Anti-aging therapy through fitness enhancement

Manuel J Castillo-Garzón Jonatan R Ruiz Francisco B Ortega Ángel Gutiérrez

EFFECTS-262 Department of Medical Physiology, School of Medicine, University of Granada, and Sotogrande Health Experience, Spain. **Abstract:** Physical exercise is proposed as a highly effective means of treating and preventing the main causes of morbidity and mortality – most of which are associated with aging – in industrialized countries. Low physical fitness is an important risk factor for cardiovascular and all-causes morbidity and mortality; indeed, it is even a predictor of these problems. When properly measured, the assessment of physical fitness can be a highly valuable indicator of health and life expectancy and, therefore, should be performed routinely in the clinical setting. Individually adapted training programs could be prescribed based on fitness assessment results and an adequate knowledge of patient lifestyle and daily physical activity. Such training programs would allow people to develop their maximum physical potential, improve their physical and mental health, and attenuate the negative consequences of aging. **Keywords:** aging, physical fitness, physical activity, health

Introduction

The increase in life expectancy and the reduction in the birth rate are major problems faced by industrialized societies. From a health and social point of view, it is more important that research be orientated towards promoting healthier aging than simply finding better ways to treat aging-related illnesses (Abbott 2004). A highly effective form of promoting healthy aging is the practice of physical exercise with the aim of improving physical fitness. Several studies have clearly shown that physical fitness is an important predictor of both cardiovascular and all-cause mortality. In addition it is a good predictor of being able to live an independent life at old age (Myers et al 2002; Myers 2003; Gulati et al 2003; Kurl et al 2003; Piepoli et al 2004). This work discusses the importance of physical fitness as an index of health, the relationship between physical fitness and aging, how to assess physical fitness in a clinical setting, and the prescription of exercise for improving physical fitness and, consequently, positively influencing the aging process.

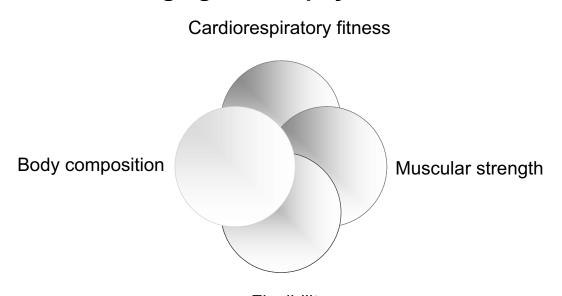
Physical exercise as an anti-aging intervention

Appropriately undertaken, physical exercise is the best means currently available for delaying and preventing the consequences of aging, and of improving health and wellbeing.

It is important to differentiate between three different but inter-related concepts: physical activity, physical exercise, and physical fitness. Physical activity refers to any body movement produced by muscle action that increases energy expenditure. Exercise refers to planned, structured, repetitive, and purposeful physical activity. Physical fitness is the capacity to perform physical exercise. Physical fitness makes reference to the full range of physical qualities, eg, aerobic capacity, strength, speed, agility, coordination, and flexibility. It can be understood as an integrated measurement of all the functions (skeletomuscular, cardiorespiratory, hematocirculatory, psychoneurological, and endocrine-metabolic) and structures involved in the

Correspondence: Manuel J Castillo-Garzón Departamento de Fisiología Médica,

Facultad de Medicina, Universidad de Granada, 18071 Granada, Spain Tel +34 958 243540 Fax +34 958 249015 Email mcgarzon@ugr.es



Anti-aging-related physical fitness

Flexibility

Figure 1 Components of physical fitness associated with aspects of good health and disease prevention, or both.

performance of physical activity or physical exercise or both. Thus, being physically fit implies that the response of these functions and structures will be adequate. A person cannot be more physically fit than that allowed by the function or structure in poorest condition in their body.

Anti-aging-related physical fitness includes those components of physical fitness associated more with aspects of good health and/or disease prevention (Figure 1).

The importance of physical fitness

The physical fitness of both men (Myers et al 2002; Myers 2003) and women (Gulati et al 2003) is an excellent predictor of life expectancy, both for those who are healthy (Kurl et al 2003) and for those who suffer some form of heart disease (Piepoli et al 2004).

Over the last 15 years, numerous epidemiological and prospective studies have reported a strong association between physical fitness and the morbidity–mortality index of the population (Balady 2002; Carnethon et al 2003), even in overweight and obese persons (Blair and Brodney 1999). Being physically fit drastically reduces all-cause mortality (Myers 2003). Improving one's physical fitness can reduce the risk of death by 44% (Blair et al 1995). In addition, several studies have shown that improving physical fitness has a favorable influence on self image, self-esteem, and depression, as well as anxiety and panic syndromes (Kirkcaldy et al 2002; Strawbridge et al 2002; Goodwin 2003). It has even been reported that, while pharmacological anti-depression treatment may induce a more rapid initial response, the efficacy of exercise is the same at 16 weeks (Blumenthal et al 1999) (Table 1).

The aerobic capacity as an index of health

The aerobic capacity is one of the most important components of physical fitness. Maximum aerobic capacity is expressed in terms of maximum oxygen consumption (VO_{2max}) . The VO_{2max} can be expressed with respect to subject weight (ml/kg/min), in absolute terms (L/min), or

 Table I Beneficial effects on health of practicing regular

 physical exercise

Reduction in the risk of developing ischemic heart disease and other cardiovascular diseases. Reduction in the risk of developing obesity and diabetes.

Reduction in the risk of developing (and control of) high blood pressure and dyslipidemia.

Reduction in the risk of developing breast and colon cancer.

Helps in the control of body weight and improves 'body image'.

Tonifies muscles and preserves or increases muscular mass.

Strengthens bones and joints.

Increases coordination and neuro-motor responses; reduces the risk of falls.

Improves immune system activity.

Reduces depression and anxiety.

Promotes wellbeing and social integration.

in metabolic equivalents (METs) (1 MET is the energy expenditure at rest [~3.5 ml/kg/min]). Thus, if a subject has a VO_{2max} of 42 ml/kg/min, he also has an energy expenditure of 12 METS (ie, he is able to increase his resting energy expenditure 12-fold).

A number of important prospective studies have shown that the VO_{2max} is the most important predictor of all-cause mortality, and in particular of cardiovascular death. This is true both for healthy persons and those with cardiovascular disease (Carnethon et al 2003), and for both men (Laukkanen et al 2001; Balady 2002; Kurl et al 2003) and women (Gulati et al 2003; Mora et al 2003) of different ages (Myers et al 2002). An almost linear reduction in mortality is seen as the aerobic capacity increases (Myers et al 2002; Mora et al 2003) (Figures 2, 3). For each increase of 1 MET there is a 12% increase in the life expectancy of men (Myers et al 2002) and a 17% increase in women (Gulati et al 2003; Figures 2 and 3, respectively). This is even more evident if cardiovascular mortality is considered alone, and is true for both men (Carnethon et al 2003; Kurl et al 2003) and women (Gulati et al 2003; Mora et al 2003). An inverse relationship has also been found between aerobic capacity and mortality due to cancer - a relationship quite independent of age, alcohol intake, the suffering of diabetes mellitus, and even the use of tobacco (Lee and Blair 2002; Evenson et al 2003; Lee et al 2003; Sawada, Muto, et al 2003). Similarly, it has been shown that the VO_{2max} is an important determinant of insulin sensitivity (Seibaek et al 2003; Sawada, Lee, et al 2003); low VO_{2max} levels are associated with metabolic syndrome (abdominal obesity, glucose intolerance, type II diabetes, hypertension, hyperlipidemia and insulin

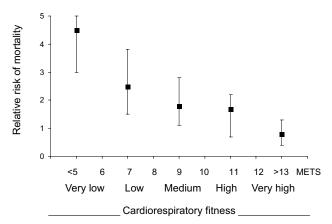


Figure 2 The maximum aerobic capacity is a powerful predictor of all-cause mortality in men (drawn from data contained in Myers et al 2002). The figure shows percentage survival as a function of the aerobic capacity (VO_{2max} expressed in METs). Survival is worse in subjects with lower aerobic capacity. **Abbreviations:** METs, metabolic equivalents; VO_{2max} , maximum oxygen consumption.

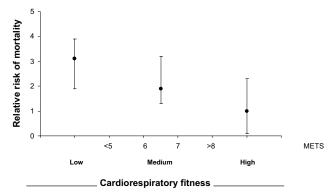


Figure 3 The maximum aerobic capacity is a powerful predictor of all-cause mortality in women (drawn from data contained in Mora et al 2003). The figure shows percentage survival as a function of the aerobic capacity (VO_{2max} expressed in METs). Survival is worse in subjects with lower aerobic capacity. **Abbreviations:** METs, metabolic equivalents; VO_{2max} , maximum oxygen consumption.

resistance) (Bertoli et al 2003; Lakka et al 2003). A good aerobic capacity reduces the neuronal losses associated with aging (Colcombe et al 2003) and protects against cognitive dysfunction (Barnes et al 2003).

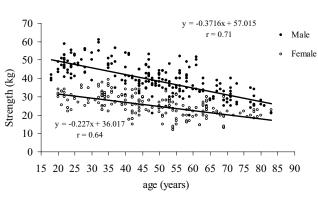
Muscular strength as an index of health

Hand grip strength, assessed by the manual dynamometer test, is currently considered to be a reliable marker of health and wellbeing (Lord et al 2003; Chang et al 2004; Hulsmann et al 2004) and a potent predictor of mortality and the expectancy of being able to live independently (Metter et al 2002; Seguin and Nelson 2003). Figure 4 shows the decline in this quality with the passage of time. Given its importance, efforts should be made to reduce the errors associated with its measurement (Ruiz et al 2002).

A recent study performed with patients with heart disease shows that the isokinetic strength of the extensor muscles (quadriceps) and especially the flexors of the knee (ischiotibial muscles), is strongly associated with mortality – and has even better predictive power than variables such as VO_{2max} (Hulsmann et al 2004). In addition, the maintenance of good muscular tone in the legs is directly related to a drastic reduction in the number of falls (and therefore of bone fractures) suffered (Lord et al 2003; Chang et al 2004).

Assessment of physical fitness

Knowing a person's true physical fitness is fundamental for prescribing any program of physical exercise to help prevent the consequences of aging. Physical fitness is assessed by a battery of validated tests that provides a complete evaluation



Hand grip strength

Figure 4 Deterioration of hand grip strength with age (cross-sectional study performed on healthy Spanish people [222 men, and 208 women]).

of the physical qualities associated with physical fitness (Laukkanen et al 1992; EC and UKK 1998). These tests should always include the assessment of aerobic capacity, the muscular strength of the upper and lower body, flexibility, and psychokinetic capacities (ie, agility, coordination, balance, visual and auditory reaction times). Table 2 shows the tests most commonly used in clinical practice for the evaluation of physical fitness orientated towards anti-aging therapy.

Prescription of exercise as an antiaging therapy

The prescription of exercise with the aim of attenuating the physiological consequences of aging should be orientated towards increasing daily physical activity and improving physical fitness. The aim is to provoke optimum stimulation (training) in order to achieve maximum adaptation, but without over-stimulating (Figure 5). In exercise physiology terms, the aim is to train to the maximum but not to overtrain (Castillo and Gutiérrez 2001; Gutiérrez et al 2003). Thus, it is very important to correctly individualize exercise and to monitor functional adaptation; this will allow adjustments to be made according to the medical and physiological condition of the subject at each moment. In general terms, exercise prescription is based upon the frequency, intensity and duration of training, the type of activity, and the initial level of fitness (the main determinant).

Exercise prescription for aerobic training

Physical activities that develop cardiorespiratory fitness lie at the heart of any exercise program (Delgado et al 2004). These activities are designed to improve both the capacity and efficiency of cardiovascular and metabolic systems. They also help in the control and reduction of body fat.

The results of aerobic exercise, eg, walking, are very positive, especially for cardiovascular health. These improvements are independent of race, sex, age, and body mass index (Manson et al 2002). A program of regular aerobic exercise of three to six months duration can improve aerobic capacity by 15%-30% (ACSM 1998). Undertaking weekly aerobic exercise lasting 60-90 minutes leads to significant reductions in the systolic and diastolic blood pressure in hypertensive men and women. No further improvement is seen if this time is extended (Ishikawa-Takata et al 2003). There is substantial evidence that aerobic training exerts a favorable influence on the blood lipid and lipoprotein profiles at any age (Pate et al 1995; Fletcher et al 1996). The dose-response relationships between the amount of exercise and favorable blood lipid and lipoproteins changes suggest that exercise can exert a positive influence on blood lipids even at low training volumes, although the effects may not be observed until certain exercise thresholds are met (ACSM 1998). Another important benefit of aerobic exercise is the reduction it causes in insulin resistance (Sato et al 2003). Similar results have been obtained in the treatment of diabetes and metabolic syndrome (Watkins et al 2003; Swartz et al 2003). Finally, aerobic exercise performed for 30 min at least three times per week has been shown to have a potent therapeutic effect on certain mental illnesses such as depression and anxiety and panic syndromes (Babyak et al 2000; Paluska and Schwenk 2000).

Table 2 Some of the most used clinical tests	for assessing
physical fitness with a view to anti-aging thera	РУ

Physical fitness-related capacities	Tests
Aerobic capacity	2 km walking (UKK test)
	Bruce test
	Power work capacity 170
Muscular strength (upper extremity)	Hand grip strength
	Arm flexions
	Bent arm hang
Muscular strength (lower extremity)	Squat jump
	Counter movement jump
	Abalakov
Muscular strength (trunk strength)	Curl up test
Flexibility	Seat and reach
Agility	Standing reaching up
Eye-hand coordination	Plate tapping
Eye-toe coordination	Ladder test
Static balance test (right and left leg)	Flamingo

Abbreviations: UKK, Urho Kaleka Kekkonen.

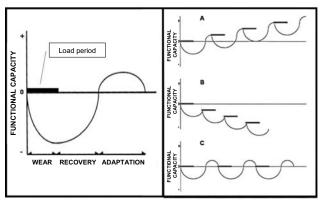


Figure 5 Left: Physical exercise (Load period) implies organic wear that reduces functional capacity (Wear). With rest and correct nutrition, lost functional capacity can be recovered (Recovery). This is followed by a period of overcompensation to exertion (Adaptation). This forms the theoretical basis of training. Right: The timing of training (A, B o C) influences functional capacity - either improving it (A), causing it to worsen (B) or having no effect (C) (Delgado et al 2004).

A training frequency of 3-5 days a week is recommended. It is preferable to avoid single, hard bouts of exercise once a week (Ruiz et al 2004). Training intensity should be at some 55%/65%-90% of the maximum heart rate, or of the maximum reserve heart rate (maximum HR rest HR) (ACSM 1998). Lower intensity values, eg, 40%-49% of the maximum reserve heart rate and 55%-64% of the maximum heart rate, are recommended for unfit individuals. The duration of training should be 30-60 min of continuous or intermittent (10 min or longer bouts accumulated over the day) aerobic activity. The duration is dependent on the intensity of the activity; thus, lowerintensity activity should be conducted over 30 min or more, while individuals training at higher intensity levels should do so for 20 min or more. Because of the importance of "total fitness", that this is more readily attained with exercise sessions of longer duration, and given the potential hazards and adherence problems associated with high-intensity activity, moderate-intensity activity of longer duration is recommended for adults not training for athletic competition (ACSM 1998). Any activity that uses the large muscle groups (eg, walking, hiking, running, jogging, cycling, cross-country skiing, aerobic dancing, rope skipping, rowing, stair climbing, swimming, skating, endurance game activities, etc.), that can be maintained continuously and is rhythmical and aerobic in nature, is recommendable. Brisk walking is preferable for older people since this has a low impact on the joints, although recreational sports are also recommended. These guidelines for healthy adults are those published by the American College of Sports Medicine (ACSM 1998).

Prescribing exercise for improving muscular strength

Resistance training has been shown to be the most effective method for developing skeletomuscular strength, and it is currently prescribed by many major health organizations for improving health and fitness (AACPR 1999; ACSM 2002). Resistance training reduces the risk factors associated with coronary heart disease (Fahlman et al 2002), noninsulin-dependent diabetes (Fluckey et al 1994), and colon cancer (Koffler et al 1992), it prevents osteoporosis (von Stengel et al 2005), promotes weight loss and weight maintenance, improves dynamic stability, preserves functional capacity (Evans 1999), and fosters psychological well-being (Ewart 1989). These benefits can be safely obtained when an individualized program is prescribed.

Appropriate strength training produces a significant increase in muscular strength in a relatively short time, as shown in studies that have followed men and women (aged 45–65 years) involved in a six month training program (unpublished; Figure 6). Table 3 shows the gains in strength that can be obtained.

Muscular strength and endurance can be developed by means of static (isometric) or dynamic (isotonic or isokinetic) exercises (ACSM 2002). Although each type of training has its advantages and limitations, for healthy adults, dynamic resistance exercises are recommended since they best mimic everyday activities (Iki et al 2002). Resistance training for the average participant should be rhythmical, performed at a moderate-to-slow and controlled speed, involve a full range of motion, and demand a normal breathing pattern during lifting movements. Heavy resistance exercise can cause a dramatic acute increase in both systolic and diastolic blood pressure (Lachowetz et al 1998), especially when a Valsalva manoeuvre is undertaken (ACSM 2002).

Resistance training should be an integral part of any adult fitness program and should be of sufficient intensity to enhance strength, muscular endurance, and maintain fatfree mass. Resistance training should be progressive in nature, individualized, and provide a stimulus to all the major muscle groups. In the American College of Sports Medicine's Position Stand (ACSM 2002), "The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults," the initial standard for a resistance training program was the performance of one set of 8–12 repetitions of 8–10 exercises, including one

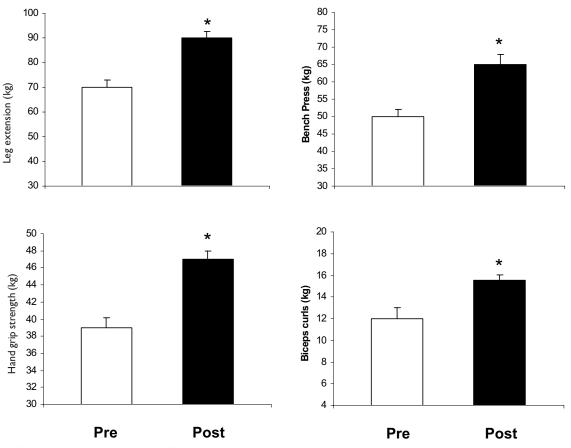


Figure 6 Effects of a resistance training program (3 days/week) for 3 months on maximum strength in older people. Note: $p \le 0.05$. Bars are mean \pm standard error of mean.

exercise for all major muscle groups (10–15 repetitions for older or more frail persons) (Armstrong 1984).

It is recommended that novice lifters train with loads of 60%–70% of a one repetition maximum (RM) for 8– 12 repetitions. Advanced individuals should use loading ranges of 70%–90% of the RM in a periodic fashion to maximize muscular strength (ACSM 2002). For progression in those individuals training at a specific RM load (eg, 8–12 repetitions), it is recommended that a 2%– 10% increase be applied on the basis of muscle group size and involvement (ie, greater load increases may be used for large muscle groups and for multiple-joint exercises) when the individual can perform at his/her current intensity for one or two repetitions more than the desired number in two consecutive training sessions (ACSM 2002).

Recently, it has been reported that power training is more effective than strength training for maintaining bone mineral density in postmenopausal women (von Stengel et al 2005). This suggests that fast movements provide greater benefit than slow movements.

Prescribing exercise for flexibility

Flexibility exercise usually supplements exercises performed during the warm-up or cool-down period, and are useful for those who have poor flexibility or muscle and joint problems (such as low back pain).

Flexibility exercises do not improve resistance or strength, but several studies have shown that they increase muscular performance and tendon flexibility, and that they extend the amplitude of movement and the functionality of the joints (ACSM 1998). It is therefore a good idea to incorporate these exercises into any program directed towards improving physical fitness (Pollock et al 2000).

A general stretching program that exercises the major muscle/tendon groups (lower extremity anterior chain, lower extremity posterior chain, shoulder girdle, etc) should be developed using static, ballistic, or modified proprioceptive neuromuscular facilitation (contract/relax, hold/relax, active/ assisted) techniques. Static stretches should be held for 10–20 s, whereas proprioceptive neuromuscular facilitation techniques should include a 6 s contraction followed by 10–20 s assisted stretch (ACSM 2000).

Study	Studies of resistance training in older subjects			
	Age (y)	Gender	Training program	Strength gain (%)
Hendwood and Taaffe 2005	60–80	М	8 weeks	21–82
Capodaglio et al 2005	75	M + W	12 months	21
Thompson et al 2003	69	W	12 weeks	40–60
Englund et al 2005	67–87	W	12 months	10
Hung et al 2004	60–80	W	8 weeks	10-20
Izquierdo et al 2004	65–74	Μ	16 weeks	35–45

 Table 3 Strength gains after a resistance training period in older people

Abbreviations: F, female; M, male.

Conclusion

Aging is a physiological process that can be influenced for the better (delaying it) or worse (accelerating it). The most recent scientific evidence shows that regularly and appropriately practiced physical exercise, in order to improve physical fitness, is currently the best way to delay or even prevent the consequences of aging. Such exercise always brings benefits, irrespective of the age, sex, health, or the physical condition of the person who undertakes it. In contrast, a lack of exercise clearly accelerates aging and its consequences, including one's physical appearance. Among people of the same age and genetic background, those who remain physically active, who eat correctly, and who avoid risk factors, look younger and maintain a more youthful nature.

Recent research has shown that a person's degree of physical fitness is an excellent predictor of life expectancy and quality of life. Improving one's physical fitness increases life expectancy and prevents age-associated diseases. To be effective, the aerobic capacity needs to be increased, along with strength and joint mobility.

In conclusion, potentiating physical fitness is undoubtedly the best medicine available today for combating the inexorable process of aging.

References

[AACPR] American Association of Cardiovascular and Pulmonary Rehabilitation. 1999. Guidelines for Cardiac Rehabilitation and Secondary Prevention Programs. 3rd Ed. Champaign, IL: Human Kinetics.

Abbott A. 2004. Growing old gracefully. Nature, 428:116-18.

- [ACSM] American College of Sports Medicine. 1998. Position stand: the recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc*, 30:975-91.
- [ACSM] American College of Sports Medicine. 2002. Position stand on progression models in resistance training for healthy adults. *Med Sci Sports Exerc*, 34:364-80.
- Armstrong RB. 1984. Mechanisms of exercise-induced delayed onset muscular soreness: a brief review. *Med Sci Sports Exerc*, 16:529-38.

- Babyak M, Blumenthal JA, Herman S, et al. 2000. Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months. *Psychosom Med*, 62:633-8.
- Balady GJ. 2002. Survival of the fittest-more evidence. N Engl J Med, 346:852-4.
- Barnes DE, Yaffe K, Satariano WA, et al. 2003. A longitudinal study of cardiorespiratory fitness and cognitive function in healthy older adults. *J Am Geriatr Soc*, 51:459-65
- Bertoli A, Di Daniele N, Ceccobelli M, et al. 2003. Lipid profile, BMI, body fat distribution, and aerobic fitness in men with metabolic syndrome. *Acta Diabetol*, 40:130S-133S.
- Blair SN, Brodney S. 1999. Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. *Med Sci Sports Exerc*, 31:S646-62.
- Blair SN, Kohl HW, Barlow CE, et al. 1995. Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. JAMA, 273:1093-8.
- Blumenthal JA, Babyak MA, Moore KA, et al. 1999. Effects of exercise training on older patients with major depression. *Arch Intern Med*, 159:2349-56.
- Capodaglio P, Capodaglio EM, Ferri A, et al. 2005. Muscle function and functional ability improves more in community-dwelling older women with a mixed-strength training programme. *Age Ageing*, 34:141-7.
- Carnethon MR, Gidding SS, Nehgme R, et al. 2003. Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. *JAMA*, 290:3092-100.
- Castillo MJ, Gutiérrez A. 2001. Entrenamiento y sobre-entrenamiento. Entrenar para ganar o entrenar para perder. Técnicas de entrenamiento para deportes de equipo. Granada: Editorial Universitaria.
- Chang JT, Morton SC, Rubenstein LZ, et al. 2004. Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ*, 328:680.
- Colcombe SJ, Erickson KI, Raz N, et al. 2003. Aerobic fitness reduces brain tissue loss in ageing humans. *J Gerontol A Biol Sci Med Sci*, 58:176-80.
- Delgado M, Gutiérrez A, Castillo MJ. 2004. Entrenamiento físicodeportivo y alimentación. De la infancia a la edad adulta. 3rd ed; Barcelona: Paidotribo.
- [EC and UKK] European Council and UKK institute. 1998. Eurofit para adultos: evaluación de la aptitud física en relación con la salud. Ed. Española. Madrid: Ministerio de Educación y Cultura.
- Englund U, Littbrand H, Sondell A, et al. 2005. A 1-year combined weightbearing training program is beneficial for bone mineral density and neuromuscular function in older women. *Osteoporos Int*, 16:1117-23.
- Evans WJ. 1999. Exercise training guidelines for the elderly. *Med Sci* Sports Exerc, 31:12-17.
- Evenson KR, Stevens J, Cai J, et al. 2003. The effect of cardiorespiratory fitness and obesity on cancer mortality in women and men. *Med Sci Sports Exerc*, 35:270-7.
- Ewart CK. 1989. Psychological effects of resistive weight training: implications for cardiac patients. *Med Sci Sports Exerc*, 21:683-8.

- Fahlman MM, Boardley D, Lambert CP, et al. 2002. Effects of endurance training and resistance training on plasma lipoprotein profiles in elderly women. *J Gerontol A Biol Sci Med Sci*, 57:54-60.
- Fletcher GF, Balady G, Blair SN, et al. 1996. Statement on exercise: benefits and recommendations for physical activity programs for all Americans: a statement for health professionals by the Committee on Exercise and Cardiac. Rehabilitation of the Council on Clinical Cardiology, American Heart Association. *Circulation*, 94:857-62.
- Fluckey JD, M. Hickey JK, Brambrink KK, et al. 1994. Effects of resistance exercise on glucose tolerance in normal and glucose-intolerant subjects. J Appl Physiol, 77:1087-92.
- Goodwin RD. 2003. Association between physical activity and mental disorders among adults in the United States. *Prev Med*, 36:698-703.
- Gulati M, Pandey DK, Arnsdorf MF, et al. 2003. Exercise capacity and the risk of death in women: the St James Women Take Heart Project. *Circulation*, 108:1554-9.
- Gutiérrez A, González-Gross M, Ruiz JR, et al. 2003. Exposure to hypoxia decreases growth hormone response to physical exercise in untrained subjects. J Sports Med Phys Fitness, 43:554-8.
- Henwood TR, Taaffe DR. 2005. Improved physical performance in older adults undertaking a short-term programme of high-velocity resistance training. *Gerontology*, 51:108-15.
- Hulsmann M, Quittan M, Berger R, et al. 2004. Muscle strength as a predictor of long-term survival in severe congestive heart failure. *Eur J Heart Fail*, 6:101-7.
- Hung C, Daub B, Black B, et al. 2004. Exercise training improves overall physical fitness and quality of life in older women with coronary artery disease. *Chest*, 126:1026-31.
- Iki M, Saito Y, Dohi Y, et al. 2002. Greater trunk muscle torque reduces postmenopausal bone loss at the spine independently of age, body size, and vitamin D receptor genotype in Japanese women. *Calcif Tissue Int*, 71:300-7.
- Ishikawa-Takata K, Ohta T, Tanaka H. 2003. How much exercise is required to reduce blood pressure in essential hypertensives: A doseresponse study. *AJH*, 16:629-33.
- Izquierdo M, Ibanez J, Hakkinen K, et al. 2004. Once weekly combined resistance and cardiovascular training in healthy older men. *Med Sci Sports Exerc*, 36:435-43.
- Kirkcaldy BD, Shephard RJ, Siefen RG. 2002. The relationship between physical activity and self-image and problem behaviour among adolescents. Soc Psychiatry Psychiatr Epidemiol, 37:544-50.
- Koffler KH, Menkes RA, Redmond WE, et al. 1992. Strength training accelerates gastrointestinal transit in middle-aged and older men. *Med Sci Sports Exerc*, 24:415-19.
- Kurl S, Laukkanen JA, Rauramaa R, et al. 2003. Cardiorespiratory fitness and the risk for stroke in men. *Arch Intern Med*, 163:1682-8.
- Lachowetz T, Evon J, Pastiglione J. 1998. The effect of an upper body strength program on intercollegiate baseball throwing velocity. J Strength Cond Res, 12:116-19.
- Lakka TA, Laaksonen DE, Lakka HM, et al. 2003. Sedentary lifestyle, poor cardiorespiratory fitness, and the metabolic syndrome. *Med Sci Sports Exerc*, 35:1279-86.
- Laukkanen JA, Lakka TA, Rauramaa R, et al. 2001. Cardiovascular fitness as a predictor of mortality in men. *Arch Intern Med*, 161:825-31.
- Laukkanen R, Oja P, Pasanen M, et al. 1992. Validity of a two kilometre walking test for estimating maximal aerobic power in overweight adults. *Int J Obes Relat Metab Disord*, 16:263-8.
- Lee CD, Blair SN. 2002. Cardiorespiratory fitness and smoking-related and total cancer mortality in men. *Med Sci Sports Exerc*, 34:735-9.
- Lee CD, Folsom AR, Blair SN. 2003. Physical activity and stroke risk. *Stroke*, 34:2475.
- Lord SR, Castell S, Corcoran J, et al. 2003. The effect of group exercise on physical functioning and falls in frail older people living in retirement villages: a randomized, controlled trial. *J Am Geriatr Soc*, 51:1685-92.

- Manson JE, Greenland P, LaCroix AZ, et al. 2002. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med*, 347:716-25.
- Metter EJ, Talbot LA, Schrager M, et al. 2002. Skeletal muscle strength as a predictor of all-cause mortality in healthy men. *J Gerontol A Biol Sci Med Sci*, 57:B359-65.
- Mora S, Redberg RF, Cui Y, et al. 2003. Ability of exercise testing to predict cardiovascular and all-cause death in asymptomatic women: a 20-year follow-up of the lipid research clinics prevalence study. *JAMA*, 290:1600-7.
- Myers J, Prakash M, Froelicher V, et al. 2002. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med, 346:793-801.
- Myers J. 2003. Exercise and cardiovascular health. *Circulation*, 107:2-5.
- Paluska SA, Schwenk TL. 2000. Physical activity and mental health: Current Concepts. *Sports Med*, 29:167-80.
- Pate RR, Pratt M, Blair SN, et al. 1995. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA*, 273:402-7.
- Piepoli MF, Davos C, Francis DP, et al. 2004. Exercise training metaanalysis of trials in patients with chronic heart failure (ExTraMATCH). *BMJ*, 328:189.
- Pollock ML, Franklin BA, Balady GJ, et al. 2000. AHA Science Advisory. Resistance exercise in individuals with and without cardiovascular disease: benefits, rationale, safety, and prescription: An advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association; Position paper endorsed by the American College of Sports Medicine. *Circulation*, 101:828-33.
- Ruiz JR, Mesa JL, Castillo MJ, et al. 2002. Hand size influences optimal grip span in women but not in men. *J Hand Surg*, 27:897-901.
- Ruiz JR, Mesa JLM, Mingorance I, et al. 2004. Sports Requiring Stressful Physical Exertion Cause Abnormalities in Plasma Lipid Profile. *Rev Esp Cardiol*, 57: 499-506.
- Sato Y, Nagasaki M, Nakai N, et al. 2003. Physical exercise improves glucose metabolism in lifestyle-related diseases. *Exp Biol Med*, 228:1208-12.
- Sawada SS, Lee IM, Muto T, et al. 2003a. Cardiorespiratory fitness and the incidence of type 2 diabetes: prospective study of Japanese men. *Diabetes Care*, 26:2918-22.
- Sawada SS, Muto T, Tanaka H, et al. 2003b. Cardiorespiratory Fitness and Cancer Mortality in Japanese Men: A Prospective Study. *Med Sci Sports Exerc*, 35:1546-50.
- Seguin R, Nelson ME. 2003. The benefits of strength training for older adults. *Am J Prev Med*, 25:S141-9.
- Seibaek M, Vestergaard H, Burchardt H, et al. 2003. Insulin resistance and maximal oxygen uptake. *Clin Cardiol*, 26:515-20.
- Strawbridge WJ, Deleger S, Roberts RE, et al. 2002. Physical activity reduces the risk of subsequent depression for older adults. *Am J Epidemiol*, 156:328-34.
- Swartz AM, Strath SJ, Bassett DR, et al. 2003. Increasing daily walking improves glucose tolerance in overweight women. *Prev Med*, 37:356-62.
- Thompson KR, Mikesky AE, Bahamonde RE, et al. 2003. Effects of physical training on proprioception in older women. J Musculoskelet Neuronal Interact, 3:223-31.
- von Stengel S, Kemmler WK, Lauber D, et al. 2005. Power training is more effective than strength training for maintaining bone mineral density in postmenopausal women. *J Appl Physiol*, 3:S8750-87.
- Watkins LL, Sherwood A, Feinglos M, et al. 2003. Effects of exercise and weight loss on cardiac risk factors associated with syndrome X. Arch Intern Med, 163:1889-95.