Fitness Assessment as an Anti-Aging Marker: A Narrative Review

Francisco J Amaro-Gahete1,2*, Alejandro De La O1, Lucas Jurado-Fasoli1, Manuel J Castillo1 and Angel Gutiérrez1

1Department of Medical Physiology, School of Medicine, University of Granada, Spain
2PROmoting FITness and Health through Physical Activity Research Group (PROFITH), Department of Physical Education and Sports, University of Granada, Spain

Corresponding author: Francisco J. Amaro-Gahete, Department of Medical Physiology, School of Medicine, University of Granada, Spain, Tel: +34 697 287 022; E-mail: amaroj@ugr.es

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Abstract
Aging is a natural, physiological, and inevitable process, but it can be also influenced. Although aging is not a disease, it has several characteristics that could indicate so, such as a functional decline at different levels, which may determine clinical manifestations, and it is associated with several disease processes. Consequently, it is essential to create and adopt strategies to delay the aging process. Nowadays, any strategy adopted without including physical exercise seems inconceivable. Recent studies published in relation to this population have shown that the maintenance of acceptable levels of physical fitness is associated with the prevention of many of premature aging consequences, good rates of health, and quality of life of the person. Cardiorespiratory fitness and muscular strength (as physical fitness components) are excellent life expectancy and quality of life predictors. Therefore, reaching a good fitness level is the most powerful clinical method to prevent and delay the aging process. Not only their years to live increase, but also their quality, with health and without diseases or mobility dependence.

Keywords: Aging; Physical activity; Health; Cardiorespiratory fitness; Muscular strength

Introduction
One major concern of humans has been to live a long life in good physical and mental conditions, and free of diseases. Aging is not a disease, it is a natural and physiological, progressive, and unavoidable process, but it can be influenced. The aging process is accompanied by a functional decline at different levels. At advanced stages it gives clinical manifestations, and finally, death [1].

Today, people live longer, and aging, as a health problem, affects a growing percentage of the population. It implies addressing the problem with several strategies in order to minimize its effects and avoid its consequences. In this context, a new concept has appeared: “successful aging” [1]. This concept refers to slowing down the functional decline and preventing diseases produced by aging. In this sense, the aim would not be to add years to life, but to add life to years [2]. That is not to prolong life, but to living a full and active life for as long as possible.

To achieve this goal, it is essential to create and adopt strategies to slow down the aging process. Among these strategies, it is imperative to be physically and mentally active, as well as self-sufficient and socially integrated [3]. It is well known that regular physical exercise practice has a fundamental role in this process. Previous studies suggested that doing physical exercise with an adequate intensity and duration could contribute to maintain or even improve the level of fitness, producing powerful anti-aging effects [3]. After that, many studies related to this topic have been published. Thus, the main aim of this review was to update the role of physical fitness as an anti-aging treatment, particularly bearing in mind the measurement of physical fitness as a diagnostic marker of health and biological age.

Literature Review
Physical fitness components
Physical fitness is the ability to do physical activity and/or physical exercise using most of the body structures and functions involved in body movements such as the musculoskeletal, cardiorespiratory, hemato-circulatory, endocrine-metabolic system, etc. [3]. Physical fitness integrates several components: (i) cardiorespiratory fitness, (ii) muscular strength, (iii) neuromuscular factors, (iv) body composition, and (v) other factors that include coordination, static and dynamic balance, flexibility, posture, and reaction time [4].

Changes in physical fitness throughout human life span
Physical fitness is an excellent marker of exercise performance. It is well known that humans suffer a progressive physiological and functional decline (10% per decade). A previous study showed that the maximum functional capacity occurs between the ages of 20 and 30 approximately, and the clinical manifestations of functional failure occur when 80% of the functional capacity has been depleted [5]. We can estimate that, in well conditions, excellent health could be maintained until the age of 100. Two decades later, the exhaustion of functional capacity would be generalized. Reducing the slowdown of the functional capacity to 8% to 9% would be a real and effective anti-aging therapy. Consequently, measuring the level of physical fitness as a method to determine the functional capacity, health status, expectancy, and quality of life is of great importance [6].

Cardiorespiratory fitness as a health predictor
Cardiorespiratory fitness is the most important component of physical fitness, and maximum oxygen uptake (VO2 max) is the physiological variable which has defined it both traditionally [7] and nowadays [8]. The VO2 max can be measured with indirect calorimetry
through a maximal or sub maximal test with a gas analyzer, as well as with laboratory and field tests [9,10]. Some studies clearly show that VO₂max is a powerful predictor of all-cause mortality (especially of cardiovascular diseases) in both healthy men and women of different ages [11,12], and this correlation is independent of different factors such as alcohol, tobacco, or metabolic syndrome [13-15].

A recent review showed that people with high cardiorespiratory fitness have a lower mortality risk (45% less) for any type of cancer, when compared to individuals with a low level of cardiorespiratory fitness [16]. Lakoski et al. confirmed the existence of an inverse association between cancer mortality (lung and/or colorectal) and high cardiorespiratory fitness in middle-aged adults [17]. Several studies have found a clear association between cardiorespiratory fitness and cognitive impairment. A recent study showed that high levels of cardiorespiratory fitness in early and middle ages are associated with a lower incidence of senile dementia or/and cerebrovascular diseases [18,19]. Another study described a relationship between high levels of cardiorespiratory fitness and higher verbal memory and psychomotor speed [20]. Moreover, a negative relationship between high levels of cardiorespiratory condition and the loss of executive function and episodic memory has also been reported [21].

Finally, it has been demonstrated that adequate levels of cardiorespiratory fitness in adults have a strong association with lower public health care costs during the last period of life [22].

Muscular strength as a preventive factor of morbi-mortality and aging

Muscular strength is a physical fitness parameter that has acquired great relevance in the aging process. Regardless of different factors such as age [23], body fatness, smoking, hypertension [24], or alcohol consumption [25], and even without considering cardiorespiratory fitness [25], an inverse association between muscular strength and mortality risk has been suggested [26].

The aging process implies a slow, but inexorable loss of muscular mass, strength, and functional capacity (sarcopenia and dynapenia). Therefore, the maintenance and improvement of these parameters should be considered as a prevention strategy to fight against the aging process [27,28]. The muscular strength level depends on the lean mass [29] and/or the level of physical activity [28]. Consequently, a pronounced loss of muscular strength is positively associated with an accelerated aging and an increase of all-cause mortality risk [26]. Sarcopenia, for instance, is a typical syndrome caused fundamentally by the aging process [30]. The maintenance of muscular strength through physical exercises has been described as a factor which can counteract the natural decline of the lean mass and delay the sarcopenia process [31].

Another factor that also influences aging acceleration is osteoporosis. This process is especially prevalent in postmenopausal women [32], who have traditionally experimented more bone fractures than men [33]. A specific study has shown a positive relationship between hip fractures in osteoporosis population and the risk of morbidity and mortality for all-causes [34]. In addition, another study found a positive relationship between bone mineral density and muscular strength in knee extensor strength and hand grip values [35]. Therefore, it is important to maintain and increase muscular strength as an anti-aging therapy and to fight against the osteopenia process.

On the other hand, recent studies have shown that skeletal muscle has an endocrine and metabolic function related to chronic systemic inflammation [36]. The skeletal muscle produces myokines which are involved in the lipolysis process, improving insulin sensitivity and contributing to the muscle hypertrophy process [37]. An adequate production of myokines is necessary for the metabolic regulation related to obesity, insulin resistance, atherosclerosis, neurodegenerative process, and tumoral diseases [38,39]. Therefore, the loss of lean body mass (associated with the loss of muscular strength) may predispose the development of metabolic diseases such as insulin resistance, diabetes mellitus type II, or metabolic syndrome [27,29], and premature mortality [25] associated to the aging process.

Body composition as a health biomarker in aging

Body composition is considered an important health biomarker associated with the development or prevention of several diseases [3]. It is well known that the aging process is characterized by an increase in the body fat mass and a decrease in the lean body mass [40].

It has been found that the overweight and obesity prevalence rates increase during the aging process. In fact, it has been estimated that 37% of men and 42% of women are obese in the USA [41]. This fact is a public health problem due to a body mass index >30 kg/m², which is positively associated with aging related diseases [42]. Body fat mass is strongly associated with a higher risk of suffering different chronic diseases (cardiovascular disease, diabetes, and/or cancer) [43]. Furthermore, it contributes to a reduction of the functional capacity [44,45] and, consequently, to the acceleration of the aging process.

Another important factor to consider is body fat mass distribution. Several studies have found that central adiposity (android distribution) is strongly associated with the appearance of cardiovascular diseases in comparison with gynoid distribution [46].

The loss of muscular strength is faster than the loss of lean body mass, suggesting a significant decrease in muscle quality. Therefore, it is essential to investigate strategies which increase muscle quality during the aging process in addition to maintaining or increasing the lean body mass in order to prevent or delay functional impairment as an anti-aging therapy [47].

Adiposity and sarcopenia are two factors that contribute to the decline of the functional capacity and personal autonomy in the elderly. Its synergistic effects are known as sarcopenic obesity. This pathology is associated with an accelerated aging process [48] and greater prevalence of several diseases such as atherosclerosis, diabetes type II, or metabolic syndrome [49].

Other determinants of fitness

There are other factors that can be included as part of physical fitness. The intra-individual variability of reaction time is considered a functional index of the central nervous system, associating low variability with healthy aging [50]. Coordination (oculomanual/oculopedical) is also included in the concept of physical fitness. Several studies have shown that coordination training combined with aerobic training increases cognitive performance in the elderly, thus achieving a potent anti-aging effect [51,52]. Finally, low levels of dynamic balance are positively associated with a risk of fractures and falls [53]. Therefore, high levels of this parameter provide a protective role in the prevention of falls in the elderly population [54].
Physical Fitness Evaluation

Cardiorespiratory fitness

To measure cardiorespiratory fitness, we have to consider different facts: (i) the availability of a physiology lab with technological equipment (gas analyser, ergometer, etc.), (ii) the evaluation purpose, (iii) the patients' characteristics, and (iv) the evaluation context.

Maximum ergometer exercise test (with indirect calorimetry)

This method is considered the "gold standard" [55] and it can follow specific protocols which depend on the patients' characteristics. All of them start at low intensity and progressively increase over time. The criteria to achieve VO$_2$max are usually (i) to reach a respiratory exchange ratio ≥ 1.1, (ii) to observe a plateau in VO$_2$ (change of <100 ml/min in the last three consecutive 10s stages), (iii) to achieve a heart rate within 10 beats/min of the age-predicted maximal heart rate (208-0.7 * age [56]), and (iv) to obtain a serum lactate >8.6 Mmol*L$^{-1}$ [55]. Different ergometers can be used (treadmill, cycloergometer, remoergometer, etc.).

Submaximum ergometer lab test

Bruce treadmill test: It is an incremental submaximal treadmill test. It is characterized by its progressive incremental stage with an increase of speed and slope every 3 minutes [57]. The use of the modified Bruce protocol is the most extended currently [58,59].

Single-stage submaximal treadmill walking test: This test starts with a 3-minute warm-up, walking at 5 km/h on a treadmill; the speed is gradually increased until the participants reach a comfortable speed which they can maintain for several minutes. The protocol consists of two parts, walking for 5 minutes. In the first part, the speed must be adjusted between 50 and 70% of heart rate reserve. The second stage is characterized by an increase of 5% of the inclination maintaining the same speed. Finally, a 2-minute recovery stage is carried out at 4 km*h$^{-1}$ [60]. The VO$_2$max is calculated applying a specific equation [61].

Astrand and rhyming cycle ergometer test: It is done on a cycloergometer, and it calculates the VO$_2$max from the heart rate reached after a 6-minute period at different intensities. The stable heart rate for each stage can be calculated through the mean of the last 2 minutes of each stage. If the difference is higher than 5 beats*minute$^{-1}$, the stage has to be prolonged one additional minute. The first load is specific for sex and age [62]. This test has been used in recent studies [63,64].

Other submaximum lab tests: (i) Using less frequency on the treadmill: Madder test [65] and Self-Paced Walking test [66]; (ii) On the ergometer: Astrand and Rhyning Cycle Ergometer test [62], YMCA test [67], Hollman Cycle Ergometer test [68]; (iii) On the step: Astrand and Rhyning Step test [62], Nagle Step test [69].

Indirect field tests

The 2-km walk-test (UKK test): It consists in walking at a comfortable and constant speed for 2 kilometres as fast as possible without running. It is necessary to register the test duration and the final heart rate. We can estimate the VO$_2$max applying a specific equation, and compare by sex and age using the reference values [70]. It is an easy and feasible test to do in elderly population, and it has been used in recent studies [71].

Rockport one-mile fitness walking test: The aim of the test is to complete 1 mile at maximum speed without running [72]. It has been considered a reference value, and its use is currently widespread [73,74].

The 6-min walk test: It consists in walking during 6 minutes at the maximum speed in order to complete the maximum distance without running [75]. It has been applied in elderly populations to assess cardiorespiratory fitness as a predictor of morbidity and mortality [75-81]. It has been used to assess cardiorespiratory fitness in several recent studies [82,83].

The 20-meter shuttle run test (Test of Montreal, Course Navette or Léger Boucher): It consists in running between two points separated by 20 meters. It is synchronized with an audio tape which includes a software that generates beeps at set intervals. As the test progresses, the time interval decreases until the participant cannot maintain the imposed intensity. The starting speed is 8.5 km*h$^{-1}$, and it increases 0.5 km*h$^{-1}$ each stage [84]. The VO$_2$max can be estimated applying a specific equation [85]. It has been used to assess cardiorespiratory fitness in several studies [86,87].

The 3-minute YMCA step test: It is a submaximal step test. The participant has to step up and down a specific step following an imposed rhythm produced by a metronome (96 pulses per minute) for 3 minutes. We can estimate the VO$_2$max introducing the final heart rate after the effort applying a specific equation by sex and age [88]. It has been used in some recent studies [89,90].

Muscular strength

Muscular strength has several dimensions, but in elderly people we can consider two predominantly: (i) "Maximum strength", which is evaluated at a specific instant, and b) "Endurance strength", which is evaluated using a submaximal load in different situations [91].

Maximum strength

Isokinetic dynamometry test: It is considered the gold standard method performed in lab conditions. It is based on the realization of specific movements with an established load at a constant speed. It has shown a direct relationship between isokinetic strength in the lower limbs and lower risk of all-cause mortality [92].

Strength assessment by linear encoders: A linear encoder is a dynamometer which allows to obtain variables such as power and mechanical work, force, or speed. The main advantages compared with 1 RM test are that the linear encoder provides valid and reliable values and that it also reduces injury risk [93].

Hand grip test: It is a manual dynamometry which is commonly used as a health marker in elderly population [94]. The starting position is standing and holding a manual dynamometer, which has been regulated and adapted previously, with one hand [95]. The arm has to be separated from the body and the maximum strength must be applied without arm flexion. Two attempts are allowed in each hand, and the sum of the maximum levels are considered the valid measure.

1 RM test: It is considered the gold standard in non-lab situations [96]. It is defined as the maximum weight that can be lifted from a particular exercise on one attempt [97]. The results can be obtained directly through a specific protocol [98] or indirectly, applying another protocol and using a predictive equation after performing a specific number of repetitions [99,100].
Muscular endurance

Linear encoders (fatigue curve): In lab conditions, the most commonly used method to measure muscular endurance is doing a strength test with a submaximal load during a pre-established time in order to get a fatigue curve (force-velocity curve) [93].

Bent arm hang test: This test allows to measure the muscular endurance of the upper limb traction muscles. The participant has to be suspended on a bar with a specific hand position. The performance is assessed through the maximum suspended time [91].

Push up test: This test measures the muscular endurance of the upper limb push muscle. The participant has to be in a prone position with 4 supports (feet and hands on the ground). The number of repetitions performed in 30 seconds is considered the test result [91].

Body composition

The body composition can be measured using lab techniques or field procedures, according to the precision required and the aim established [101,102].

Lab methods

Computed axial tomography and magnetic resonance: It provides an evaluation of the tissue-system components in vivo. With both techniques, tissue volume can be determined including the adipose tissue (visceral, subcutaneous, and total), muscular tissue, brain, and organs, skin tissue and bone tissues among others [103].

Dual-energy X-ray absorptiometry (DXA): It assesses the amount of fat free mass (bone content and lean mass) and fat mass by X-rays [104].

Densitometry (hydro-densitometry and air displacement plethysmography): The body density is the ratio of the body weight (BW) to the body volume. In this way, the body density can easily be calculated from hydro-densitometry. The body density is used to estimate body fat percentage. Air displacement plethysmography is a method based on air displacement and it uses the relationship between pressure and volume to obtain body fat [105].

Total body electric conductance (TOBEC): This method enables the measurement of body composition through the differences encountered in the electrical conductivity. It has a good reproducibility, accuracy, and precision [106].

Field methods

Anthropometry: Body mass index is the most commonly used index to elucidate health problems related to body composition. However, it only includes weight and height variables, and it does not consider differences in lean mass, fat mass, or bone content. Nevertheless, it usually has a good correlation with body fat mass [107,108]. Cutaneous folds measure the skinfold thickness as a method to estimate body fat mass [109]. This method cannot calculate visceral mass, being this its main limitation.

Near-infrared interactance: The major constituents of body composition (fat, protein, and water) can be estimated using a diffuse reflectance spectrophotometry by introducing two wavelength signals, one at peak and the other at minimum absorption, for each compartment [105].

Bioelectrical impedance analysis: It is based on the electrical conductance through biological tissues [110]. This method measures the impedance or opposition to the electric flow through the body fluids [111].

Battery test used for physical fitness assessment

It is necessary to consider the concept of a battery test, since it allows a complete evaluation of the most important physical fitness qualities. These batteries include individual tests, the results of which can provide a general physical fitness value.

The most used battery test to determine physical fitness are:

ALPHA-FIT test battery for Adults, aged 18-69 [112]: It has been used in several recent studies [113-115]. The ALPHA-FIT battery consists on seven tests, which include the assessment of the main components of physical fitness: (i) the 2 km walk-test for cardiorespiratory fitness, (ii) the hand-grip test, which indicates the upper limb grip value, (iii) the jump-and-reach test, which determines the muscle strength of the lower extremities, (iv) a modified push-up test, which indicates the upper-train strength and trunk-muscle endurance, (v) the one-leg stand test, which measures static balance, and (vi) body mass index and (vii) waist circumference, both to measure body composition. It is recommended to include three additional tests: (i) dynamic sit-up, which indicates trunk-muscle endurance, (ii) shoulder-neck mobility, which shows flexibility, and (iii) figure-of-eight run, for the dynamic balance and agility [112].

Battery senior fitness test: It is one of the most used battery tests to determine physical fitness in senior or elderly population, and it has been applied in several recent studies [116,117]. This battery tries to evaluate the most important factors related to fitness and health: cardiorespiratory fitness, hip and shoulders mobility, hip extensor strength, and the ability to get up and move [118]. The tests included are 1) the 30-second chair test, 2) the arm curl test, 3) the back-scratch test, 4) the chair sit and rest test, 5) the 2-minute step test, 6) the 6-minute walk test, 7) the foot up and go test.

Short physical performance battery: It measures the functionality and the fitness condition in the elderly [119]. It includes several specific tests: the side to side test, the semi tandem stand test and tandem stand test, the gait speed walking speed test, and the lower limbs strength test [120]. It has been used in numerous studies in populations over the age of 69 [121].

When we compare all the previous battery tests, it is suggested that “short physical performance battery” is the most recommended taking into account that it presents the higher values in terms of validity, reliability, and accuracy [122].

Conclusion

The gradual aging of the population in the last decades suggests the importance of the promotion of a healthy aging based on keeping good physical and mental conditions. Although aging involves a progressive loss of functionality, it is possible to delay or attenuate this functional decline, improving health through physical fitness.

It can be argued that maintaining acceptable levels of physical fitness is associated with the prevention of many consequences of premature aging, as well as good health and quality of life.

It is well-known that physical fitness is an excellent predictor of life expectancy and quality of life, being this association stronger when muscular strength parameters are included. The improvement of physical fitness increases the functional capacity related to aging. Thus,
it is essential to begin with a correct evaluation of the physical fitness, following the standardized methods, and to follow specific exercise programs based of physical activity recommendations.

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