The instrument was administered through personal interview, and norm-based scores for the SF-36 were calculated using the methods set out by Ware, Snow, Kosinski, & Gandek (1993) and Ware & Kosinski (2001). In the norm-based scales and components, a score of 50 represented the mean. Therefore, all scores above or below 50 can be interpreted as above or below the general population (US population) norm.

Habitual physical activity. Physical activity levels were assessed using accelerometers (Actigraph GT1M, Actigraph LLC, Pensacola, FL) as an objective measure of daily physical activity. The Actigraph accelerometer is an uniaxial monitor that measures the intensity of movement averaged over 1-minute sampling intervals called 'epochs' (Mark & Janssen, 2008). Monitors were programmed to start recording at midday of the second meeting and recorded activity for the following seven days. Subjects were instructed to wear the accelerometer over their right hip (Freedson, Melanson, & Sirard, 1998) for a seven-day period (five week days and two weekend days). Exceptions included time spent sleeping, showering, and during water-based activities. Subjects were asked to maintain their usual activities and record them in a diary. Data from each monitor were downloaded by the investigators and compared with data from a diary before the average counts/min had been calculated. This unit of measurement (counts/min) was generated based on magnitude and frequency of movement (Mark & Janssen, 2008). To the best of our knowledge, there are no appropriate counts/min cut-points that represent meaningful intensity categories (sedentary, moderate and vigorous) in older adults. Therefore, in the current study, physical activity levels were expressed as the average counts per minute (obtained from the Actigraph monitor) over the 7 days.

Dietary intake. Dietary intake was measured by a four-day dietary record (DR) (three weekdays and one weekend day), before and after the intervention.

Subjects were asked to record all food and drink consumed on each recording day, trying to not change their eating habits. To ensure standardization in the recording, a nutritionist individually instructed the subjects on how to fill out the DR correctly. After receiving the completed DRs, nutritionists checked them for missing information, and when necessary, the subjects were asked to add extra information (generally quantities and food preparation issues) for the following visit. Dietary records were analyzed using an adapted national version of the software Food Processor Plus® (ESHA Research Inc, Salem, Oregon, USA), a nutritional analysis software that converts food intake into total energy and nutrients, based on food composition tables available from the USDA (United States Department of Agriculture) and national data from typical national foods.

Statistical Analysis

The characteristics of the subjects were initially described using tabulations of frequency and percentage distributions. The results were shown as means and standard deviations (M±SD). A one-way analysis of variance (ANOVA) was used to identify between group differences in baseline values. When a significant main effect was detected at a significance level of $p<0.05$, a Bonferonni correction was used for post-hoc comparison. To detect changes within groups (pre-test vs. post-test), a paired t-test was employed. The pre-to-post changes (Δ) for each subject were related to the individual baseline level to define the relative change (%Δ). In order to identify differences in pre-to-post changes between groups, General Linear Models were used, with the relative change as the dependent variable and the group as the fixed factor. Afterwards, baseline values, age, gender, %BF and medication were inserted into the models as covariates. Pearson (r) correlation coefficients were used to investigate correlations between relative changes in body composition variables, physical function tests and HRQoL domains. A Mann-Whitney U test was used to identify, in each group, differences between dropouts and compliant subjects. Statistical significance was set at a p value equal to or less than 0.05, and all analyses were performed with SPSS (version 17.0).

Results

Drop-out and Characteristics of the Subjects

After randomization, 11 individuals (8 RT, 3 AT) out of the 85 left the study due to incompatibility with the training timetable. Therefore, only 74 older adults began the protocol. During the eight months, another 24 (32.4%) subjects dropped out of the study (8 RT, 4 AT, 12 WL) for different reasons: low back pain and arthrosis (3 RT); knee surgery (1 RT, 1 WL); cerebral stroke (1 AT, 1 WL); medical advice (2 RT, 1 AT); loss of motivation and moved out of the city (2RT, 1 AT) and 11 (1 AT, 10 WL) were lost because they did not complete the final assessment.

Thus, the total dropout rate was 41.2%, and the final sample was comprised of fifty community-dwelling older adults (68.0±5.5 years), mainly women (n=39, 78.0%); 56.0% had controlled hypertension, 42.0% suffered from dislipidemia, and 18.0% had controlled diabetes. According to BMI criteria, 21.0% were classified as overweight (25-29) and 28.0% as obese (>30). None of the subjects were currently smokers. Finally, four (10.3%) out of thirty-nine women were on hormone replacement therapy (HRT). Table 1 presents the main characteristics of the subjects for each group at baseline and the flow of subjects during the study is presented in Figure 2.

Differences Between Groups at Baseline

Before the protocol, the RT group had better performance than the WL group in the 6MWT ($p \leq 0.01$), 8FUG ($p=0.01$), and sit-to-stand five times ($p<\leq 0.01$). On the contrary, the WL group had better GH perceptions than the RT group ($p \leq 0.01$). When compared with the WL group, the AT group had higher perceptions of their RP ($Pp \leq 0.01$). The AT group also demonstrated better performance in the sit-to-stand five times than the WL group ($p=0.01$). The WL group had a higher dietary intake when compared with the AT group ($p=0.01$). No significant differences were observed at baseline in either body composition outcomes or in physical activity levels.

Table 1. Baseline characteristics of the sample.

	Resistance n=11	Aerobic n=20	Waiting List n=19
Gender	4 men, 7 women	3 men, 17 women	4 men, 15 women
Age (years)	67.3±4.9	69.9±5.7	67.8±5.5
BMI (kg/m^2)	29.5 ± 5.0	28.1 ± 4.1	27.2 ± 3.5
Controlled hypertension, n (%)	6 (54.5%)	9 (45.0%)	13 (68.4%)
Controlled dislipidemia, n (%)	4 (36.4%)	10 (50.0%)	7 (36.8%)
Controlled diabetes, n (%)	1 (9.1%)	2 (10.0%)	6 (31.6%)
Smoking status			
Never, n (%)	9 (81.8%)	18 (90.0%)	17 (89.5%)
Former, n (%)	2 (18.2%)	2 (10.0%)	2 (10.5%)
Smoker, n (%)	0	0	0
HRT, n (%)	1 (9.1%)	3 (15.0%)	0

BMI – body mass index; HRT – hormone replacement therapy.

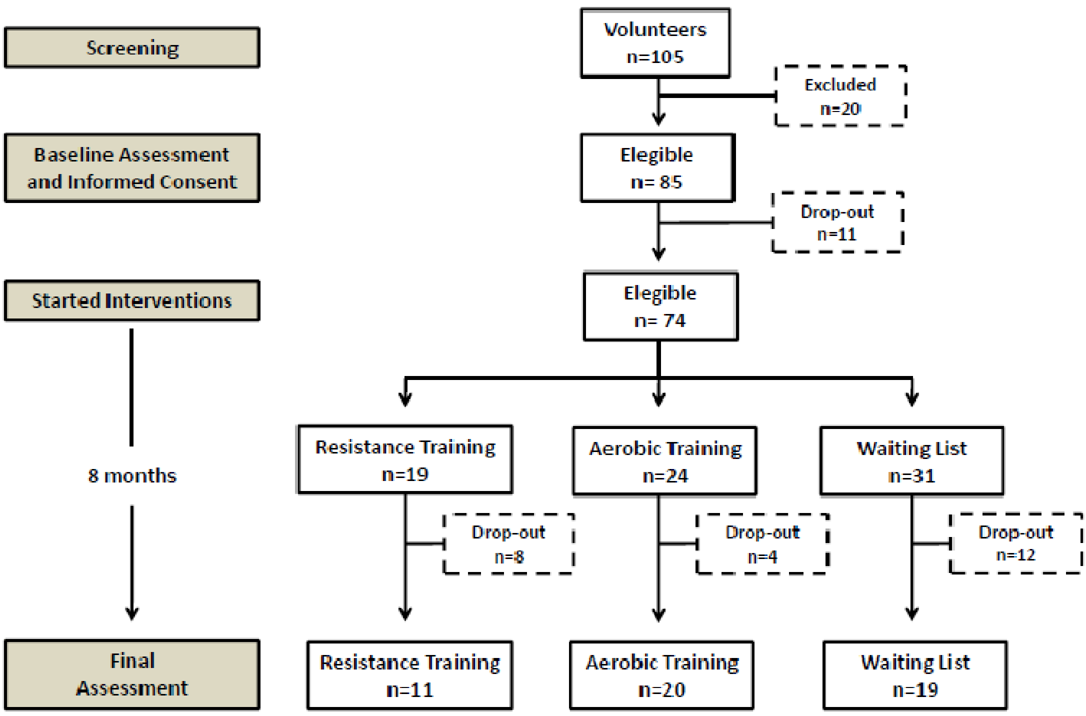

Figure 2. Flowchart describing retention of participants.

Differences Within Groups after the Protocol

After the protocol, the RT and AT groups demonstrated a lower %BF (RT, $p=0.02$; AT, $p\leq 0.01$), while the WL group had greater %BF ($p=0.02$). No changes were observed in older adults' BMI or lean mass across the eight months. As expected, the RT and AT groups also increased their fitness through the training. The AT group had a better performance in the 6MWT ($p\leq 0.01$), and the RT group had higher hand-grip strength ($p\leq 0.01$). Additionally, both training groups decreased the time needed to perform the sit-to-stand five-times (RT, $p\leq 0.01$; AT, $p\leq 0.01$), stair ascent (RT, $p\leq 0.01$; AT, $p\leq 0.01$) and the 8FUG (RT, $p\leq 0.01$; AT, $p\leq 0.01$) tests. Interestingly, the WL group also decreased the time needed to perform the sit-to-stand five times test ($p=0.02$). Besides improvements in body composition and fitness, the older adults in the AT group scored higher on PF ($p=0.04$), GH ($p\leq 0.01$) and MH ($p=0.03$), and older adults in the RT group also scored higher on GH ($p=0.04$). On the contrary, worse scores on GH ($p=0.04$) and MH ($p=0.04$) were observed in the WL group after the protocol (Table 2). At baseline, in the single separate item of SF-36 that was used to assess any change in health from one year before, the majority of the subjects (70.0%), independent of group, reported no changes in their health status during the last year. On the other hand, after intervention, 72.7% and 65.0% of the RT and AT groups, respectively, evaluated their health as somewhat better or much better than one year ago, while 47.4% of the WL group self-reported their actual health status as somewhat worse now than one year ago. Moreover, none of the subjects in this group reported his or her health as somewhat better or much better than one year ago (Table 3).

Subjects did not change their physical activity levels ($p=0.39$) or their dietary patterns ($p=0.95$) across the eight-month study period.

Differences in Relative Changes Between Groups

General linear models demonstrated significant differences in relative changes between groups for BMI, %BF, 6MWT, 8FUG, stair ascent, sit-to-stand, GH, MH, and PCS. Post-hoc comparisons demonstrated that relative changes in BMI were more pronounced in the RT group than in the WL group ($p=0.03$). Greater differences were also identified in the RT and AT groups than in the WL group regarding %BF ($p \leq 0.01$). Concerning changes in functional fitness, individuals in the AT group demonstrated a greater improvement in 6MWT ($p \leq 0.01$) and in stair ascent ($p \leq 0.01$) than those in the WL group. Relative changes in 8FUG and sit-to-stand five times were more pronounced in both training groups than in the WL group ($p \leq 0.03$). Finally, the relative differences for GH ($p=0.01$) and MH ($p \leq 0.01$) were greater in the AT group than in the WL group, and the PCS relative difference was greater in the RT group than in the WL group ($p=0.02$). No significant differences in relative changes were observed between the AT and RT groups.

Table 2. Outcomes at baseline (before) and after protocol.

Outcomes	Resistance (n=11)			Aerobic (n=20)			Waiting List (n=19)		
	Before	After	Δ%	Before	After	Δ%	Before	After	Δ%
Body composition									
BMI (kg/m^2)	29.5 ± 5.0	28.1 ± 4.0	-2.4 ± 4.4	28.1 ± 4.1	27.9 ± 3.8	-0.6 ± 1.5	27.2 ± 3.5	27.6 ± 3.0	2.0 ± 4.6
%BF	34.5 ± 7.1	32.9 ± 8.3*	-5.4 ± 6.3	38.4 ± 5.3	37.2 ± 5.6*	-3.3 ± 2.9	34.5 ± 5.9	35.2 ± 6.0*	2.1 ± 3.5
Lean mass (kg)	43.7 ± 9.8	43.8 ± 9.8	0.4 ± 4.8	37.2 ± 5.5	37.0 ± 4.5	0.1 ± 5.5	42.9 ± 10.2	42.5 ± 9.7	-0.6 ± 2.5
Functional fitness									
6MWD (m)†	630.5 ± 57.0	659.1 ± 73.5	4.6 ± 7.4	541.8 ± 70.4	592.4 ± 76.9*	9.5 ± 6.9	524.5 ± 97.0	533.2 ± 82.7	-0.4 ±9.7
Stair ascent (s)	4.56 ± 0.7	3.95 ± 0.5*	-12,8 ± 9.9	5.29 ± 1.1	4.20 ± 0.7*	-20.1 ± 11.4	5.19 ± 0.8	4.98 ± 1.0	-4.8 ± 10.3
8FUG (s)†	5.14 ± 0.5	4.62 ± 0.4*	-8.8 ± 9.7	5.88 ± 1.0	5.08 ± 0.7*	-13.3 ± 9.6	6.12 ± 0.9	5.94 ± 1.0	-2.7 ± 12.9
Sit-to-stand 5-times (s)†	7.99 ± 1.0	6.45 ± 0.7*	-18.2 ± 10.8	8.73 ± 2.1	6.71 ± 1.4*	-21.5 ± 13.9	9.92 ± 2.5	9.05 ± 2.5*	-8.0 ± 16.2
Hand-grip Strength(kg) / Body weight (kg)	0.43 ± 0.11	0.46 ± 0.11*	9.0 ± 8.4	0.40 ± 0.9	0.41 ± 0.8	4.5 ± 13.9	0.42 ± 0.9	0.41 ± 0.1	0.8 ± 11.1
Health-related quality of life									
(Standardized scales)									
PF	47.6 ± 8.8	51.3 ± 4.3	13.8 ± 27.8	49.3 ± 6.2	51.1 ± 3.6*	4.4 ± 8.1	48.2 ± 9.3	46.8 ± 9.8	1.5 ± 36.2
RP†	53.6 ± 6.6	52.9 ± 8.6	5.5 ± 13.2	55.1 ± 2.6	54.0 ± 6.5	-1.9 ± 11.7	52.4 ± 6.8	47.2 ± 12.4	-9.0 ± 26.3
BP	48.3 ±11.2	50.2 ± 10.1	5.6 ± 14.0	49.2 ± 11.0	53.1 ±9.0	14.0 ± 36.8	49.2 ± 10.7	45.0 ± 8.7	-4.7 ± 27.2
GH	43.4 ± 7.5	48.5 ± 5.7*	16.8 ± 17.0	45.8 ± 6.7	51.5 ± 6.0*	14.4 ± 19.7	50.4 ± 6.4	47.0 ± 8.3*	-6.6 ± 13.1
VT	55.2 ± 10.0	53.0 ± 11.9	-1.5 ± 16.2	56.1 ± 10.4	57.3 ± 11.4	2.3 ± 17.6	53.9 ± 8.6	51.2 ± 11.3	-4.3 ± 17.9
SF	53.8 ± 5.7	53.8 ±4.5	3.2 ± 13.4	51.9 ± 10.4	52.5 ± 7.1	11.6 ±61.0	51.1 ± 5.9	51.1 ± 5.9	1.7 ± 20.5
RE	50.7 ± 8.4	52.6 ± 9.3	14.0 ± 24.7	46.2 ± 12.8	50.3 ± 10.2	20.9 ± 51.4	49.5 ± 9.9	47.3 ± 11.1	-0.9 ± 34.6
MH	45.4 ± 15.0	44.0 ±14.6	2.9 ± 27.0	45.2 ± 12.7	52.2 ± 13.0*	21.9 ± 37.3	47.9 ± 10.6	43.0 ± 13.9*	-10.5 ± 20.8
PCS†	48.7 ± 7.2	52.7 ± 3.3	10.0 ± 15.3	52.2 ± 5.2	52.9 ± 5.3	2.1 ± 12.2	50.6 ± 6.2	47.4 ± 8.9	-6.0 ± 16.3
MCS	50.7 ± 9.1	50.9 ± 8.6	2.1 ± 16.4	47.6 ± 12.9	52.5 ± 12.3	19.7 ± 43.5	50.2 ± 9.1	47.6 ± 8.8	-3.1 ± 19.8
Physical Activity levels (Count/min)	368.9 ± 106.8	438.9 ± 185.1	17.1 ± 26.3	318.4 ± 82.3	334.8 ± 74.3	9.1 ± 25.7	354.9 ± 156.0	361.0 ± 139.3	8.9 ± 40.0
Dietary Intake (kcal)	1 531.2± 359.7	1 678.8 ± 647.4	9.9 ± 44.3	1 368.2 ± 281.7	1 428.9 ± 301.6	-0.1±24.8	1 724.6 ± 486.4	1 798.7 ± 260.9	0.5 ± 27.3

† Outcomes that presented differences between groups at baseline. *Differences within groups (before and after interventions/observation). $p<0.05$.

BMI – body mass index; %BF – percentage of body fat; 6MWD – six-minute walk distance; 8FUG – eight-foot up-and- go; PF – physical functioning; RP – role-physical; BP – bodily pain; GH - general health; VT – vitality; SF – social functioning; RE – role-emotional; MH - mental health; PCS – Physical Component Summary; MCS – Mental Component Summary.

Table 3. Frequencies and percentages for each self-rating option in the item "changes in general health", before and after protocol.

	Resistance		**Aerobic**		**Waiting List**	
	Before	After	Before	After	Before	After
1. Much better now than one year ago, n (%)	-	1 (9.1)	2 (10.0)	6 (30.0)	1 (5.2)	-
2. Somewhat better now than one year ago, n (%)	-	7 (63.6)	3 (15.0)	7 (35.0)	3 (15.8)	1 (5.2)
3. About the same, n (%)	9 (81.8)	3 (27.3)	14 (70)	7 (35.0)	12 (63.2)	9 (47.4)
4. Somewhat worse now than one year ago, n (%)	2 (18.2)	-	1 (5.0)	-	3 (15.8)	9 (47.4)
5. Much worse now than one year ago, n (%)	-	-	-	-	-	-

Further adjustments for baseline values, age, gender, %BF and medication use slightly changed results. In the adjusted models, the factor group did not explain the relative changes in BMI. In addition, the relative changes between the RT and the WL groups in the sit-to-stand five times test and in the PCS lose significance. On the contrary, in the adjusted models, relative changes in the stair ascent were greater in both the AT and RT groups than in the WL group. Finally, the mean differences of the RE and MCS were greater in the AT group than in the WL group (see Table 4).

Table 4. General Linear Models: between group comparisons of mean relative changes (%Δ).

Dependent Variable	Unadjusted Model			Adjusted Model†			
	F	*p*	Partial Eta² (%)	*F*	*p* Model	*p* Factor	Partial Eta² (%)
Body composition							
%Δ BMI	4.0	0.03	14.5	4.0	<0.01	0.06	50.0
%Δ %BF	17.7	<0.01	42.9	6.4	<0.01	<0.01	59.0
%Δ Lean mass	0.2	0.81	0.9	1.0	0.44	0.56	45.0
Functional fitness							
%Δ 6MWT	6.9	<0.01	23.8	2.9	<0.01	<0.01	44.2
%Δ Stair ascent	9.4	<0.01	29.0	5.4	<0.01	<0.01	58.7
%Δ 8FUG	6.9	<0.01	23.1	3.6	<0.01	<0.01	47.8
%Δ Sit-to-stand five times	7.1	<0.01	23.9	2.0	0.06	0.04	34.5
%Δ Hand-grip strength/Body weight	2.1	0.13	8.3	5.9	<0.01	0.08	60.0
Health-related quality of life							
%Δ PF	0.5	0.58	2.3	5.2	<0.01	0.84	57.2
%Δ RP	1.9	0.17	7.5	2.6	0.02	0.13	40.1
%Δ BP	1.9	0.16	7.7	4.8	<0.01	0.12	55.9
%Δ GH	4.6	0.02	16.6	4.7	<0.01	0.03	54.4
%Δ VT	0.8	0.46	3.2	0.9	0.57	0.19	18.1
%Δ SF	0.4	0.70	1.5	4.7	<0.01	0.81	55.4
%Δ RE	1.4	0.27	5.4	4.9	<0.01	0.02	59.0
%Δ MH	5.9	<0.01	20.2	2.8	0.01	0.03	41.5
%Δ PCS	4.2	0.02	15.4	2.7	0.01	0.04	41.2
%Δ MCS	2.7	0.08	10.6	8.2	0.01	0.02	68.4

Independent variable – mean change (%Δ) in outcomes; Factor – Group.

†Adjusted for baseline values, age, gender, %BF, and medication use.BMI – body mass index; %BF – percentage of body fat; 6MWD – six-minute walk distance; 8FUG – eight-foot up-and- go; PF – physical functioning; RP – role-physical; BP – bodily pain; GH - general health; VT – vitality; SF – social functioning; RE – role-emotional MH - mental health; PCS – Physical Component Summary; MCS – Mental Component Summary.

Correlation Between Relative Changes

All changes in functional fitness tests were significantly correlated with changes in %BF. The observed correlations between a change in %BF and changes in 6MWT and handgrip strength ($-0.32 \leq r \leq -0.40$; $p \leq 0.02$) were negative, while the correlations between the change in %BF and a change in time to perform each of stair ascent, 8FUG, and sit-to-stand five times were positive ($0.28 \leq r \leq 0.41$; $p \leq 0.05$). A change in one´s performance in the stair ascent test negatively correlated with changes in BP (r=-0.41; $p \leq 0.01$) and MH (r=-0.39; $p \leq 0.01$).

There was a trend that a change in 6MWT would positively correlate with changes in BP (r=0.27; p=0.06) and MH (r=0.29; p=0.05). Finally, changes in body composition did not correlate with changes in HRQoL domains.

Baseline Differences Between Individuals With and Without Missing Data

When compliant individuals were compared with individuals who had dropped out, minimal differences were observed. In the RT group, the dropout subjects had lower aerobic fitness than the compliant subjects (p=0.04). The opposite was observed in the AT group: the compliant subjects had a worse performance at baseline on the aerobic fitness test than the subjects who dropped out (p=0.03). Compliant subjects in the WL group had a better performance on the stair ascent (p=0.04) and a better perception of their RP

(p=0.02) and PCS (p=0.03) than volunteers who gave up along the study period.

Discussion

The decline in HRQoL generally observed during aging is multi-factorial, including among other factors, biological aging, disease, fat mass increase and redistribution, sarcopenia, death of relatives and friends, and certain lifestyle patterns (Halvorsrud & Kalfoss, 2007). Therefore, any intervention designed to improve the HRQoL of older adults also has to combat multiple factors. In the present study it was demonstrated that after exercise training, older adults decreased their total body fat percentage and improved their overall functional fitness. Additionally, the AT group was able to increase their self-reported PF, GH, and MH, while the RT group increased self-reported GH. Finally, the magnitude of relative changes for all variables was not different among training groups, suggesting that they have similar benefits for body fat control, functionality, and self-reported HRQoL of community-dwelling older adults.

In this study, body composition was investigated because the common decrease in skeletal muscle mass (Visser, et al., 2005) and the increase in body fat put older adults at a higher risk of chronic conditions and disability (Bouchard, et al., 2007). Moreover, it has been demonstrated that increased body fat was associated with decreased PF and RP domains for SF-36 (Villareal, Banks, Siener, Sinacore, & Klein, 2004). Studies addressing the impact of exercise training on body composition have provided conflicting results. In accordance with the present observations, others have demonstrated resistance (Sillanpaa, et al., 2008) and aerobic training (Okita, et al., 2004) as valuable for reducing body fat. Nevertheless, the contrary was also observed (Heffernan, et al., 2009; Timmerman, Flynn, Coen, Markofski, & Pence, 2008; Wanderley, Oliveira, Mota, & Carvalho, 2010). It is likely that differences in results are due methodological bias, like lower intensity and the duration of interventions, as well as the use of different methods for assessing body composition. Another explanation may be the lack of control of diet intake. None of the studies previously mentioned have controlled for this possible confounding factor. In the present study, the energy intake of subjects was assessed at baseline and at the end of the protocol, and no significant change within groups was observed. Moreover, subjects did not report any illness or medication that could interfere in their weight or body fat. In this regard, it is likely that the observed changes in body composition were probably mostly related to the exercise training.

Taking into account that social contacts (Farquhar, 1995), the number of chronic conditions (Leinonen, et al., 2001), functionality (Leinonen, et al., 2001; Netuveli & Blane, 2008), disability (Lebrun, et al., 2006), and independence

(Netuveli & Blane, 2008) are relevant aspects when older adults assess their HRQoL, it was hypothesized that if AT and RT increased physical function and fitness of subjects to levels that permitted them to carry out an array of activities relevant to effective community living, such as walking, climbing, lifting, standing from a seated position, and handling everyday objects without fatigue, it would ameliorate HRQoL. Confirming the hypothesis, and in accordance with previous findings (Henwood, Riek, & Taaffe, 2008; Hung, et al., 2004; Levinger, Goodman, Hare, Jerums, & Selig, 2007; Tsai, et al., 2002), the observed improvements in body composition and in functional fitness after training were followed by better perceptions of HRQoL in both the AT and RT groups.

Indeed, the AT group obtained higher scores in three out of eight SF-36 domains (PF, GH and MH) while the RT group scored higher on the GH domain only. It is also important to mention that before intervention, the AT and RT groups had, on average, five and four out of eight domains that scored lower than normative values, respectively. But, at the end of the protocol, the AT group scored above the norm in all SF-36 domains and the RT group in six out eight. In addition, more than 60% of the individuals in the training groups rated their general status as better after the protocol, while almost 50% of individuals in the WL group rated their health as worse after the 8-month study period. Despite the AT group demonstrated within-group changes in a greater number of HRQoL domains than the RT group, the mean relative changes between the training groups for HRQoL domains were not different. Hence, these results are consistent with previous research (Kimura, et al., 2010; Martins, Assis, Nahas, Gauche, & Moura, 2009; Tsai, et al., 2002) suggesting that HRQoL improves with exercise, whatever the training type performed.

Despite relationships between body composition and HRQoL that were demonstrated in observational studies (Lebrun, et al., 2006; Lorraine, Hammock, & Blanton, 2005), in the present study the changes observed in body composition were not related with the changes in the domains of HRQoL. On the contrary, changes in performance in all the functional fitness tests correlated with changes in %BF, suggesting that maybe the relationship between body composition and HRQoL is, to a certain degree, mediated by functional fitness. The observed change in the stair ascent performance also related with changes in the BP and MH domains. It is not surprising that a surrogate measure of lower limb strength and mobility related with one's subjective HRQoL. Several studies have reported that a loss of strength and power in older adults seems to be more pronounced in the lower limbs than in the upper limbs (Landers, Hunter, Wetzstein, Bamman, & Weinsier, 2001) and that this lower limb muscle impairment is associated with disability and the loss of one's mobility and independence. Therefore, it is possible that increases in functional fitness, namely in lower limb strength and mobility, may provide a global indicator of health and functioning through which the improvements in health and functional performance can be perceived and reflected in everyday life (Rejeski & Mihalko, 2001) and, for that reason, in training-induced improvements in the self-reported HRQoL of the subjects.

Other possible mechanisms include the effects of exercise on an array of positive health outcomes in older adults, including mitigating cardiovascular disease risk factors and reducing one's risk of falling (King, et al., 2000). The psychological benefits of social interaction and support were also suggested to be possible mediating factors of the exercise training effects on subjective HRQoL (Liu-Ambrose, et al., 2005). Finally, it has been suggested that exercise training might improve serotonin and endorphin levels, which can lead to beneficial effects on one's mood and feelings of well-being (Kritz-Silverstein, Barrett-Connor, & Corbeau, 2001). However, these variables were not controlled for in the present study.

Some caution is warranted when interpreting the results of this study. Firstly, the sample was comprised of independent, community-dwelling older volunteers with no serious medical conditions, and thus, does not represent a true randomized sample. In addition, a higher withdrawal rate was observed particularly in the RT group. This increased rate of dropouts may undercut the benefits of randomization. In order to explore possible bias in the results, the baseline values of compliant individuals and dropouts were compared in each group. In the RT group, the dropouts had a worse performance in 6MWT than compliant subjects, while the opposite was observed in the AT group. In general, lower fitness levels at baseline are related to greater improvements after training, which suggests that, most likely, if the dropouts in the RT group had followed the protocol, the mean increase in the 6MWT of this group would be higher than the observed increase. The contrary it would probably happened with the AT group. In the WL group, compliant subjects had a better performance on the stair ascent test and a better perception of their RP and PCS than dropouts, suggesting that if all subjects had adhered to the protocol, the mean change differences between the WL group and the training groups would be higher than the observed differences. Nevertheless, previous studies (Ring-Dimitriou, et al., 2007) with long-duration exercise programs like that seem in the present study have reported a similar withdrawal rate.

Despite these limitations, this study has several strengths. Potential confounding variables were controlled for, such as habitual physical activity levels objectively measured by accelerometers, dietary intake, number of chronic conditions, and medication.Considering the study's limitations and strengths, the results led us to conclude that eight months of moderate to vigorous exercise training – independent of the exercise type (aerobic or resistance) – is an effective intervention for decreasing body fat mass percentage, improving overall physical function, and improving several domains of self-reported HRQoL in community-dwelling older adults. With the number of older adults constantly increasing, a public health approach based on the dissemination of aerobic and/or resistance exercise programs seems to be of paramount importance to avoid an increased number of disabled older individuals living with a poor HRQoL. However, additional studies with larger samples are needed to clarify this issue.

Acknowledgments

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CHAPTER VIII

FINAL REMARKS

8. FINAL REMARKS

This section aims to answer the three major questions of this thesis based on the main findings of the descriptive, correlational and RCT studies.

Are simple physical/functional fitness field tests capable of identifying, in a group of community-dwelling older adults, those who are at an increased risk of CVD and those with a lower HRQoL?

The findings from Study II demonstrated that the performance of community-dwelling older adults on the 6MWT was associated with cardiovascular function at rest and with several CVDs risk factors. These findings reinforce results from previous studies which demonstrated that lower levels of aerobic fitness are related with an increased CVD risk. Moreover, this study adds to the body of literature providing evidence that a simple field-test is able to identify older individuals with high %BF, SBP, and RPP_{rest}, independent of age and sex.

Results from previous observational studies have demonstrated that lower levels of aerobic fitness and muscular strength were related with decreased functionality and increased disability and dependence in older adults. Considering that older adults generally report disability and the loss of autonomy as contributing factors to a poor QoL/HRQoL, this study aimed to observe if aerobic fitness and muscular strength, as surrogate measures of functional limitation, and assessed by simple field tests were capable of identifying older adults with a low self-reported HRQoL.

The results confirmed that, at least in this group of community-dwelling older adults, the way they reported some aspects of HRQoL were related to general physical fitness as assessed by 6MWT and hand-grip strength. The fit older adults were twice as likely to score higher in the PF, RP and VT domains, as compared to their less-fit peers. Moreover, the observed positive associations between 6MWT and hand-grip strength with PF, RP and VT seemed to be independent of BMI, the number of chronic conditions and education.

Altogether, the findings from descriptive studies suggested that (i) simple fitness tests like 6MWT are able to identify older adults with an increased CVD risk and (ii) that physical fitness is positively related with self-reported physical health domains.

However, the findings from the descriptive correlational studies do not prove causality. Thus, to observe the direct effects of increasing physical fitness on CVD risk factors, cardiovascular function, functional fitness and HRQoL of community-dwelling older adults, a RCT was designed. Although fitness is greatly influenced by genetics, exercise training seems to be the better way to improve individuals´ fitness. Therefore, two different exercise training typesAT and RT were chosen in order to achieve this goal.

Does exercise training improve the CVD risk profile, cardiovascular function, functional fitness, and HRQoL of community-dwelling older adults?

After the eight months of exercise training, subjects in both AT and RT groups improved their overall performance in physical and functional fitness tests as well as decreased total %BF and trunk fat. Additionally, RT was able to increase overall HRV whereas AT was able to decrease resting BP and resting HR, increase efferent vagal activity, and decrease low-grade systemic inflammation, in community-dwelling older adults. Finally, AT was able to increase self-reported PF, GH, and MH, while RT increased self-reported GH, and independent of training type, 67.7% of trained subjects reported their health as much better or somewhat better now than one year ago.

Are there differences in the effects of aerobic versus resistance training on the CVD risk profile, cardiovascular function, functional fitness, and HRQoL of community-dwelling older adults?

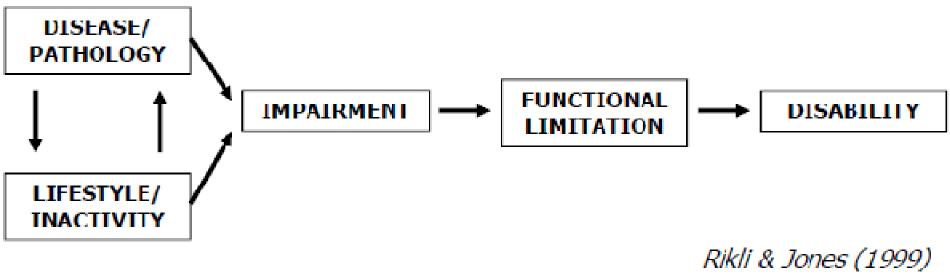
The magnitude of relative changes for body composition, autonomic function (HR, BP, and HRV), lipidic profile, fasting glycemia, inflammation markers, performance on functional fitness tests, and HRQoL domains were not different among exercise training types, suggesting that they have similar benefits for cardiovascular function, CVD risk factors, functionality, and self-reported HRQoL of community-dwelling older adults.

Altogether, the findings from the RCT studies suggested that aerobic or resistance exercise training is an effective intervention for: (i) improving overall physical function; (ii) decreasing body fat mass percentage; (iii) improving autonomic function; (iv) decreasing low-grade chronic inflammation, as assessed by hs-CRP; and (v) improving several domains of self-reported HRQoL. The last finding from the RCT studies is that AT and RT seem to induce changes of similar magnitude on the variables investigated in this thesis.

Briefly, it seems that in physically independent, community-dwelling older adults, with no serious medical conditions, the type of exercise training does not matter for increasing functionality, reducing CVD risk or increasing HRQoL; the most important is that they exercise.

Based on the present results and those from previous disability models, we suggested a new amended model, in Figure 1, in order to explain the interactions between CVD risk factors, inactive lifestyle, functional fitness, impairment-disability evolution, and HRQoL in older adults, as well as the role of physical activity and exercise training on these interactions.

It is now proposed that changing an inactive lifestyle by increasing the quantity and intensity of PA, which can be done through formal and structured PA like the exercise program presented in this thesis, will lead to an increase in physical and functional fitness. Both were demonstrated to be negatively related with CVD risk. A decreased risk for CVD added to an increased fitness and functionality will decrease the one's susceptibility to impairment, functional limitation, and disability. Finally, reducing older adults' CVD risk and disability and increasing their functionality will favor a higher subjective HRQoL.



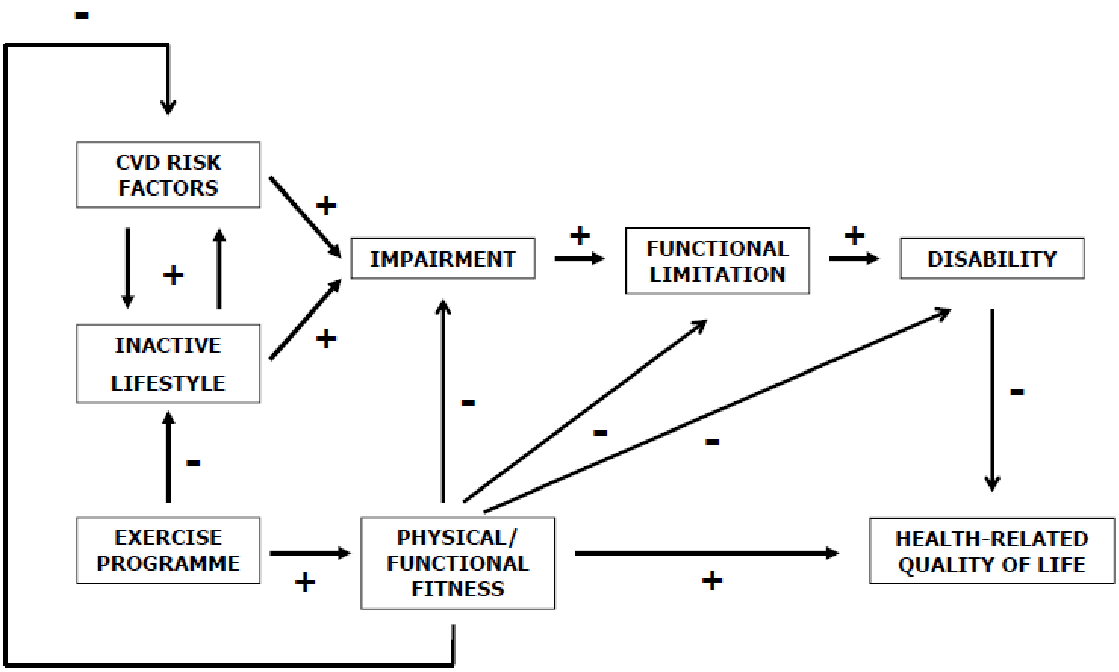


Figure 1. The first model was suggested by Rikli & Jones (1999). The second model was amended based on the results obtained in this thesis and aims to explain the interactions between CVD risk factors, an inactive lifestyle, functional fitness, impairment-disability evolution, and HRQoL in physically independent, community-dwelling older adults with no serious medical conditions.

CHAPTER IX

CONCLUSION

9. CONCLUSION

Based on the analysis of the results drawn from the different studies presented in this thesis, it is possible to conclude that, in physically independent, community-dwelling, older adults with no serious clinical conditions:

A worse cardiovascular profile (higher %BF, trunk fat, SBP) is related with lower aerobic fitness as assessed by 6MWT.

An elevated aerobic fitness level, as assessed by 6MWT, is correlated with favorable cardiovascular function at rest.

Higher levels of physical fitness, as assessed by hand-grip strength and 6MWT, are associated with higher self-reports in several domains of HRQoL, especially those included in the physical health component.

Eight months of moderate to vigorous aerobic or resistance exercise training: (i) improves physical and functional fitness, (ii) decreases CVD risk profile, (iii) increases cardiovascular function, and (iv) improves subjective HRQoL

Aerobic and resistance training seem to induce changes of similar magnitude on physical and functional fitness, CVD risk profile, and subjective HRQoL.

For future research, it is recommend a larger sample and the use of different exercise types as well as different training intensities and duration. An investigation into the effects of exercise training on different indexes of autonomic dysfunction and other biochemical and inflammatory markers related to CVD is also recommended.

APPENDIX 1

Written Informed Consent

U.PORTO
FACULDADE DE DESPORTO
UNIVERSIDADE DO PORTO

FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

Centro de Investigação em Actividade Física, Saúde e Lazer

Carta de Consentimento/ Termo de Responsabilidade

Para a presente investigação, os participantes serão submetidos a uma série de procedimentos de avaliação de parâmetros relacionados com a aptidão física e a saúde, nomeadamente:

- Avaliação da composição corporal;
- Análises de amostra sanguínea;
- Medidas de Pressão Arterial e Frequência Cardíaca em repouso e em exercício;
- Inquérito sobre estado de saúde percebido;
- Inquérito sobre hábitos nutricionais;
- Avaliação do nível de actividade física habitual;
- Testes de Aptidão física (equilíbrio, força muscular e aptidão cardiorespiratória).

Os dados recolhidos na pesquisa terão fins exclusivamente científicos, a identidade de cada participante será preservada. Espera-se, que os resultados deste estudo forneçam subsídios para o melhor entendimento do papel do exercício em algumas variáveis da aptidão física e saúde. Os resultados deste estudo estarão à disposição dos participantes mediante a solicitação dos mesmos, ao professor responsável. Nos casos onde forem detectadas restrições à prática de exercícios de intensidade moderada a vigorosa, serão sugeridos: 1) o afastamento provisório do programa de exercício e 2) a procura a um fisioterapeuta para tratamento adequado. Os voluntários têm ainda, o direito de abandonar a pesquisa, a qualquer momento, caso não se sintam satisfeitos.

Estando informado das intenções e dos propósitos desta pesquisa, eu,

____

declaro que participo voluntariamente nos projectos de doutorado da M.S. Flávia Wanderley, do Programa de Doutoramento em Actividade Física e Saúde da Faculdade de Desporto da Universidade do Porto, com orientação pela Profa. Dra. Joana Carvalho.
Ainda, ciente de que a realização de actividade física pode acarretar algum risco clínico, declaro que **me assegurei, previamente, de que não tenho quaisquer contra-indicações para a prática da actividade física e aceito todas as responsabilidades** inerentes à participação no Programa de Actividade Física Sénior.
Pela presente declaração, **isento de qualquer responsabilidade** a Faculdade de Desporto por alguma alteração do meu estado de saúde, decorrente directa ou indirectamente do programa de exercícios.

Porto, ____ de ____________________ de 2008

____

Assinatura do participante

APPENDIX 2

Medical Outcomes Study 36-Item Short-Form Health Study questionnaire, adapted and validated for the Portuguese population

MOS SF-36

Para responder coloque uma cruz no número que melhor descreve a sua saúde

1. Em geral, diria que sua saúde é:

Óptima	Muito boa	Boa	Razoável	Fraca
1	2	3	4	5

2. Comparando com o que acontecia há um ano, como descreve o seu estado geral actual:

Muito melhor	Com algumas melhoras	Aproximadamente igual	Um pouco pior	Muito pior
1	2	3	4	5

3. As perguntas que se seguem são sobre actividades que executa no seu dia-dia. Será que a sua saúde o/a limita nestas actividades? Se sim, quanto?

	Sim, muito limitado/a	Sim, um pouco limitado/a	Não, nada limitado/a
a) Actividades violentas, tais como participar em desportos violentos ou mesmo correr ou levantar pesos.	1	2	3
b) Actividades moderadas, tais como deslocar uma mesa ou aspirar a casa.	1	2	3
c) Levantar ou pegar nas compras da mercearia.	1	2	3
d) Subir vários lanços de escadas	1	2	3
e) Subir um lanço de escadas	1	2	3
f) Inclinar-se, ajoelhar-se ou baixar-se	1	2	3
g) Andar mais de 1Km	1	2	3
h) Andar vários quarteirões ou grupos de casas	1	2	3
i) Andar um quarteirão ou grupo de casas	1	2	3
j) Tomar banho ou vestir-se sozinho/a	1	2	3

4. Durante as últimas 4 semanas teve, no seu trabalho ou actividades diárias, algum dos problemas apresentados a seguir como consequência do seu estado de saúde físico?

	Sim	Não
a) Diminuiu o tempo gasto a trabalhar, ou noutras actividades	1	2
b) Fez menos do que queria	1	2
c) Sentiu-se limitado/a no tipo de trabalho ou noutras actividades	1	2
d) Teve dificuldade em executar o seu trabalho ou noutras actividades	1	2

(por exemplo foi preciso mais esforço)		

5. Durante as últimas 4 semanas teve, no seu trabalho ou actividades diárias, algum dos problemas apresentados a seguir devido a quaisquer problemas emocionais (tal como sentir-se deprimido/a ou ansioso/a)?		
	Sim	Não
a) Diminuiu o tempo gasto a trabalhar, ou noutras actividades	1	2
b) Fez menos do que queria	1	2
c) Não executou o trabalho ou outras actividades tão cuidadosamente como era costume	1	2

6. Durante as últimas 4 semanas, em que medida é que a sua saúde física ou problemas emocionais interferiram no seu relacionamento social normal com a família, amigos, vizinhos ou outras pessoas?				
Absolutamente Nada	Pouco	Moderadamente	Bastante	Imenso
1	2	3	4	5

7. Durante as últimas 4 semanas teve dores?					
Nenhumas	Muito fracas	Ligeiras	Moderadas	Fortes	Muito Fortes
1	2	3	4	5	6

8. Durante as últimas 4 semanas, em que medida é que a dor interferiu com o seu trabalho normal (tanto o trabalho de casa como o trabalho doméstico)?				
Absolutamente nada	Pouco	Moderadamente	Bastante	Imenso
1	2	3	4	5

9. As perguntas que se seguem pretendem avaliar a forma como se sentiu e como lhe correram as coisas nas últimas quatro semanas.

Por cada pergunta, coloque por favor, uma cruz na resposta que melhor descreve a forma como se sentiu

Quanto tempo, nas últimas quatro semanas	Sempre	A maior parte do tempo	Bastante tempo	Algum tempo	Pouco tempo	Nunca
a) Se sentiu cheio/a de vitalidade?	1	2	3	4	5	6
b) Se sentiu muito nervoso/a?	1	2	3	4	5	6
c) Se sentiu tão deprimido/a que nada o/a animava?	1	2	3	4	5	6
d) Se sentiu calmo/a e tranquilo/a?	1	2	3	4	5	6
e) Se sentiu com muita energia?	1	2	3	4	5	6
f) Se sentiu triste e em baixo?	1	2	3	4	5	6
g) Se sentiu estafado/a?	1	2	3	4	5	6
h) Se sentiu feliz?	1	2	3	4	5	6
i) Se sentiu cansado/a?	1	2	3	4	5	6

10. Durante as últimas 4 semanas teve, até que ponto é que a sua saúde física ou problemas emocionais limitaram a sua actividade social (tal como visitar amigos ou familiares próximos)?				
Sempre 1	A maior parte do tempo 2	Algum tempo 3	Pouco tempo 4	Nunca 5

11. Por favor, diga em que medida são verdadeiras ou falsas as seguintes afirmações:

Ponha uma cruz em cada linha	Absolutamente verdade	Verdade	Não sei	Falso	Absolutamente Falso
a) Parece que adoeço mais facilmente do que os outros	1	2	3	4	5
b) Sou tão saudável como qualquer outra pessoa	1	2	3	4	5
c) Estou convecido/a que a minha saúde vai piorar	1	2	3	4	5
d) A minha saúde é óptima	1	2	3	4	5

APPENDIX 3

Physical Activity Diary

Diário

O aparelho que vai usar a partir de agora é um monitor de actividade. Pretende medir a quantidade de movimento que vai efectuar ao longo do dia. Deve por isso usá-lo durante todo o dia, colocando-o à cintura logo pela manhã e retirando-o quando se for deitar. Tem que ser colocado sempre no mesmo lado da cintura e sempre na mesma posição. Enquanto usar o aparelho deve fazer tudo o que costuma fazer habitualmente. <u>Este aparelho ***não é à prova de água***, por isso quando for tomar banho, ou nadar, não o pode usar</u>. Registar sempre, todos os dias, a hora que o colocou e o retirou.

Nome: ________________________________ Código: _______

Data de início:_______ Hora:____ Data do fim:_______ Hora:_____

Dia da semana	Ao levantar	Antes de ir dormir	Só se realizou uma <u>actividade aquática (nadar, hidroginástica)</u>	
	Hora que colocou	**Hora que retirou**	**Hora que retirou** (antes da actividade)	**Hora que colocou** (depois da actividade)
2ª Feira				
3ª Feira				
4ª Feira				
5ª Feira				
6ª Feira				
Sábado				
Domingo				

Obrigado pela colaboração!

APPENDIX 4

Dietary Record

INSTRUÇÕES PARA O PREENCHIMENTO DO DIÁRIO ALIMENTAR DE 4 DIAS

Por favor anote tudo o que comer ou beber durante 4 dias seguidos, a começar no próximo domingo. Faça descrições pormenorizadas de alimentos e bebidas como, por exemplo, tipo de pão (trigo, mistura, integral, etc.) ou tipo de leite (magro, meio-gordo ou gordo). Mencione também o tipo de confecção culinária como, por exemplo, carne de vaca guisada, ovos estrelados, costeleta de porco frita em margarina, etc..

Quando comer fora de casa, por favor anote tudo o que comer ou beber, imediatamente após o consumo. Não se esqueça de apontar tudo o que for comido ou bebido no intervalo das refeições como, por exemplo, cachorros, bolachas, café, açúcar, etc.

Como fazer o registo:

Inicie o registo com a página correspondente a esse dia (existem 2 páginas para cada dia); por favor assegure-se que preencheu as partes correspondentes a: HORA, LOCAL, ALIMENTOS E BEBIDAS CONSUMIDOS, TAMANHO DAS PORÇÕES.

Quanto às quantidades e aos tamanhos das porções:

Mencione o tamanho dos alimentos e a quantidade das bebidas. Para tal, use medidas caseiras como, por exemplo, 1 colher de chá de manteiga, 9 colheres de sopa cheias de arroz, 3 conchas de massa, 1 tigela de sopa, 1/2 chávena almoçadeira de leite (ou 1/2 chávena de chá, se for mais pequena), 1 copo de cerveja, etc. Seguem-se alguns exemplos:

Bebidas

Use copos ou chávenas e refira o tipo como, por exemplo, chávena almoçadeira, de chá ou de café. Quando misturar leite com café, mencione as quantidades de cada uma das bebidas (por exemplo, 1/4 de chávena almoçadeira com leite magro e o restante com café).

Sopas

Use tigelas (semelhantes à da cantina), número de conchas ou pratos (cheio, meio prato).

Molhos

Para cada molho (de fritos, guisados, maionese, etc.) use colheres de sopa ou de chá.

Carne, pescado, aves e pizza

Indique as quantidades consumidas especificando os alimentos e classificando as porções em pequenas, médias, grandes, fatias, unidades, cubos de carne, latas (de atum, por exemplo), ou medidas caseiras (colheres de sopa, chávena almoçadeira, etc.).

Hortaliças e legumes

Use rodelas (por exemplo, tomate, cebola, pepino), parte do prato (meio prato, um quarto de prato) ou chávenas almoçadeiras (meia chávena de alface, por exemplo).

Arroz, massa, feijão, ervilhas ou grão

Indique o número de colheres de sopa.

Batatas

Se forem cozidas, indique o número de batatas do tamanho de um ovo; em puré, diga o número de colheres de sopa. Se forem fritas, indique a que parte do prato corresponde (meio prato, um quarto de prato); em pacote, diga se é pequeno, médio ou grande.

Óleos, manteiga e margarina
Use colheres de sopa ou de chá

Açúcar, cacau, chocolate, mel
Use pacotes de açúcar ou colheres de chá

Pão, pastelaria e doces
Use o número de pães ou fatias e mencione o tipo de pão se não for corrente (de trigo).
Bolos: 1 unidade ou 1 fatia

Fruta
Refira o nome da fruta e indique o número de porções médias; se forem uvas, a unidade é 1 cacho.

NOTA: Se tiver balança ou conhecer o peso do alimento pode referi-lo

Dia da semana: Data:_____/_____/_____

Hora	Local	Alimento	Quantidade

APPENDIX 5

Individual Physical Fitness Report

RELATÓRIO

AVALIAÇÕES DA APTIDÃO FÍSICA E ANTROPOMÉTRICA

Aluno(a):______________________________________

Aptidão Funcional

CAPACIDADE AERÓBIA – TESTE DE 6 MINUTOS DE CAMINHADA

Outubro 2008	Julho 2009	Alteração
m	m	

FORÇA E RESISTÊNCIA MUSCULAR LOCALIZADA

SUBIR DEGRAUS

Outubro 2008	Julho 2009	Alteração
Segundos	Segundos	

5 VEZES SENTAR E LEVANTAR DA CADEIRA

Outubro 2008	Julho 2009	Alteração
Segundos	Segundos	

Agilidade e Equilíbrio

Outubro 2008	Julho 2009	Alteração
Kg	Kg	

Força de Preensão Manual

Outubro 2008	Julho 2009	Alteração
Kg	Kg	

Nota: O símbolo **—** significa que piorou e o **+** que melhorou

Força Isocinética

FORÇA ISOCINÉTICA

Pico de torque 60º	Out/Nov 2008	Julho 2009	Alteração
Músculos Flexores do Joelho Direito			
Músculos Flexores do Joelho Esquerdo			
Músculos Extensores do Joelho Direito			
Músculos Extensores do Joelho Esquerdo			

Pico de torque 180º	Out/Nov 2008	Julho 2009	Alteração
Músculos Flexores do Joelho Direito			
Músculos Flexores do Joelho Esquerdo			
Músculos Extensores do Joelho Direito			
Músculos Extensores do Joelho Esquerdo			

Nota: O símbolo **−** significa que piorou e o **+** que melhorou

Antropometria

PESO

Os Meus Resultados **Alteração**

Out/Nov 2008	**Julho 2009**
Kg	Kg

☐

ÍNDICE DE MASSA CORPORAL – IMC

Os Meus Resultados **Encontro-me:** **Alteração**

Out/Nov 2008	**Julho 2009**
Kg/m^2	Kg/m^2

☐ Dentro da Zona Saudável

☐ Fora da Zona Saudável

PERÍMETRO DO ABDÓMEN

Os Meus Resultados **Encontro-me:** **Alteração**

Out/Nov 2008	**Julho 2009**
cm	cm

☐ Dentro da Zona Saudável

☐ Fora da Zona Saudável

PERCENTUAL DE GORDURA CORPORAL

Os Meus Resultados **Encontro-me:** **Alteração**

Out/Nov 2008	**Julho 2009**
%	%

☐ Dentro da Zona Saudável

☐ Fora da Zona Saudável

RELAÇÃO CINTURA QUADRIL – RCQ

Os Meus Resultados **Alteração**

Out/Nov 2008	**Julho 2009**

Nota: O símbolo **–** significa que piorou e o **+** que melhorou

Tensão Arterial e Frequência Cardíaca de Repouso

TENSÃO ARTERIAL

Os Meus Valores **Alteração**

Out/Nov 2008		**Julho 2009**	
PAS	**PAD**	**PAS**	**PAD**
	mmHg		mmHg

FREQUÊNCIA CARDÍACA EM REPOUSO

Os Meus Valores **Alteração**

Out/Nov 2008	**Julho 2009**
bpm	bpm

Assiduidade

ASSIDUIDADE

Nº faltas **Frequência (%)**

Nota: O símbolo **–** significa que piorou e o **+** que melhorou

OBRIGADO PELA SUA COLABORAÇÃO

Atenciosamente,

M.S. Flávia Wanderley

APPENDIX 6

Acknowledgement Letter

Carta de Agradecimento

Caro Sr(a).,

A aluna Flávia Accioly Canuto Wanderley, do Programa Doutoral em Actividade Física e Saúde bem como sua orientadora, Professora Dra. Joana Carvalho, ambas da Faculdade de Desporto da Universidade do Porto vêm por meio desta agradecer vossa enorme colaboração. Sem vossa disponibilidade para responder aos inquéritos, realizar testes, e retirar amostras de sangue nossa pesquisa não teria sido possível.

Aproveitamos a oportunidade para nos desculpar pela demora referente a entrega deste último relatório. Infelizmente, tivemos alguns problemas técnicos que impossibilitaram que as análises de sangue ficassem prontas com maior rapidez.

Temos também o prazer de informar que alguns dos resultados desta pesquisa já foram apresentados em eventos científicos nacionais e internacionais. Nestas ocasiões, tomou-se sempre o cuidado de preservar a identidade de cada participante. Por fim, lembramos que os resultados deste estudo estarão à disposição dos participantes mediante a solicitação dos mesmos, ao professor responsável.

Com os melhores cumprimentos,

M.S. Flávia A. C. Wanderley

Porto, Setembro de 2010