Revista SOCHMEDEP
Sociedad Chilena de Medicina del Deporte

Revisión Narrativa

Is physical exercise a protective agent against the way we currently age? A narrative review.

Emilio Jofré S. Msc.[1,3,*]; Álvaro Villalobos G. Msc.[4]; Paloma Ferrero H. Msc.[5]; Claudio Farías V. Msc.[2,6]; Gemma Gea G. PhD.[3,7]

[1] Instituto del Deporte, Universidad de las Américas, Escuela Licenciatura en Ciencias de la Actividad Física, Santiago, Chile.
[2] Laboratorio de Ciencias de la Actividad Física, el Deporte y la Salud, Universidad de Santiago de Chile (USACH), Santiago, Chile.
[3] Departamento de Ciencias del Deporte, Facultad de Ciencias del Deporte, Universidad Católica San Antonio de Murcia, Murcia, España.
[4] Programa de Fisiología y Biofísica, Instituto de Ciencias Biomédicas (ICBM), Facultad de Medicina, Universidad de Chile, Santiago, Chile.
[5] Facultad de Educación y Cultura, Universidad SEK, Santiago, Chile.
[6] Departamento de Didáctica de la Expresión Musical, Plástica y Corporal, Facultad de Educación, Universidad de Granada, Granada, España.
[7] Grupo de Investigación en Salud, Actividad Física, Fitness y Comportamiento Motor (GISAFFCOM), Departamento de Ciencias de la Actividad Física y del Deporte, Universidad Católica San Antonio de Murcia, Murcia, España.

* Correspondence to: Emilio Eduardo Jofré Saldía, Universidad de las Américas, Avenida 5 de Abril, 0620 Maipú, Región Metropolitana, Chile. E-mail: emiliojofre@me.com Telephone: 56 9 9701 0666

Abstract: Aging is an inherent process to living beings that involves a deterioration of homeostatic regulation and functional reserve. Currently, the aging population has high levels of physical inactivity that aggravates muscle disuse, which in turn drastically affects functional capacity and quality of life. The aim of this narrative review is to present aging conditions and the protective role of physical exercise in functional reserve and capacity in relation to how we currently age. The regular practice of physical exercise provokes several favorable responses to the preservation of neuromuscular and cardiorespiratory function, which has a direct impact on physical capacity, even benefiting cognitive function. Physical exercise has been shown to have a protective effect on different systems, apart from contributing to the preservation of functionality and self-efficacy, which is why it is essential for healthy aging, since it favors a better resolution to stressful events such as falls and/or diseases. In conclusion, even though physical exercise does not prevent the deleterious conditions of aging, its effects are positively related to the maintenance of systemic functional reserve and capacity, which translates into greater autonomy, independence and quality of life related to health in the last stage of the life cycle.

Keywords: Aging; functional capacity; physical exercise; quality of life

INDEX

Revista Archivos de la Sociedad Chilena de Medicina del Deporte.
ISSN: 0719-7322

Recibido:
15 de febrero de 2021
Aceptado:
26 de junio de 2021
Publicado
12 de agosto de 2021

1. INTRODUCTION

Aging is a complex process of which even in our times there is no universal agreement in its definition (1). Despite the existence of an endless number of theories with scientific validity, none manages to fully address the understanding of this phenomenon by itself (2). A main aspect of aging consists of a deterioration and even loss of homeostatic regulatory mechanisms (3), beginning at some indeterminate moment when the individual's stage of development, growth and maturation ends (4). From this stage, a gradual decrease in physiological reserves begins, which directly affects the physical and functional capacity of the organism (5, 6). From the age of 65, these changes accelerate and affect to a greater extent the functional reserve of the neuromuscular and cardiorespiratory system, causing a loss of autonomy and independence (7). In addition, muscle disuse because of the drastic reduction in daily physical activity carried out by this population increases these effects to a greater degree, impairing quality of life and increasing the risk of morbidity and mortality (8). In recent decades, the proportion of older adults has increased dramatically, due to a longer life expectancy and a decrease in the fertility rate (9). This rapid demographic transition has led us to witness a phenomenon never described before in the history of humanity: the "aging of aging", which translates into a significant increase in eighty and even ninety-year-old individuals in the world population (10). Despite the increase in life expectancy and a greater protected environment, these last years are not fully lived, due to a reduction in functionality (11). Therefore, aging today must be addressed in terms of quality over the number of years completed, since a notable increase in chronic non-communicable diseases is expected in the coming decades, mainly attributed to musculoskeletal conditions (12). In this context, physical exercise could be an essential alternative for the treatment and prevention of the effects of aging, as it is low cost and without adverse effects (13). The main benefits of physical exercise in the elderly are related to the maintenance and / or improvement of functional capacity, physiological reserve, and quality of life (14, 15, 16). Although there is abundant scientific evidence on the deleterious effects of aging on the different functions and systems of the human being, it is not clear at present how influential physical inactivity is in this natural process and how the benefits of physical exercise could counteract the effects derived from both factors. Therefore, the present research aims to review the conditions of aging and physical inactivity on the body's physiological reserve, and the protective role that physical exercise could play against the way we age today.

2. EFFECTS OF AGING AND PHYSICAL INACTIVITY ON FUNCTIONAL RESERVE

Aging is a multifactorial process, but fundamentally biological and physiological, which induces changes that limit the adaptability of the organism in relation to the environment (17). These changes have consequently, a greater difficulty to carry out the basic and instrumental activities of daily life, regardless of the presence or absence of diseases and / or a sedentary lifestyle (18, 19). Added to this, 92% of older adults globally do not accomplish the physical activity recommendations proposed by the World Health Organization (WHO) (20). This represents between 60-70% (14-17 hours) of the day performing sedentary activities, and in relation to other age groups, older adults are the most inactive (21). Muscle disuse because of physical inactivity causes a drastic decrease in the capacity of the cardiorespiratory and neuromuscular system to perform tasks with greater energy demand (7). This deficit of physical activity implies a deterioration of the functional reserve, understood as the difference between the minimum and maximum capacity that an organ or system has to perform its functions (22), which accelerates neurodegenerative and musculoskeletal processes that expose the individual to a loss of control of cardiorespiratory and metabolic diseases, added to an increased risk of falls and fractures that could directly affect their levels of autonomy, independence and quality of life (23). In addition, the suffering of chronic pain that is common in this population could trigger mental alterations, such as fear of moving and falling, causing voluntary confinement that paradoxically will further deteriorate their functional reserve (24).

2.1. Effects of aging and physical inactivity on the Neuromuscular System (NMS)

As a result of aging, the Central Nervous System (CNS) cells present certain conditions such as increased oxidative stress, accumulation of damage to proteins, lipids and nucleic acids, increased generation of reactive oxygen and nitrogen species, which involve cell damage due to mitochondrial dysfunction (25, 26). This degeneration causes a decrease in force levels and alteration of mechanisms such as reinnervation and denervation of motor neurons, delays in the process of stimulation and conduction of the nerve impulse towards muscle fibers, and alterations in muscle recruitment patterns (27). Regarding muscle tissue, a decrease in strength with age is observed, essentially due to a progressive loss of muscle mass (sarcopenia) and / or selective loss of type II fibers mainly, causing important changes in the qualitative characteristics of the same tissue (28). However, it seems that sarcopenia plays a relatively minor role in the mechanisms involved in force reduction (29), since deficits in the structure, function, and intrinsic force-generating properties of the NMS, is due to dynapenia (loss of strength) (30). Within these deficits, the changes associated with oxidative stress and inflammation generate damage, loss and failure in the innervation of α motor neurons, considerably affecting neuromuscular coordination (31). The first studies that demonstrated the loss of motor units over the years date from the 1970s (32). Adults older than ~ 75 years have less than 50% motor units in relation to younger individuals and even older people may have less than 10% of their remaining motor units (33) and the action potentials are mostly complex, so the stability of their transmission decreases (34). These alterations trigger an enlargement of the motor units as a compensatory mechanism for the loss of functional motor units, a phenomenon known as “sprouting” (35). This mechanism leads to an adaptive remodeling in which the remaining fast motor neurons seek the reinnervation of type I fibers but generating a motor unit of poor performance (36). These conditions will result in a significant reduction in muscle power that is reflected in a walking speed equal to or less than 0.8 m/s, which is related to a syndrome known as "muscle insufficiency", which is used as a clinical indicator to apply therapeutic interventions (37). Muscle mass and strength vary throughout the life cycle, decreasing considerably in advanced ages (38). After the age of 50, the loss of muscle mass in the lower limbs is 1-2% per year and in strength 1.5-5% per year (39). This decline in neuromuscular morphology and function considerably affects the regulation of the endocrine system and homeostatic mechanisms, characterized by multiple hormonal dysregulations with disruption in the secretion axes of insulin-like growth factors (IGF-1), testosterone and growth hormone mainly (40). Among the alterations involved in the structure of muscle tissue, we find anabolic resistance, which is the main moderator of atrophy of the musculoskeletal system, which will result in low-grade systemic inflammation, added to a reduction in the number and activity of satellite cell (41). At the same time, anabolic resistance is associated with malnutrition, regardless of whether this condition originates from a reduced caloric intake (42) and it has been proposed in recent studies that low muscle mass is part of a poor nutritional status (43). All these adverse changes that accumulate throughout life, added to the muscular disuse especially present in elderly people, cause a serious functional limitation at the time of long-term activities, which further encourages avoiding physical activity, generating a significant deterioration of the physiological reserve of the organism (44).

2.2. Effects of aging and physical inactivity on the Cardiovascular System (CVS)

Aging causes a decrease in cardiovascular capacity due to the decrease in maximum cardiac output (CO max), which results from the decrease in maximum stroke volume (SV) and maximum heart rate (HR max) (45). The gradual loss of contractile force in cardiomyocytes, caused to a great extent by a decrease in the activity of the myosin-ATPase enzyme and by the loss of elasticity of the walls of the heart, hinders an adequate and rapid ventricular filling, having therefore a decrease in CO (46). HRmax is similarly reduced between active and inactive people over the years (47). For example, people who are physically active have the same HRmax than long-distance runners when they are in their middle life (48). The decrease in HRmax can be attributed to morphological and electrophysiological changes in the cardiac conduction system, specifically in the sinoatrial node and the atrio-ventricular bundle, which would slow down cardiac conduction (49). In addition, dysregulation of β1-adrenergic receptors in the myocardium also reduces cardiac sensitivity to catecholaminergic stimulation (50). Over the years, systolic function does not deteriorate excessively, but diastolic function is significantly altered since rapid filling is considerably delayed by the age of 80 (51). The delay in ventricular filling is due to the increased stiffness of the hearth walls and an increase in the isovolumic relaxation time, due to the decrease in calcium in the sarcoplasmic reticulum of cardiac myocytes (52). This factor triggers a reduction in maximum SV in elderly people, due to increases in the end systolic volume (ESV) in the left ventricle and decrease in ejection fraction (EF) (53). These mechanisms are mainly altered by a decrease in end diastolic volume (EDV), the product of less peripheral venous return and slow relaxation of the ventricular wall (54). The increase in total peripheral resistance (TPR) with age increases cardiac afterload, causing the myocardium to work harder to bring blood to the periphery, which increases myocardial oxygen consumption for a given effort (55). Greater peripheral resistance also causes higher systolic blood pressures and is considered one of the most important factors that justify the decrease in stroke volume with age (56). In the blood vessels there is a progressive fragmentation and even a breakdown of the elastic components over the years (57). These ruptures are replaced by highly cross-linked collagen, which leads to hardening and stiffness of the aorta mainly (58). Furthermore, this stiffness is associated with a generalized increase in the intimate-medial thickness of the arteries, generating a very important underlying mechanism known as endothelial dysfunction, the product of high oxidative stress and low-grade inflammation (59, 60). Regarding blood, there is a decrease in blood and plasma volume, a reduction in the number of red blood cells, hemoglobin and their transport capacity, and consequently in hematocrit, regardless of the level of physical activity performed (61). White blood cells are almost unchanged, but the immune capacity of lymphocytes is reduced, exposing the individual to a higher risk of infections (62). In general, aging per se is a degenerative biological process that reduces the function of the CVS, but to a lesser extent than the physical deconditioning mediated by sedentary behavior highly present in this population (63).

2.3. Effects of aging and physical inactivity on the Respiratory System (RS)

Throughout the aging process there is a reduction in the physiological capacity of the RS and especially, of sedentary people (64). Regarding structural changes, a decrease in lung compliance, greater rigidity of the rib cage and a decrease in the curvature of the diaphragm can be seen, which are associated with a significant loss of strength and respiratory muscle mass (65). At the intrapulmonary level, there are alterations in the collagen fiber networks that lead to a dilation of the alveolar duct and consequently, an enlargement of the air spaces (66). Together, these changes cause alterations in ventilatory mechanics that are interrelated with other effects, such as decreased airway caliber, expiratory flows, and overall lung function (67). At the same time, alterations associated with respiratory mechanics generate changes in lung volumes (68). For example, the residual volume increases by approximately 50% from 20 to 70 years, due to greater rigidity of the rib cage and consequently causing an occlusion of the airway (69). The strength of the diaphragm is considerably reduced at advanced ages, being up to 25% lower in relation to young people (20-30 years), which is mainly associated with changes in its intrinsic properties and decrease in its curvature (70, 71). The strength of the rest of the inspiratory and expiratory muscles also decreases gradually after the age of 65 in men and women (72). Regarding other respiratory parameters, it has been shown that older adults present a lower tidal volume, lower forced vital capacity, and higher respiratory frequency, having therefore, pulmonary oxygenation disorders and poor cardiorespiratory capacity (73, 74). Another important parameter that is impaired by a loss in elasticity in the various lung tissues is the forced expiratory volume in one second (FEV_1) (75). With advancing age, this parameter begins to decline steadily, generating a greater risk of suffering from cardiopulmonary diseases (76). Starting at age 30, FEV_1 decreases by approximately 30 ml each year and accelerates even more after age 65, greatly affecting expiratory flow volume (77, 78). All the lung conditions reviewed show even more drastic changes when aging with sedentary behavior, especially a limitation of expiratory flow when trying to perform physical exercise (79). In addition, sedentary behavior added to tobacco consumption and/or exposure to environments with high levels of air pollution and respiratory irritants, further worsen lung structure and function, increasing the risk of developing serious respiratory diseases such as disease. chronic obstructive pulmonary disease (COPD), pulmonary hypertension, pulmonary emphysema, among others (80).

2.4. Effects of aging and physical inactivity on Functional Capacity (FC)

In contemporary societies, levels of voluntary physical activity begin to decline with advancing age, avoiding all kinds of activities that involve generating muscle tension (81). Physical inactivity leads to a deterioration in the capacity of the systems, especially the NMS, CVS and RS, which affects tolerance to strenuous effort, as a result of the decrease in Maximum Oxygen Consumption (VO_2max) (82). The VO_2max decreases gradually with age (83) and after the age of 20-30, it decreases approximately 10% per decade (84). This reduction is largely explained by a decrease in the capacity of the physiological determinants of VO_2max (COmax and maximum arterio-venous oxygen difference) (85). The main consequences of these changes in the elderly person, result in an accelerated decline in both power and cardiorespiratory capacity (86), which leads to reaching a functional threshold that will cause greater difficulty in performing their everyday life activities (44). This limitation and loss of function generates a decline in the ability to remain independent from the community, increasing the risk of frailty and mortality (87). Faced with this situation, basic actions such as getting up from a chair can be highly demanding for elderly people, which is an important risk factor for a possible diagnosis of frailty (88). Frailty is a biological syndrome associated with age characterized by a poor resolution of the organism to maintain homeostasis in situations of low stress or demand (89, 90). Older people diagnosed with this syndrome have reduced levels of mobility, muscle strength and physical-cognitive function in general, which is associated with a higher probability of falls and higher rates of hospitalization, increasing the risk of morbidity and mortality (91, 92). Within these conditions, the risk and number of falls are a frequent cause of unintentional injuries that can cause eventual disability (93). Approximately 30% of people aged ~ 65 and 50% of people ~ 80 years old fall at least once a year, and of those who fall, 50% fall again the same year (94, 95). The main causes of falls in the elderly are muscle weakness and deficiencies in gait and balance associated with age (96). A close relationship between gait speed (GS) and the probability of falling has been demonstrated, since a GS <0.7 m/s is associated with a higher risk of falls in any environment and with adverse outcomes (97). These limitations are the result of reduced levels of strength in the upper and lower extremities (40-70%), cardiorespiratory endurance (45%), flexibility (50%) and, to a greater extent, neuromuscular coordination (90%) in people aged ~ 75 years compared to 20-year-olds (98, 99). Finally, all these conditions together generate a significant loss of function that leads to severe limitations on the autonomy of the elderly person, increasing their physical dependence on their family nucleus or some technical element that conditions their independence and quality of life (100, 101).

2.5. Effects of aging and physical inactivity on Quality of Life

All the degenerative processes associated with aging, added to muscle disuse, gradually reduce the functional reserve of the systems, leading to a significant risk of suffering adverse events that can condition autonomy and quality of life (102). Quality of life is closely related to physical health and the ability to remain independent, which in turn will have an impact on the personal satisfaction of each individual (103, 104). Studies on quality of life in older people have focused on factors such as emotional state, depression, stress, income, and functional level (105). Therefore, quality of life is a useful index to assess the physical functioning, well-being and health status of older people (106). Despite the importance of evaluating this index, current policies and public services promote aging at home rather than at institutionalized contexts, which seems to be positive due to the security that this environment represents, but which to some extent could threaten their quality of life (107), since aging at home could mean an excessively safe environment, having as a possible consequence a high prevalence of physical inactivity in this population due to various factors such as the presence of diseases, fear of injury and falls, lack of energy and motivation, added to the lack of companions that allow them to socialize (108). Older people who experience mobility restrictions have difficulties in improving their quality of life through physical activity, which could lead to a state of fragility (109). It has been shown in a cross-sectional study that frail older people report a much lower health-related quality of life compared to those who are not frail on all scales, especially the physical and mental component of the SF-36 questionnaire (110). On the other hand, in a recent longitudinal study, it has been shown that frailty is negatively associated with quality of life, especially in older people who suffered a hip fracture in the last year (111), due to because of this syndrome, the incidence of falls is higher in this population and therefore, early identification of frailty is essential for its treatment (112). There is a phenotypic diagnosis for frailty syndrome based on certain criteria (113). These criteria are involuntary weight loss, self-reported exhaustion, decreased grip strength, slow gait speed and low level of physical activity, considering an elderly person frail when they present 3 or more of these criteria (114). However, frailty is potentially preventable, even when it becomes a severe condition that could lead to death and therefore, it is essential to apply strategies to prevent and/or slow the progression of this syndrome (115). Within the criteria for the diagnosis of frailty, two of them are directly related to conditioning aspects of physical capacity and that in turn, can be improved with training, such as decreased grip strength and slow gait speed (116). Faced with all the conditions regarding aging in conjunction with muscle disuse, which severely deteriorate the physiological reserve, functional capacity and quality of life, it is imminent to review the benefits derived from the regular practice of physical activity on the way we age and the maintenance and/or improvement of the functional reserve of the organism, with the purpose of arguing and promoting an autonomous and independent aging of the community.

3. BENEFITS OF PHYSICAL EXERCISE ON FUNCTIONAL RESERVE

Even though it is quite common to relate the increase in age with the decrease in well-being and the increase in frailty (117), it is also true that two older people with the same chronological age can vary in their functional reserve and health status (118). Frailty syndrome and the decrease in functional reserve represent adverse factors that lead to possible disability, but which in turn, can be modifiable with different types of intervention and specific health strategies, which aim to prevent, maintain and even reverse these factors (119). In this sense, it has been shown that the regular practice of physical exercise causes a series of favorable responses that contribute to healthy aging (120), because it causes improvements in many aspects of health such as physical-functional capacity (121), cognitive and mental function (122, 123), benefits in muscle (124) and cardiopulmonary function (125, 126). Therefore, physical exercise should be fully recommended in the elderly because it works as a protective agent against different adverse outcomes, which will improve their functionality and quality of life (127, 128). Next, the benefits of physical exercise on physiological reserve, functional capacity and quality of life will be reviewed.

3.1. Benefits of Physical Exercise on the Neuromuscular System

The aging process results in morphological and functional changes in brain tissue and its constituent components, affecting the volume, size, number of neurons, white and gray matter and synaptic connections (129). Evidence has shown the benefits of physical exercise on the neuromuscular system, even in advanced ages (130). In this sense, the main benefits are seen in increases in muscle mass and, more importantly, significant improvements in muscle strength and power (131, 132). Longitudinal studies in older people, date the relevance of muscle strength over structural components such as muscle mass (133), whose deterioration is two to five times greater, in strength levels than in the loss of muscle mass, according to annual follow-up records in this population (134). A condition that is accentuated in untrained people given the hypoexcitability of the motor cortex, compromising the ability to generate tension in a maximum voluntary contraction by 20% (135). Mechanical response, conditioned by the frequency of discharge and the recruitment of motor units, determining factors of the functionality of the skeletal muscle (136). In this sense, physical exercise plays a protective role in the preservation of motor units (137), which is a condition related to the contractile properties of skeletal muscle, which generates a preventive anti-inflammatory effect through the expression neurotrophic factors (138). In addition to having a local effect on active muscle tissue, it also favors the interaction of the musculoskeletal system with other organs through various anti-inflammatory myokines that promote a protective effect on the motor units themselves and other tissues (139). In turn, these anti-inflammatory mechanisms play an important role in neuronal plasticity and survival, dendritic branching and synaptic connections (140, 141), which favors processes related to memory, learning and cognitive functions (142). Among the physical exercise modalities, strength training is considered an important tool to combat the effects of aging on the NMS (143). Programs of 8 to 12 weeks (144, 145) of progressive strength training, with moderate-high intensity, close to 70% of 1RM (146), have shown improvements between 25-30% of the levels of strength in lower extremities (147) and in upper extremities (148). The muscle deteriorates by the loss of neurological control, rather than the intrinsic ability to generate tension in the muscle fibers. Strength training and myofibrillar hypertrophy improve mechanical efficiency by reducing the demand for activation of motor units in the face of a specific movement (143). Remodeling in motor units (144) and reinnervation of denervated muscles (149) could explain the neuromuscular adaptations and the short-term benefits of strength training in older people (150). Novel and innovative methodologies have been used to optimize the benefits of strength and power training programs in older adults. Adapted pliometric training has proven to be a reliable and safe option for older people (151), demonstrating improvements in neuromotor control of functional tests such as: climbing stairs, contraction speed in repetitive jumps and in power and height of the vertical jump (152). Results that relate a higher speed of the stretch-shortening cycle product of the preservation of medium and large motor units, type IIa and IIx fibers and a greater amount of skeletal appendicular muscle mass (153). Not only the load is important for the maintenance of the neuromuscular function, but also the speed of execution. A 19-year follow-up (154) of (n: 2629) men and (n: 1249) women between 41 and 85 years of age, showing that in both sexes, the loss of muscle power levels was related to a greater incidence of mortality, while higher power levels were related to higher survival. Controlling the speed of execution and the overload used are fundamental aspects to be taken into consideration when designing training programs for older people. On the other hand, aerobic exercise has also shown benefits in neuromuscular function with significant improvements in contractile capacity and maximum power, determined by the expression of the heavy head myosin isoforms I and II (155). Aerobic exercise and repetitive muscle contractions produce a large amount of reactive oxygen species (156), if not counteracted, these could accentuate the damage of tissues and constituent proteins, inflammation and subsequent cellular apoptosis, affecting excitability of CNS, favoring neurodegeneration and neuronal aging (157). Despite the above, there is no convincing evidence that prolonged and/or high-intensity aerobic exercise produces tissue damage and impaired neuromuscular function related to the production of reactive oxygen species (158). Contrary to the above and from a mechanical perspective, it is common to refer to neuromuscular limitations, which influence central parameters. A decrease in muscle efficiency, because of the increased coactivation of the antagonist muscles of the lower limb, contributes to the higher cost of oxygen during walking, both in sedentary and active older adults (159). Results that are determined by a series of factors such as: muscle morphology, elastic elements and joint mechanics in the efficient conversion of chemical energy into mechanical speed, a situation that translates into greater efficiency in the use of oxygen at a determined speed (160).

3.2. Benefits of Physical Exercise on the Cardiovascular System

Scientific evidence has widely shown that physical exercise can have an anti-aging effect on different systems (161), and that the benefits it may have outweigh the risks of practicing it in older adults (162). In this population, periods of physical inactivity of only 60 days can lead to a considerable loss of VO2max and maximum workload, however, intensive jump training can already be effective in counteracting cardiovascular deterioration (163). Exercise involves extra work on the cardiovascular system and myocardium, with the main cardiovascular responses being an increase in VO2max, CO and HR, as well as an early increase in SV, regardless of intensity level (164). Exercise has been considered as an effective complementary therapy in the treatment of hypertension (165) and its performance for life, in addition to increasing VO2max, can significantly reduce the risk of mortality because it preserves capillarization of skeletal muscle and aerobic enzymes (166), representing an important protective factor in advanced ages. Cardiovascular deterioration in the elderly is mainly due to structural changes including vascular stiffness (167), which can lead not only to cardiovascular events or heart attacks, but also to increased frailty and decreased functionality. Arterial dilation and compliance are yet unknown mechanisms that deteriorate with age and may be modified with exercise (168). Many authors have shown the need for physical exercise in older people for the prevention of CV diseases (169) and the improvement of quality of life. Resistance exercise has proven to have beneficial effects on cardiac function (170) and on the decrease in blood pressure by 5-7 mmHg after a training session, an effect that lasts up to 22 hours post-exercise, through neuro-humoral, vascular and structural adaptation mechanisms (171). In groups with impaired cardiovascular health after a heart attack, exercise has shown significant improvements in arterial compliance, resting systolic pressure, and distance in the 6-minute walk test (172). During exercise, blood flow to the metabolically inactive muscle and viscera decreases, which increases to the active muscle. Occlusion training, defined as blood flow restriction training, has also shown an increase in diastolic and systolic blood pressure, heart rate, stroke volume, and cardiac output in older women (173). Endothelium-dependent vasodilation of skeletal muscle, angiogenic markers, and capillarity also show a positive response to flexibility training (174), which is a good alternative in older populations. High intensity exercise can lead to greater improvements in aerobic capacity and cardioprotective effect (175), in addition to endothelial function and quality of life (176), from which it is inferred that the exercise intensity can have an impact on its protective effect at the cardiovascular level and can be an important factor in maintaining and/or improving the aerobic capacity of older adults.

3.3. Benefits of Physical Exercise on the Respiratory System

RS can also be benefited by the multisystemic effect of exercise in advanced ages. Studies show that respiratory capacity can be maintained over the years with regular physical activity (177), which presumably can improve the quality of life of older adults. Aerobic exercise at the ventilatory threshold can induce a significant improvement in maximal exercise capacity, respiratory muscle strength, and inspiratory muscle performance in obese subjects (178), which as in older adult populations, may decrease the sensation of dyspnea or shortness of breath. Likewise, an aerobic exercise program, combined with high-intensity training of the respiratory muscles, can significantly increase the maximum inspiratory and expiratory pressures (179), representative of the strength of the respiratory muscles and the maximum capacity to exercise. The improvement in exercise tolerance is correlated with the improvement in inspiratory vital capacity and even more so with the BODE index (180), a measurement that has been used as a predictor of mortality in older adults with COPD (181). Aging induces pulmonary alterations that may have implications in the response to exercise, which implies greater work of breathing during exertion due to greater elastic and expiratory resistive inspiratory work (182). Resistance exercise can help counteract this deterioration by having positive effects on ventilatory capacity and on the resistance of respiratory muscles to exertion (183), which can reduce pulmonary complications and improve the dyspnea scale during effort (184). On the other hand, aerobic exercise in combination with flexibility exercises of the respiratory muscles has been shown to contribute to a greater efficiency of the respiratory muscles, by improving abdominal contribution and compartment volume, in addition to improving mobility and functional exercise capacity with decreased dyspnea (185). This improvement in the exertional dyspnea scale is mainly due to a reduced activation of the diaphragm, thus reducing changes in ventilation, respiratory rate and operating lung volumes (186), contributing to the improvement of the maximum inspiratory pressure (187). Calisthenic exercise in conjunction with breathing exercises has shown improvements in thoracoabdominal mobility, in addition to lower values on the dyspnea scale in the 6-minute walk test (188), which may induce improvements in its performance, used as a measure of functional capacity during exercise in older populations (189). Evidence suggests that a decrease in exercise capacity or physical activity level may be related to a decrease in maximum inspiratory pressure and exercise tolerance (190), so training programs are suggested to prevent respiratory diseases and improve lung functions in the elderly population (191), thus improving their long-term quality of life.

3.4. Benefits of Physical Exercise on Functional Capacity

Regular physical activity in older populations is essential for healthy aging and for the prevention of chronic diseases (192), being multicomponent exercise, which includes strength, resistance and balance training, the most recommended to improve the ability to walk and avoid falls in physically frail older adults (193), thus contributing to maintaining the functional capacity of this population. Improvements in physical fitness in terms of aerobic capacity, endurance, muscular strength and dynamic balance have been observed as a result of combined training in older adults (194), as well as in walking capacity, capacity of standing and sitting and functionality in general (195). Multimodal programs that include resistance and high-speed training, weight-bearing impact exercises, and challenging mobility and balance exercises appear to be the most effective in improving musculoskeletal function (196), by helping to slow down the loss of muscle mass and strength associated with aging. Resistance training interventions have resulted in significant improvements in muscle strength and functional results (16), due to the direct impact on the cross-sectional area of the muscle fiber, increasing not only the number of myofibrils, if not also muscle size and strength (123). Likewise, resistance training in this population can improve microvascular blood flow, blood vessel regulation, endothelial function, and muscle oxygen availability and extraction, resulting in better muscle oxidative capacity (197). Aquatic exercise programs have also shown benefits in older adults, improving the strength and flexibility of the upper and lower body, functional mobility and balance (198), thus contributing to the improvement of physical and perceptual aspects, reducing the risk of falls in older adults with reduced physical capacity (199). The effect of exercise can partially reverse the physiological deterioration associated with aging, having a preventive role for sarcopenia, osteopenia, neurodegeneration and reducing the risk of CV mortality, by generating profound effects, related to a favorable physiological feedback cycle (200). Thus, training contributes to the maintenance and improvement of maximum strength, the 6-minute walk test and muscle strength and power (201), associated with an improved innate immune response and reduction risk of infection, inflammatory potential and disease (202). The gains in functional capacity and strength in response to training in older adults can be maintained for long periods of time, independent of the training load (203). However, regular and long-term participation in resistance training programs is necessary to maintain the muscle volume gained, as well as to maintain the protective effect of exercise against functional deterioration and disability (204), representing a valuable tool to combat frailty, falls and cognitive deterioration in the elderly (87).

3.5. Benefits of Physical Exercise on Quality of Life

The lack of physical activity in older populations has been shown to be one of the most common components of frailty (119), so the prescription of exercise, which must consider the state of health and functional capacity (192), will be vital to contribute to a better quality of life. Studies have shown that aerobic exercise, in conjunction with adequate sleep hygiene, can benefit the quality of sleep, mood, and quality of life of older adults (205). This close relationship between physical activity and quality of life could be explained by the improvement in the positive indexes of psychological health, such as self-esteem, and the decrease in the negative ones, such as symptoms of anxiety and depression (206). In sedentary older adults who begin an exercise program, a positive change has been observed in terms of pain reduction, better quality of life and greater self-efficacy (207), in addition to mental and social health benefits independently of the frequency of exercise (208), contributing to the independence and vitality of this population. In older adults, physical exercise has been shown to have positive effects on quality of life, even in those groups that suffer from certain conditions such as type 2 diabetes (209), arthritis (knee and hip) (210) and osteoporosis (211), among others; demonstrating even a high clinical relevance to improve the quality of life in breast cancer survivors (212), by demonstrating benefits in emotional, social and family well-being (213). In the elderly with depressive disorders, exercise programs have been shown to have a significant effect by reducing scores on the depression rating scales (214). The result of multimodal exercise programs is associated with significant changes in executive functioning and quality of life associated with health (215), like the effects of resistance exercise programs performed at least twice per week, which have been shown to improve quality of life and sense of coherence in older adults (216). Team training has also been implemented in older populations, showing benefits in physical function, psychological well-being, and quality of life (217), in addition to contributing to intrinsic motivation for the practice of physical activity. Other movement alternatives in the elderly, such as exercise programs at home or software games that enhance activities of daily life, can contribute to improving the physical and mental state in this population (218). Due to the high risk of falls in the elderly population and the consequence of burdens for both people and health system, a relationship is established between exercise programs to prevent falls and quality of life (219), Therefore, the daily practice of multimodal physical activity oriented to functionality is recommended to improve quality of life associated with health in this population (220).

4. Conclusions

In the present work, fundamental aspects of aging conditions added to muscle disuse and the benefits of physical exercise and its protective role in different systems, functional capacity and quality of life were reviewed. The general conclusions for each of the areas addressed in the review are presented below.

4.1 Neuromuscular System

The physiological and structural changes of the nervous and muscular system in the aging process are normal and can be accentuated to a greater extent with a sedentary behavior. This translates into lower levels of strength, power and muscle mass that are priority components in health care and autonomy. Physical exercise is essential for the preservation of neuromuscular function and other systems. Sustained muscle contraction over time is a mechanical tool that prevents deterioration due to disuse, causing a protective effect at a multisystemic level.

4.2 Cardiovascular System

Aging can deteriorate cardiovascular function, mainly due to a decrease in COmax and age-related endothelial dysfunction. Exercise can improve VO2max, CO and HR, in addition to showing improvements in arterial compliance, angiogenic markers, and capillarity, helping to lower blood pressure.

4.3 Respiratory System

Because of aging and unhealthy behaviors, there is a decrease in the capacity of the RS that causes alterations in ventilatory mechanics, respiratory flows, and compliance of the rib cage, which are associated with various respiratory pathologies. Physical exercise can preserve respiratory capacity, due to improvements in pulmonary pressures and functions, reducing the sensation of dyspnea and increasing tolerance to prolonged efforts.

4.4 Functional Capacity

Levels of physical activity tend to get lower and lower over the years, which affects VO2max and its physiological determinants. This condition will cause reaching a functional threshold that will limit the development of daily activities, increasing the risk of frailty and morbidity and mortality. Physical exercise improves the physical fitness of the elderly, having a preventive role against the various physiological deteriorations associated with aging and muscle disuse, due to increases in functional capacity that would ensure that this population is removed from the threshold of frailty.

4.5 Quality of Life

Quality of life can be negatively affected with aging, due to deterioration in physical health and functional capacity. Physical exercise contributes to improving the quality of life of older adults by improving psychological health, self-efficacy, and independence, reducing levels of depression.

In conclusion, the degenerative effect of aging at a multisystem level, added to muscle disuse, can reduce the functional capacity of older adults, limiting their daily life activities and negatively affecting their quality of life. This can lead to frailty syndrome and increased risk of contracting chronic diseases. However, physical exercise has been shown to have a protective effect on the different systems, in addition to contributing to the preservation of functionality and self-efficacy, which is why it has been established as a fundamental tool for healthy aging and as a preventive measure against disease. Despite its potential benefits, physical exercise does not prevent the deleterious effects of aging. However, it plays an important role as a protective agent for both the reserve and the functional capacity of the different systems, delaying a possible frailty and physical disability, which is associated with higher levels of independence, autonomy, and quality of life in older adults.

5. Conflicts of interests.

The authors declare no conflict of interest.

6. References

1. da Costa JP, Vitorino R, Silva GM, Vogel C, Duarte AC, Rocha-Santos T. A synopsis on aging-Theories, mechanisms and future prospects. Ageing Res Rev. 2016;29:90-112. doi:10.1016/j.arr.2016.06.005
2. Guarente L. Aging research-where do we stand and where are we going?. Cell. 2014;159(1):15-19. doi:10.1016/j.cell.2014.08.041
3. Serna E, Gambini J, Borras C, et al. Centenarians, but not octogenarians, up-regulate the expression of microRNAs [published correction appears in Sci Rep. 2013;3:1575. Mohammed, Kheira [corrected to Abdelaziz, Kheira M]]. Sci Rep. 2012;2:961. doi:10.1038/srep00961
4. Rodríguez Mañas L. El informe de la Organización Mundial de la Salud sobre envejecimiento y salud: un regalo para la comunidad geriátrica [The World Health Organization report on ageing and health: A gift for the geriatrics community]. Rev Esp Geriatr Gerontol. 2016;51(5):249-251. doi:10.1016/j.regg.2015.12.013
5. Justice JN, Cesari M, Seals DR, Shively CA, Carter CS. Comparative Approaches to Understanding the Relation Between Aging and Physical Function. J Gerontol A Biol Sci Med Sci. 2016;71(10):1243-1253. doi:10.1093/gerona/glv035
6. Sbardelotto ML, Costa RR, Malysz KA, et al. Improvement in muscular strength and aerobic capacities in elderly people occurs independently of physical training type or exercise model. Clinics (Sao Paulo). 2019;74:e833. doi:10.6061/clinics/2019/e833
7. Valenzuela PL, Morales JS, Pareja-Galeano H, et al. Physical strategies to prevent disuse-induced functional decline in the elderly. Ageing Res Rev. 2018;47:80-88. doi:10.1016/j.arr.2018.07.003
8. Lindahl E, Tilton K, Eickholt N, Ferguson-Stegall L. Yoga reduces perceived stress and exhaustion levels in healthy elderly individuals. Complement Ther Clin Pract. 2016;24:50-56. doi:10.1016/j.ctcp.2016.05.007
9. Rezola-Pardo C, Arrieta H, Gil SM, et al. A randomized controlled trial protocol to test the efficacy of a dual-task multicomponent exercise program in the attenuation of frailty in long-term nursing home residents: Aging-ONDUAL-TASK study. BMC Geriatr. 2019;19(1):6. Published 2019 Jan 8. doi:10.1186/s12877-018-1020-z
10. Rodríguez Rodríguez V, Rodríguez Mañas L, Sancho Castiello M, Díaz Martín R. Envejecimiento. La investigación en España y Europa [Ageing: research in Spain and Europe]. Rev Esp Geriatr Gerontol. 2012;47(4):174-179. doi:10.1016/j.regg.2012.02.005

11. Arai H, Ouchi Y, Yokode M, et al. Toward the realization of a better aged society: messages from gerontology and geriatrics. Geriatr Gerontol Int. 2012;12(1):16-22. doi:10.1111/j.1447-0594.2011.00776.x

12. Briggs AM, Cross MJ, Hoy DG, et al. Musculoskeletal Health Conditions Represent a Global Threat to Healthy Aging: A Report for the 2015 World Health Organization World Report on Ageing and Health. Gerontologist. 2016;56 Suppl 2:S243-S255. doi:10.1093/geront/gnw002

13. Fiuza-Luces C, Garatachea N, Berger NA, Lucia A. Exercise is the real polypill. Physiology (Bethesda). 2013;28(5):330-358. doi:10.1152/physiol.00019.2013

14. Daskalopoulou C, Stubbs B, Kralj C, Koukounari A, Prince M, Prina AM. Physical activity and healthy ageing: A systematic review and meta-analysis of longitudinal cohort studies. Ageing Res Rev. 2017;38:6-17. doi:10.1016/j.arr.2017.06.003

15. Marzetti E, Calvani R, Tosato M, et al. Physical activity and exercise as countermeasures to physical frailty and sarcopenia. Aging Clin Exp Res. 2017;29(1):35-42. doi:10.1007/s40520-016-0705-4

16. Lopez P, Pinto RS, Radaelli R, et al. Benefits of resistance training in physically frail elderly: a systematic review. Aging Clin Exp Res. 2018;30(8):889-899. doi:10.1007/s40520-017-0863-z

17. Carmona JJ, Michan S. Biology of Healthy Aging and Longevity. Rev Invest Clin. 2016;68(1):7-16.

18. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental activities of daily living. J Am Geriatr Soc. 1983;31(12):721-727. doi:10.1111/j.1532-5415.1983.tb03391.x

19. Andrade FB, Duarte YAO, Souza Junior PRB, Torres JL, Lima-Costa MF, Andrade FCD. Inequalities in basic activities of daily living among older adults: ELSI-Brazil, 2015. Rev Saude Publica. 2018;52Suppl 2(Suppl 2):14s. Published 2018 Oct 25. doi:10.11606/S1518-8787.2018052000617

20. Crombie KM, Leitzelar BN, Almassi NE, Mahoney JE, Koltyn KF. Translating a "Stand Up and Move More" intervention by state aging units to older adults in underserved communities: Protocol for a randomized controlled trial. Medicine (Baltimore). 2019;98(27):e16272. doi:10.1097/MD.0000000000016272

21. Mañas A, Del Pozo-Cruz B, Rodríguez-Gómez I, et al. Dose-response association between physical activity and sedentary time categories on ageing biomarkers. BMC Geriatr. 2019;19(1):270. Published 2019 Oct 15. doi:10.1186/s12877-019-1284-y

22. Berrazuelta-Fernández JR. Aging and Cardiovascular Diseases ANALES RANM. Real Academia Nacional de Medicina de España. An RANM. 2018; 135(03):266-280. doi:10.32440/ar.2018.135.03.rev09

23. Cooper R, Kuh D, Hardy R; Mortality Review Group; FALCon and HALCyon Study Teams. Objectively measured physical capability levels and mortality: systematic review and meta-analysis. BMJ. 2010;341:c4467. Published 2010 Sep 9. doi:10.1136/bmj.c4467

24. Klinedinst NJ, Resnick B, Yerges-Armstrong LM, Dorsey SG. The Interplay of Genetics, Behavior, and Pain with Depressive Symptoms in the Elderly. Gerontologist. 2015;55 Suppl 1(Suppl 1):S67-S77. doi:10.1093/geront/gnv015

25. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. Cell. 2013;153(6):1194-1217. doi:10.1016/j.cell.2013.05.039

26. Segel M, Neumann B, Hill MFE, et al. Niche stiffness underlies the ageing of central nervous system progenitor cells [published correction appears in Nature. 2019 Aug 29;:]. Nature. 2019;573(7772):130-134. doi:10.1038/s41586-019-1484-9

27. Hunter SK, Pereira HM, Keenan KG. The aging neuromuscular system and motor performance. J Appl Physiol (1985). 2016;121(4):982-995. doi:10.1152/japplphysiol.00475.2016

28. McKinnon NB, Connelly DM, Rice CL, Hunter SW, Doherty TJ. Neuromuscular contributions to the age-related reduction in muscle power: Mechanisms and potential role of high velocity power training. Ageing Res Rev. 2017;35:147-154. doi:10.1016/j.arr.2016.09.003

29. Correa-de-Araujo R, Hadley E. Skeletal muscle function deficit: a new terminology to embrace the evolving concepts of sarcopenia and age-related muscle dysfunction. J Gerontol A Biol Sci Med Sci. 2014;69(5):591-594. doi:10.1093/gerona/glt208

30. Clark BC, Manini TM. What is dynapenia?. Nutrition. 2012;28(5):495-503. doi:10.1016/j.nut.2011.12.002

31. Tudoraşcu I, Sfredel V, Riza AL, Dănciulescu Miulescu R, Ianoşi SL, Dănoiu S. Motor unit changes in normal aging: a brief review. Rom J Morphol Embryol. 2014;55(4):1295-1301.

32. Campbell MJ, McComas AJ, Petito F. Physiological changes in ageing muscles. J Neurol Neurosurg Psychiatry. 1973;36(2):174-182. doi:10.1136/jnnp.36.2.174

33. Piasecki M, Ireland A, Jones DA, McPhee JS. Age-dependent motor unit remodelling in human limb muscles. Biogerontology. 2016;17(3):485-496. doi:10.1007/s10522-015-9627-3

34. Deschenes MR. Motor unit and neuromuscular junction remodeling with aging. Curr Aging Sci. 2011;4(3):209-220. doi:10.2174/1874609811104030209

35. Gordon T, Hegedus J, Tam SL. Adaptive and maladaptive motor axonal sprouting in aging and motoneuron disease. Neurol Res. 2004;26(2):174-185. doi:10.1179/016164104225013806

36. Edström E, Altun M, Bergman E, et al. Factors contributing to neuromuscular impairment and sarcopenia during aging. Physiol Behav. 2007;92(1-2):129-135. doi:10.1016/j.physbeh.2007.05.040

37. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis [published correction appears in Age Ageing. 2019 Jul 1;48(4):601]. Age Ageing. 2019;48(1):16-31. doi:10.1093/ageing/afy169

38. Dodds RM, Syddall HE, Cooper R, et al. Grip strength across the life course: normative data from twelve British studies. PLoS One. 2014;9(12):e113637. Published 2014 Dec 4. doi:10.1371/journal.pone.0113637

39. Keller K, Engelhardt M. Strength and muscle mass loss with aging process. Age and strength loss. Muscles Ligaments Tendons J. 2014;3(4):346-350. Published 2014 Feb 24.

40. Maggio M, De Vita F, Fisichella A, et al. The Role of the Multiple Hormonal Dysregulation in the Onset of "Anemia of Aging": Focus on Testosterone, IGF-1, and Thyroid Hormones. Int J Endocrinol. 2015;2015:292574. doi:10.1155/2015/292574

41. Morton RW, Traylor DA, Weijs PJM, Phillips SM. Defining anabolic resistance: implications for delivery of clinical care nutrition. Curr Opin Crit Care. 2018;24(2):124-130. doi:10.1097/MCC.0000000000000488

42. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr. 2017;36(1):49-64. doi:10.1016/j.clnu.2016.09.004

43. Jensen GL, Cederholm T, Correia MITD, et al. GLIM Criteria for the Diagnosis of Malnutrition: A Consensus Report From the Global Clinical Nutrition Community. JPEN J Parenter Enteral Nutr. 2019;43(1):32-40. doi:10.1002/jpen.1440

44. Hunter GR, McCarthy JP, Bamman MM. Effects of resistance training on older adults. Sports Med. 2004;34(5):329-348. doi:10.2165/00007256-200434050-00005

45. Strait JB, Lakatta EG. Aging-associated cardiovascular changes and their relationship to heart failure. Heart Fail Clin. 2012;8(1):143-164. doi:10.1016/j.hfc.2011.08.011

46. Paneni F, Diaz Cañestro C, Libby P, Lüscher TF, Camici GG. The Aging Cardiovascular System: Understanding It at the Cellular and Clinical Levels. J Am Coll Cardiol. 2017;69(15):1952-1967. doi:10.1016/j.jacc.2017.01.064

47. Jensen MT. Resting heart rate and relation to disease and longevity: past, present and future. Scand J Clin Lab Invest. 2019;79(1-2):108-116. doi:10.1080/00365513.2019.1566567

48. Wilson TM, Tanaka H. Meta-analysis of the age-associated decline in maximal aerobic capacity in men: relation to training status. Am J Physiol Heart Circ Physiol. 2000;278(3):H829-H834. doi:10.1152/ajpheart.2000.278.3.H829

49. Kane AE, Howlett SE. Differences in Cardiovascular Aging in Men and Women. Adv Exp Med Biol. 2018;1065:389-411. doi:10.1007/978-3-319-77932-4_25

50. Jakovljevic DG. Physical activity and cardiovascular aging: Physiological and molecular insights. Exp Gerontol. 2018;109:67-74. doi:10.1016/j.exger.2017.05.016

51. Levy WC, Cerqueira MD, Abrass IB, Schwartz RS, Stratton JR. Endurance exercise training augments diastolic filling at rest and during exercise in healthy young and older men. Circulation. 1993;88(1):116-126. doi:10.1161/01.cir.88.1.116

52. He ZX, Darcourt J, Camous JP, et al. Correlations of left ventricular diastolic parameters and heart rate: assessment through right ventricular pacing. Eur J Nucl Med. 1992;19(5):343-348. doi:10.1007/BF00177056

53. Metra M, Teerlink JR. Heart failure. Lancet. 2017;390(10106):1981-1995. doi:10.1016/S0140-6736(17)31071-1

54. Obas V, Vasan RS. The aging heart. Clin Sci (Lond). 2018;132(13):1367-1382. Published 2018 Jul 9. doi:10.1042/CS20171156

55. Wolsk E, Bakkestrøm R, Thomsen JH, et al. The Influence of Age on Hemodynamic Parameters During Rest and Exercise in Healthy Individuals. JACC Heart Fail. 2017;5(5):337-346. doi:10.1016/j.jchf.2016.10.012

56. Nadruz W. Myocardial remodeling in hypertension. J Hum Hypertens. 2015;29(1):1-6. doi:10.1038/jhh.2014.36

57. Triposkiadis F, Xanthopoulos A, Butler J. Cardiovascular Aging and Heart Failure: JACC Review Topic of the Week. J Am Coll Cardiol. 2019;74(6):804-813. doi:10.1016/j.jacc.2019.06.053

58. O'Rourke MF, Hashimoto J. Mechanical factors in arterial aging: a clinical perspective. J Am Coll Cardiol. 2007;50(1):1-13. doi:10.1016/j.jacc.2006.12.050

59. Moreau KL. Intersection between gonadal function and vascular aging in women. J Appl Physiol (1985). 2018;125(6):1881-1887. doi:10.1152/japplphysiol.00117.2018

60. van den Munckhof ICL, Jones H, Hopman MTE, et al. Relation between age and carotid artery intima-medial thickness: a systematic review. Clin Cardiol. 2018;41(5):698-704. doi:10.1002/clc.22934

61. Davy KP, Seals DR. Total blood volume in healthy young and older men. J Appl Physiol (1985). 1994;76(5):2059-2062. doi:10.1152/jappl.1994.76.5.2059

62. Duggal NA, Niemiro G, Harridge SDR, Simpson RJ, Lord JM. Can physical activity ameliorate immunosenescence and thereby reduce age-related multi-morbidity?. Nat Rev Immunol. 2019;19(9):563-572. doi:10.1038/s41577-019-0177-9

63. de Rezende LF, Rey-López JP, Matsudo VK, do Carmo Luiz O. Sedentary behavior and health outcomes among older adults: a systematic review. BMC Public Health. 2014;14:333. Published 2014 Apr 9. doi:10.1186/1471-2458-14-333

64. Skloot GS. The Effects of Aging on Lung Structure and Function. Clin Geriatr Med. 2017;33(4):447-457. doi:10.1016/j.cger.2017.06.001

65. Miller MR. Structural and physiological age-associated changes in aging lungs. Semin Respir Crit Care Med. 2010;31(5):521-527. doi:10.1055/s-0030-1265893

66. Hochhegger B, Meirelles GS, Irion K, et al. The chest and aging: radiological findings [published correction appears in J Bras Pneumol. 2014 Jan-Feb;40(1):98. Souza, Gustavo [added]; Meireles, Gustavo Pontes de [corrected to Meirelles, Portes]]. J Bras Pneumol. 2012;38(5):656-665. doi:10.1590/s1806-37132012000500016

67. Janssens JP, Pache JC, Nicod LP. Physiological changes in respiratory function associated with ageing. Eur Respir J. 1999;13(1):197-205. doi:10.1034/j.1399-3003.1999.13a36.x

68. Roman MA, Rossiter HB, Casaburi R. Exercise, ageing and the lung. Eur Respir J. 2016;48(5):1471-1486. doi:10.1183/13993003.00347-2016

69. Skloot GS, Busse PJ, Braman SS, et al. An Official American Thoracic Society Workshop Report: Evaluation and Management of Asthma in the Elderly. Ann Am Thorac Soc. 2016;13(11):2064-2077. doi:10.1513/AnnalsATS.201608-658ST

70. Gosselin LE, Johnson BD, Sieck GC. Age-related changes in diaphragm muscle contractile properties and myosin heavy chain isoforms [published correction appears in Am J Respir Crit Care Med 1994 Sep;150(3):879]. Am J Respir Crit Care Med. 1994;150(1):174-178. doi:10.1164/ajrccm.150.1.8025746

71. Kelley RC, Ferreira LF. Diaphragm abnormalities in heart failure and aging: mechanisms and integration of cardiovascular and respiratory pathophysiology. Heart Fail Rev. 2017;22(2):191-207. doi:10.1007/s10741-016-9549-4

72. Janssens JP. Aging of the respiratory system: impact on pulmonary function tests and adaptation to exertion. Clin Chest Med. 2005;26(3):469-vii. doi:10.1016/j.ccm.2005.05.004

73. Sparrow D, Weiss ST, Vokonas PS, Cupples LA, Ekerdt DJ, Colton T. Forced vital capacity and the risk of hypertension. The Normative Aging Study. Am J Epidemiol. 1988;127(4):734-741. doi:10.1093/oxfordjournals.aje.a114854

74. Brandenberger C, Mühlfeld C. Mechanisms of lung aging. Cell Tissue Res. 2017;367(3):469-480. doi:10.1007/s00441-016-2511-x

75. Vaz Fragoso CA, Gill TM. Respiratory impairment and the aging lung: a novel paradigm for assessing pulmonary function. J Gerontol A Biol Sci Med Sci. 2012;67(3):264-275. doi:10.1093/gerona/glr198

76. Vaz Fragoso CA, McAvay G, Van Ness PH, et al. Aging-Related Considerations When Evaluating the Forced Expiratory Volume in 1 Second (FEV1) Over Time. J Gerontol A Biol Sci Med Sci. 2016;71(7):929-934. doi:10.1093/gerona/glv201

77. Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. Clin Interv Aging. 2006;1(3):253-260. doi:10.2147/ciia.2006.1.3.253

78. Sorino C, Battaglia S, Scichilone N, et al. Diagnosis of airway obstruction in the elderly: contribution of the SARA study. Int J Chron Obstruct Pulmon Dis. 2012;7:389-395. doi:10.2147/COPD.S31630

79. Taylor BJ, Johnson BD. The pulmonary circulation and exercise responses in the elderly. Semin Respir Crit Care Med. 2010;31(5):528-538. doi:10.1055/s-0030-1265894

80. Braman SS, Skloot GS. Pulmonary Disease in the Aging Patient. Clin Geriatr Med. 2017;33(4):xi-xii. doi:10.1016/j.cger.2017.08.001

81. Betik AC, Hepple RT. Determinants of VO2 max decline with aging: an integrated perspective. Appl Physiol Nutr Metab. 2008;33(1):130-140. doi:10.1139/H07-174

82. Strait JB, Lakatta EG. Aging-associated cardiovascular changes and their relationship to heart failure. Heart Fail Clin. 2012;8(1):143-164. doi:10.1016/j.hfc.2011.08.011

83. Ekblom-Bak E, Ekblom Ö, Andersson G, et al. Decline in cardiorespiratory fitness in the Swedish working force between 1995 and 2017. Scand J Med Sci Sports. 2019;29(2):232-239. doi:10.1111/sms.13328

84. Fleg JL, Lakatta EG. Role of muscle loss in the age-associated reduction in VO2 max. J Appl Physiol (1985). 1988;65(3):1147-1151. doi:10.1152/jappl.1988.65.3.1147

85. Lawrenson L, Hoff J, Richardson RS. Aging attenuates vascular and metabolic plasticity but does not limit improvement in muscle VO(2) max. Am J Physiol Heart Circ Physiol. 2004;286(4):H1565-H1572. doi:10.1152/ajpheart.01070.2003

86. Tanaka H, Seals DR. Invited Review: Dynamic exercise performance in Masters athletes: insight into the effects of primary human aging on physiological functional capacity. J Appl Physiol (1985). 2003;95(5):2152-2162. doi:10.1152/japplphysiol.00320.2003

87. Casas Herrero Á, Cadore EL, Martínez Velilla N, Izquierdo Redin M. El ejercicio físico en el anciano frágil: una actualización [Physical exercise in the frail elderly: an update]. Rev Esp Geriatr Gerontol. 2015;50(2):74-81. doi:10.1016/j.regg.2014.07.003

88. Dent E, Morley JE, Cruz-Jentoft AJ, et al. Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management. J Nutr Health Aging. 2019;23(9):771-787. doi:10.1007/s12603-019-1273-z

89. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-M156. doi:10.1093/gerona/56.3.m146

90. Del Pozo-Cruz B, Mañas A, Martín-García M, et al. Frailty is associated with objectively assessed sedentary behaviour patterns in older adults: Evidence from the Toledo Study for Healthy Aging (TSHA). PLoS One. 2017;12(9):e0183911. Published 2017 Sep 11. doi:10.1371/journal.pone.0183911

91. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. J Am Geriatr Soc. 2010;58(4):681-687. doi:10.1111/j.1532-5415.2010.02764.x

92. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people [published correction appears in Lancet. 2013 Oct 19;382(9901):1328]. Lancet. 2013;381(9868):752-762. doi:10.1016/S0140-6736(12)62167-9

93. Robinovitch SN, Feldman F, Yang Y, et al. Video capture of the circumstances of falls in elderly people residing in long-term care: an observational study [published correction appears in Lancet. 2013 Jan 5;381(9860):28]. Lancet. 2013;381(9860):47-54. doi:10.1016/S0140-6736(12)61263-X

94. McClure R, Turner C, Peel N, Spinks A, Eakin E, Hughes K. Population-based interventions for the prevention of fall-related injuries in older people. Cochrane Database Syst Rev. 2005;(1):CD004441. Published 2005 Jan 25. doi:10.1002/14651858.CD004441.pub2

95. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev. 2012;(9):CD007146. Published 2012 Sep 12. doi:10.1002/14651858.CD007146.pub3

96. Kelsey JL, Berry SD, Procter-Gray E, et al. Indoor and outdoor falls in older adults are different: the maintenance of balance, independent living, intellect, and Zest in the Elderly of Boston Study. J Am Geriatr Soc. 2010;58(11):2135-2141. doi:10.1111/j.1532-5415.2010.03062.x

97. Inzitari M, Calle A, Esteve A, Casas Á, Torrents N, Martínez N. ¿Mides la velocidad de la marcha en tu práctica diaria? Una revisión [Do you measure gait speed in your daily clinical practice? A review]. Rev Esp Geriatr Gerontol. 2017;52(1):35-43. doi:10.1016/j.regg.2015.12.010

98. Häkkinen K, Kallinen M, Izquierdo M, et al. Changes in agonist-antagonist EMG, muscle CSA, and force during strength training in middle-aged and older people. J Appl Physiol (1985). 1998;84(4):1341-1349. doi:10.1152/jappl.1998.84.4.1341

99. Izquierdo M, Aguado X, Gonzalez R, López JL, Häkkinen K. Maximal and explosive force production capacity and balance performance in men of different ages. Eur J Appl Physiol Occup Physiol. 1999;79(3):260-267. doi:10.1007/s004210050504

100. Rodríguez-Pérez M, Abreu-Sánchez A, Rojas-Ocaña MJ, Del-Pino-Casado R. Coping strategies and quality of life in caregivers of dependent elderly relatives. Health Qual Life Outcomes. 2017;15(1):71. Published 2017 Apr 14. doi:10.1186/s12955-017-0634-8

101. da Silva GC, Cavalcante Neto JL. Quality of life and functional capability of elderly Brazilian women. Work. 2019;62(1):97-106. doi:10.3233/WOR-182844

102. Marques AI, Rosa MJ, Amorim M, et al. Study protocol: using the Q-STEPS to assess and improve the quality of physical activity programmes for the elderly. BMC Res Notes. 2012;5:171. Published 2012 Jul 9. doi:10.1186/1756-0500-5-171

103. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. Soc Sci Med. 1995;41(10):1403-1409. doi:10.1016/0277-9536(95)00112-k

104. Kim GM, Hong MS, Noh W. Factors affecting the health-related quality of life in community-dwelling elderly people. Public Health Nurs. 2018;35(6):482-489. doi:10.1111/phn.12530

105. Lee S, Cheong CH. Effect of the Physical Environment on the Health-related Quality of Life of the Low-income Korean Elderly Population. Iran J Public Health. 2018;47(12):1865-1873.

106. Kil SR, Lee SI, Yun SC, An HM, Jo MW. J Prev Med Public Health. 2008;41(6):434-441. doi:10.3961/jpmph.2008.41.6.434

107. Vanleerberghe P, De Witte N, Claes C, Schalock RL, Verté D. The quality of life of older people aging in place: a literature review. Qual Life Res. 2017;26(11):2899-2907. doi:10.1007/s11136-017-1651-0

108. Bashkireva AS, Bogdanova DY, Bilyk AY, Shishko AV, Kachan EY, Arutyunov VA. Adv Gerontol. 2018;31(5):743-750.

109. de Vries NM, van Ravensberg CD, Hobbelen JS, Olde Rikkert MG, Staal JB, Nijhuis-van der Sanden MW. Effects of physical exercise therapy on mobility, physical functioning, physical activity and quality of life in community-dwelling older adults with impaired mobility, physical disability and/or multi-morbidity: a meta-analysis. Ageing Res Rev. 2012;11(1):136-149. doi:10.1016/j.arr.2011.11.002

110. Lin CC, Li CI, Chang CK, et al. Reduced health-related quality of life in elders with frailty: a cross-sectional study of community-dwelling elders in Taiwan. PLoS One. 2011;6(7):e21841. doi:10.1371/journal.pone.0021841

111. van de Ree CLP, Landers MJF, Kruithof N, et al. Effect of frailty on quality of life in elderly patients after hip fracture: a longitudinal study. BMJ Open. 2019;9(7):e025941. Published 2019 Jul 18. doi:10.1136/bmjopen-2018-025941

112. Silva MR, Alberton CL, Portella EG, Nunes GN, Martin DG, Pinto SS. Water-based aerobic and combined training in elderly women: Effects on functional capacity and quality of life. Exp Gerontol. 2018;106:54-60. doi:10.1016/j.exger.2018.02.018

113. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. Lancet. 2019;394(10206):1365-1375. doi:10.1016/S0140-6736(19)31786-6

114. Cesari M, Calvani R, Marzetti E. Frailty in Older Persons. Clin Geriatr Med. 2017;33(3):293-303. doi:10.1016/j.cger.2017.02.002

115. Puts MTE, Toubasi S, Andrew MK, et al. Interventions to prevent or reduce the level of frailty in community-dwelling older adults: a scoping review of the literature and international policies. Age Ageing. 2017;46(3):383-392. doi:10.1093/ageing/afw247

116. Liu CK, Fielding RA. Exercise as an intervention for frailty. Clin Geriatr Med. 2011;27(1):101-110. doi:10.1016/j.cger.2010.08.001

117. Puts MT, Lips P, Deeg DJ. Sex differences in the risk of frailty for mortality independent of disability and chronic diseases. J Am Geriatr Soc. 2005;53(1):40-47. doi:10.1111/j.1532-5415.2005.53008.x

118. Mitnitski AB, Graham JE, Mogilner AJ, Rockwood K. Frailty, fitness and late-life mortality in relation to chronological and biological age. BMC Geriatr. 2002;2:1. Published 2002 Feb 27. doi:10.1186/1471-2318-2-1

119. de Labra C, Guimaraes-Pinheiro C, Maseda A, Lorenzo T, Millán-Calenti JC. Effects of physical exercise interventions in frail older adults: a systematic review of randomized controlled trials. BMC Geriatr. 2015;15:154. Published 2015 Dec 2. doi:10.1186/s12877-015-0155-4

120. American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc. 2009;41(7):1510-1530. doi:10.1249/MSS.0b013e3181a0c95c

121. Cadore EL, Casas-Herrero A, Zambom-Ferraresi F, et al. Multicomponent exercises including muscle power training enhance muscle mass, power output, and functional outcomes in institutionalized frail nonagenarians. Age (Dordr). 2014;36(2):773-785. doi:10.1007/s11357-013-9586-z

122. Kramer AF, Colcombe SJ, McAuley E, Scalf PE, Erickson KI. Fitness, aging and neurocognitive function. Neurobiol Aging. 2005;26 Suppl 1:124-127. doi:10.1016/j.neurobiolaging.2005.09.009

123. Landi F, Marzetti E, Martone AM, Bernabei R, Onder G. Exercise as a remedy for sarcopenia. Curr Opin Clin Nutr Metab Care. 2014;17(1):25-31. doi:10.1097/MCO.0000000000000018

124. Hruda KV, Hicks AL, McCartney N. Training for muscle power in older adults: effects on functional abilities. Can J Appl Physiol. 2003;28(2):178-189. doi:10.1139/h03-014

125. Ram FS, Robinson SM, Black PN. Effects of physical training in asthma: a systematic review. Br J Sports Med. 2000;34(3):162-167. doi:10.1136/bjsm.34.3.162

126. Arbab-Zadeh A, Dijk E, Prasad A, et al. Effect of aging and physical activity on left ventricular compliance. Circulation. 2004;110(13):1799-1805. doi:10.1161/01.CIR.0000142863.71285.74

127. Peterson MJ, Giuliani C, Morey MC, et al. Physical activity as a preventative factor for frailty: the health, aging, and body composition study. J Gerontol A Biol Sci Med Sci. 2009;64(1):61-68. doi:10.1093/gerona/gln001

128. Giné-Garriga M, Guerra M, Unnithan VB. The effect of functional circuit training on self-reported fear of falling and health status in a group of physically frail older individuals: a randomized controlled trial. Aging Clin Exp Res. 2013;25(3):329-336. doi:10.1007/s40520-013-0048-3

129. Harada CN, Natelson Love MC, Triebel KL. Normal cognitive aging. Clin Geriatr Med. 2013 Nov;29(4):737-52. doi: 10.1016/j.cger.2013.07.002. PMID: 24094294; PMCID: PMC4015335.

130. Drey M, Sieber CC, Degens H, McPhee J, Korhonen MT, Müller K, Ganse B, Rittweger J. Relation between muscle mass, motor units and type of training in master athletes. Clin Physiol Funct Imaging. 2016 Jan;36(1):70-6. doi: 10.1111/cpf.12195. Epub 2014 Oct 24. PMID: 25345553.

131. Steib S, Schoene D, Pfeifer K. Dose-response relationship of resistance training in older adults: a meta-analysis. Med Sci Sports Exerc. 2010;42(5):902-914. doi:10.1249/MSS.0b013e3181c34465

132. Peterson MD, Sen A, Gordon PM. Influence of resistance exercise on lean body mass in aging adults: a meta-analysis. Med Sci Sports Exerc. 2011;43(2):249-258. doi:10.1249/MSS.0b013e3181eb6265

133. Newman AB, Kupelian V, Visser M, et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. J Gerontol A Biol Sci Med Sci. 2006;61(1):72-77. doi:10.1093/gerona/61.1.72

134. Delmonico MJ, Harris TB, Visser M, et al. Longitudinal study of muscle strength, quality, and adipose tissue infiltration. Am J Clin Nutr. 2009;90(6):1579-1585. doi:10.3945/ajcn.2009.28047

135. Clark BC, Taylor JL, Hong SL, Law TD, Russ DW. Weaker Seniors Exhibit Motor Cortex Hypoexcitability and Impairments in Voluntary Activation. J Gerontol A Biol Sci Med Sci. 2015;70(9):1112-1119. doi:10.1093/gerona/glv030

136. Clark BC, Taylor JL. Age-related changes in motor cortical properties and voluntary activation of skeletal muscle. Curr Aging Sci. 2011;4(3):192-199. doi:10.2174/1874609811104030192

137. Anziska Y, Sternberg A. Exercise in neuromuscular disease. Muscle Nerve. 2013;48(1):3-20. doi:10.1002/mus.23771

138. Ogborn DI, Gardiner PF. Effects of exercise and muscle type on BDNF, NT-4/5, and TrKB expression in skeletal muscle. Muscle Nerve. 2010;41(3):385-391. doi:10.1002/mus.21503

139. Delezie J, Weihrauch M, Maier G, et al. BDNF is a mediator of glycolytic fiber-type specification in mouse skeletal muscle. Proc Natl Acad Sci U S A. 2019;116(32):16111-16120. doi:10.1073/pnas.1900544116

140. Edelmann E, Lessmann V, Brigadski T. Pre- and postsynaptic twists in BDNF secretion and action in synaptic plasticity. Neuropharmacology. 2014;76 Pt C:610-627. doi:10.1016/j.neuropharm.2013.05.043

141. Panja D, Bramham CR. BDNF mechanisms in late LTP formation: A synthesis and breakdown. Neuropharmacology. 2014;76 Pt C:664-676. doi:10.1016/j.neuropharm.2013.06.024

142. Etnier JL, Wideman L, Labban JD, et al. The Effects of Acute Exercise on Memory and Brain-Derived Neurotrophic Factor (BDNF). J Sport Exerc Psychol. 2016;38(4):331-340. doi:10.1123/jsep.2015-0335

143. Lavin KM, Roberts BM, Fry CS, Moro T, Rasmussen BB, Bamman MM. The Importance of Resistance Exercise Training to Combat Neuromuscular Aging. Physiology (Bethesda). 2019;34(2):112-122. doi:10.1152/physiol.00044.2018

144. Stec MJ, Thalacker-Mercer A, Mayhew DL, et al. Randomized, four-arm, dose-response clinical trial to optimize resistance exercise training for older adults with age-related muscle atrophy. Exp Gerontol. 2017;99:98-109. doi:10.1016/j.exger.2017.09.018

145. Petrella JK, Kim JS, Tuggle SC, Bamman MM. Contributions of force and velocity to improved power with progressive resistance training in young and older adults. Eur J Appl Physiol. 2007;99(4):343-351. doi:10.1007/s00421-006-0353-z

146. Bickel CS, Cross JM, Bamman MM. Exercise dosing to retain resistance training adaptations in young and older adults. Med Sci Sports Exerc. 2011;43(7):1177-1187. doi:10.1249/MSS.0b013e318207c15d

147. Motalebi SA, Cheong LS, Iranagh JA, Mohammadi F. Effect of low-cost resistance training on lower-limb strength and balance in institutionalized seniors. Exp Aging Res. 2018;44(1):48-61. doi:10.1080/0361073X.2017.1398810

148. Radaelli R, Fleck SJ, Leite T, et al. Dose-response of 1, 3, and 5 sets of resistance exercise on strength, local muscular endurance, and hypertrophy. J Strength Cond Res. 2015;29(5):1349-1358. doi:10.1519/JSC.0000000000000758

149. Hepple RT, Rice CL. Innervation and neuromuscular control in ageing skeletal muscle. J Physiol. 2016;594(8):1965-1978. doi:10.1113/JP270561

150. Kelly NA, Hammond KG, Bickel CS, Windham ST, Tuggle SC, Bamman MM. Effects of aging and Parkinson's disease on motor unit remodeling: influence of resistance exercise training. J Appl Physiol (1985). 2018;124(4):888-898. doi:10.1152/japplphysiol.00563.2017

151. Vetrovsky T, Steffl M, Stastny P, Tufano JJ. The Efficacy and Safety of Lower-Limb Plyometric Training in Older Adults: A Systematic Review. Sports Med. 2019;49(1):113-131. doi:10.1007/s40279-018-1018-x

152. Van Roie E, Walker S, Van Driessche S, Delabastita T, Vanwanseele B, Delecluse C. An age-adapted plyometric exercise program improves dynamic strength, jump performance and functional capacity in older men either similarly or more than traditional resistance training. PLoS One. 2020;15(8):e0237921. Published 2020 Aug 25. doi:10.1371/journal.pone.0237921

153. Singh H, Kim D, Kim E, et al. Jump test performance and sarcopenia status in men and women, 55 to 75 years of age. J Geriatr Phys Ther. 2014;37(2):76-82. doi:10.1519/JPT.0b013e3182a51b11

154. European Society of Cardiology. "Ability to lift weights quickly can mean a longer life: Not all weight lifting produces the same benefit." ScienceDaily. ScienceDaily, 12 April 2019. <www.sciencedaily.com/releases/2019/04/190412085247.htm>.

155. Harber MP, Konopka AR, Undem MK, et al. Aerobic exercise training induces skeletal muscle hypertrophy and age-dependent adaptations in myofiber function in young and older men. J Appl Physiol (1985). 2012;113(9):1495-1504. doi:10.1152/japplphysiol.00786.2012

156. He F, Li J, Liu Z, Chuang CC, Yang W, Zuo L. Redox Mechanism of Reactive Oxygen Species in Exercise. Front Physiol. 2016;7:486. Published 2016 Nov 7. doi:10.3389/fphys.2016.00486

157. Latini A, Pereira PJS, Couture R, Campos MM, Talbot S. Oxidative Stress: Neuropathy, Excitability, and Neurodegeneration. Oxid Med Cell Longev. 2019;2019:2715326. Published 2019 Jan 6. doi:10.1155/2019/2715326

158. Powers SK, Deminice R, Ozdemir M, Yoshihara T, Bomkamp MP, Hyatt H. Exercise-induced oxidative stress: Friend or foe?. J Sport Health Sci. 2020;9(5):415-425. doi:10.1016/j.jshs.2020.04.001

159. Mian OS, Thom JM, Ardigò LP, Narici MV, Minetti AE. Metabolic cost, mechanical work, and efficiency during walking in young and older men. Acta Physiol (Oxf). 2006;186(2):127-139. doi:10.1111/j.1748-1716.2006.01522.x

160. Mian OS, Thom JM, Ardigò LP, Morse CI, Narici MV, Minetti AE. Effect of a 12-month physical conditioning programme on the metabolic cost of walking in healthy older adults. Eur J Appl Physiol. 2007;100(5):499-505. doi:10.1007/s00421-006-0141-9

161. Garatachea N, Pareja-Galeano H, Sanchis-Gomar F, et al. Exercise attenuates the major hallmarks of aging. Rejuvenation Res. 2015;18(1):57-89. doi:10.1089/rej.2014.1623

162. Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc. 2011;43(7):1334-1359. doi:10.1249/MSS.0b013e318213fefb

163. Kramer A, Gollhofer A, Armbrecht G, Felsenberg D, Gruber M. How to prevent the detrimental effects of two months of bed-rest on muscle, bone and cardiovascular system: an RCT. Sci Rep. 2017;7(1):13177. Published 2017 Oct 13. doi:10.1038/s41598-017-13659-8

164. Sharman JE, Smart NA, Coombes JS, Stowasser M. Exercise and sport science australia position stand update on exercise and hypertension. J Hum Hypertens. 2019;33(12):837-843. doi:10.1038/s41371-019-0266-z

165. Williams MA, Haskell WL, Ades PA, et al. Resistance exercise in individuals with and without cardiovascular disease: 2007 update: a scientific statement from the American Heart Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity, and Metabolism. Circulation. 2007;116(5):572-584. doi:10.1161/CIRCULATIONAHA.107.185214

166. Gries KJ, Raue U, Perkins RK, et al. Cardiovascular and skeletal muscle health with lifelong exercise. J Appl Physiol (1985). 2018;125(5):1636-1645. doi:10.1152/japplphysiol.00174.2018

167. Heckman GA, McKelvie RS. Cardiovascular aging and exercise in healthy older adults. Clin J Sport Med. 2008;18(6):479-485. doi:10.1097/JSM.0b013e3181865f03

168. Kitzman DW, Brubaker PH, Herrington DM, et al. Effect of endurance exercise training on endothelial function and arterial stiffness in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. J Am Coll Cardiol. 2013;62(7):584-592. doi:10.1016/j.jacc.2013.04.033

169. Coats AJS, Forman DE, Haykowsky M, et al. Physical function and exercise training in older patients with heart failure. Nat Rev Cardiol. 2017;14(9):550-559. doi:10.1038/nrcardio.2017.70

170. Schüttler D, Clauss S, Weckbach LT, Brunner S. Molecular Mechanisms of Cardiac Remodeling and Regeneration in Physical Exercise. Cells. 2019;8(10):1128. Published 2019 Sep 23. doi:10.3390/cells8101128

171. Pescatello LS, Franklin BA, Fagard R, et al. American College of Sports Medicine position stand. Exercise and hypertension. Med Sci Sports Exerc. 2004;36(3):533-553. doi:10.1249/01.mss.0000115224.88514.3ª

172. Billinger SA, Mattlage AE, Ashenden AL, Lentz AA, Harter G, Rippee MA. Aerobic exercise in subacute stroke improves cardiovascular health and physical performance. J Neurol Phys Ther. 2012;36(4):159-165. doi:10.1097/NPT.0b013e318274d082

173. Pinto RR, Karabulut M, Poton R, Polito MD. Acute resistance exercise with blood flow restriction in elderly hypertensive women: haemodynamic, rating of perceived exertion and blood lactate. Clin Physiol Funct Imaging. 2018;38(1):17-24. doi:10.1111/cpf.12376

174. Hotta K, Behnke BJ, Arjmandi B, et al. Daily muscle stretching enhances blood flow, endothelial function, capillarity, vascular volume and connectivity in aged skeletal muscle. J Physiol. 2018;596(10):1903-1917. doi:10.1113/JP275459

175. Rognmo Ø, Moholdt T, Bakken H, et al. Cardiovascular risk of high- versus moderate-intensity aerobic exercise in coronary heart disease patients. Circulation. 2012;126(12):1436-1440. doi:10.1161/CIRCULATIONAHA.112.123117

176. Wisløff U, Støylen A, Loennechen JP, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. Circulation. 2007;115(24):3086-3094. doi:10.1161/CIRCULATIONAHA.106.675041

177. Watsford ML, Murphy AJ, Pine MJ, Coutts AJ. The effect of habitual exercise on respiratory-muscle function in older adults. J Aging Phys Act. 2005;13(1):34-44. doi:10.1123/japa.13.1.34

178. Chlif M, Chaouachi A, Ahmaidi S. Effect of Aerobic Exercise Training on Ventilatory Efficiency and Respiratory Drive in Obese Subjects. Respir Care. 2017;62(7):936-946. doi:10.4187/respcare.04923

179. Messaggi-Sartor M, Marco E, Martínez-Téllez E, et al. Combined aerobic exercise and high-intensity respiratory muscle training in patients surgically treated for non-small cell lung cancer: a pilot randomized clinical trial. Eur J Phys Rehabil Med. 2019;55(1):113-122. doi:10.23736/S1973-9087.18.05156-0

180. Kerti M, Balogh Z, Kelemen K, Varga JT. The relationship between exercise capacity and different functional markers in pulmonary rehabilitation for COPD. Int J Chron Obstruct Pulmon Dis. 2018;13:717-724. Published 2018 Feb 28. doi:10.2147/COPD.S153525

181. Roberts MH, Mapel DW, Bruse S, Petersen H, Nyunoya T. Development of a modified BODE index as a mortality risk measure among older adults with and without chronic obstructive pulmonary disease. Am J Epidemiol. 2013;178(7):1150-1160. doi:10.1093/aje/kwt087

182. Smith JR, Cross TJ, Van Iterson EH, Johnson BD, Olson TP. Resistive and elastic work of breathing in older and younger adults during exercise. J Appl Physiol (1985). 2018;125(1):190-197. doi:10.1152/japplphysiol.01105.2017

183. Laurent H, Aubreton S, Galvaing G, et al. Preoperative respiratory muscle endurance training improves ventilatory capacity and prevents pulmonary postoperative complications after lung surgery. Eur J Phys Rehabil Med. 2020;56(1):73-81. doi:10.23736/S1973-9087.19.05781-2

184. Hanada M, Kasawara KT, Mathur S, et al. Aerobic and breathing exercises improve dyspnea, exercise capacity and quality of life in idiopathic pulmonary fibrosis patients: systematic review and meta-analysis. J Thorac Dis. 2020;12(3):1041-1055. doi:10.21037/jtd.2019.12.27

185. Wada JT, Borges-Santos E, Porras DC, et al. Effects of aerobic training combined with respiratory muscle stretching on the functional exercise capacity and thoracoabdominal kinematics in patients with COPD: a randomized and controlled trial. Int J Chron Obstruct Pulmon Dis. 2016;11:2691-2700. Published 2016 Oct 28. doi:10.2147/COPD.S114548

186. Langer D, Ciavaglia C, Faisal A, et al. Inspiratory muscle training reduces diaphragm activation and dyspnea during exercise in COPD. J Appl Physiol (1985). 2018;125(2):381-392. doi:10.1152/japplphysiol.01078.2017

187. López-de-Uralde-Villanueva I, Candelas-Fernández P, de-Diego-Cano B, Mínguez-Calzada O, Del Corral T. The effectiveness of combining inspiratory muscle training with manual therapy and a therapeutic exercise program on maximum inspiratory pressure in adults with asthma: a randomized clinical trial. Clin Rehabil. 2018;32(6):752-765. doi:10.1177/0269215517751587

188. Basso-Vanelli RP, Di Lorenzo VA, Labadessa IG, et al. Effects of Inspiratory Muscle Training and Calisthenics-and-Breathing Exercises in COPD With and Without Respiratory Muscle Weakness. Respir Care. 2016;61(1):50-60. doi:10.4187/respcare.03947

189. McNamara RJ, Houben-Wilke S, Franssen FME, et al. Determinants of functional, peak and endurance exercise capacity in people with chronic obstructive pulmonary disease. Respir Med. 2018;138:81-87. doi:10.1016/j.rmed.2018.03.032

190. Aslan GK, Akinci B, Yeldan I, Okumus G. Respiratory muscle strength in patients with pulmonary hypertension: The relationship with exercise capacity, physical activity level, and quality of life. Clin Respir J. 2018;12(2):699-705. doi:10.1111/crj.12582

191. Kim BS, Kim JH, Park SH, Seo HS, Lee HS, Lee MM. Effect of a Respiratory Training Program Using Wind Instruments on Cardiopulmonary Function, Endurance, and Quality of Life of Elderly Women. Med Sci Monit. 2018;24:5271-5278. Published 2018 Jul 29. doi:10.12659/MSM.909492

192. Lee PG, Jackson EA, Richardson CR. Exercise Prescriptions in Older Adults. Am Fam Physician. 2017;95(7):425-432.

193. Cadore EL, Rodríguez-Mañas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: a systematic review. Rejuvenation Res. 2013;16(2):105-114. doi:10.1089/rej.2012.1397

194. Lange E, Kucharski D, Svedlund S, et al. Effects of Aerobic and Resistance Exercise in Older Adults With Rheumatoid Arthritis: A Randomized Controlled Trial. Arthritis Care Res (Hoboken). 2019;71(1):61-70. doi:10.1002/acr.23589

195. Ferraz DD, Trippo KV, Duarte GP, Neto MG, Bernardes Santos KO, Filho JO. The Effects of Functional Training, Bicycle Exercise, and Exergaming on Walking Capacity of Elderly Patients With Parkinson Disease: A Pilot Randomized Controlled Single-blinded Trial. Arch Phys Med Rehabil. 2018;99(5):826-833. doi:10.1016/j.apmr.2017.12.014

196. Daly RM. Exercise and nutritional approaches to prevent frail bones, falls and fractures: an update. Climacteric. 2017;20(2):119-124. doi:10.1080/13697137.2017.1286890

197. Fiogbé E, de Vassimon-Barroso V, de Medeiros Takahashi AC. Exercise training in older adults, what effects on muscle oxygenation? A systematic review. Arch Gerontol Geriatr. 2017;71:89-98. doi:10.1016/j.archger.2017.03.001

198. Moreira NB, da Silva LP, Rodacki ALF. Aquatic exercise improves functional capacity, perceptual aspects, and quality of life in older adults with musculoskeletal disorders and risk of falling: A randomized controlled trial. Exp Gerontol. 2020;142:111135. doi:10.1016/j.exger.2020.111135

199. Liu CJ, Chang WP, Araujo de Carvalho I, Savage KEL, Radford LW, Amuthavalli Thiyagarajan J. Effects of physical exercise in older adults with reduced physical capacity: meta-analysis of resistance exercise and multimodal exercise. Int J Rehabil Res. 2017;40(4):303-314. doi:10.1097/MRR.0000000000000249

200. Mendonca GV, Pezarat-Correia P, Vaz JR, Silva L, Almeida ID, Heffernan KS. Impact of Exercise Training on Physiological Measures of Physical Fitness in the Elderly. Curr Aging Sci. 2016;9(4):240-259. doi:10.2174/1874609809666160426120600

201. Zambom-Ferraresi F, Cebollero P, Gorostiaga EM, et al. Effects of Combined Resistance and Endurance Training Versus Resistance Training Alone on Strength, Exercise Capacity, and Quality of Life in Patients With COPD. J Cardiopulm Rehabil Prev. 2015;35(6):446-453. doi:10.1097/HCR.0000000000000132

202. Bartlett DB, Willis LH, Slentz CA, et al. Ten weeks of high-intensity interval walk training is associated with reduced disease activity and improved innate immune function in older adults with rheumatoid arthritis: a pilot study. Arthritis Res Ther. 2018;20(1):127. Published 2018 Jun 14. doi:10.1186/s13075-018-1624-x

203. Van Roie E, Walker S, Van Driessche S, et al. Training load does not affect detraining's effect on muscle volume, muscle strength and functional capacity among older adults. Exp Gerontol. 2017;98:30-37. doi:10.1016/j.exger.2017.07.017

204. Casas-Herrero A, Anton-Rodrigo I, Zambom-Ferraresi F, et al. Effect of a multicomponent exercise programme (VIVIFRAIL) on functional capacity in frail community elders with cognitive decline: study protocol for a randomized multicentre control trial. Trials. 2019;20(1):362. Published 2019 Jun 17. doi:10.1186/s13063-019-3426-0

205. Reid KJ, Baron KG, Lu B, Naylor E, Wolfe L, Zee PC. Aerobic exercise improves self-reported sleep and quality of life in older adults with insomnia. Sleep Med. 2010;11(9):934-940. doi:10.1016/j.sleep.2010.04.014

206. Awick EA, Ehlers DK, Aguiñaga S, Daugherty AM, Kramer AF, McAuley E. Effects of a randomized exercise trial on physical activity, psychological distress and quality of life in older adults. Gen Hosp Psychiatry. 2017;49:44-50. doi:10.1016/j.genhosppsych.2017.06.005

207. Jönsson T, Ekvall Hansson E, Thorstensson CA, Eek F, Bergman P, Dahlberg LE. The effect of education and supervised exercise on physical activity, pain, quality of life and self-efficacy - an intervention study with a reference group. BMC Musculoskelet Disord. 2018;19(1):198. Published 2018 Jun 21. doi:10.1186/s12891-018-2098-3

208. Rugbeer N, Ramklass S, Mckune A, van Heerden J. The effect of group exercise frequency on health related quality of life in institutionalized elderly. Pan Afr Med J. 2017;26:35. Published 2017 Jan 24. doi:10.11604/pamj.2017.26.35.10518

209. Tomas-Carus P, Ortega-Alonso A, Pietilainen KH, et al. A randomized controlled trial on the effects of combined aerobic-resistance exercise on muscle strength and fatigue, glycemic control and health-related quality of life of type 2 diabetes patients. J Sports Med Phys Fitness. 2016;56(5):572-578.

210. Bartels EM, Juhl CB, Christensen R, et al. Aquatic exercise for the treatment of knee and hip osteoarthritis. Cochrane Database Syst Rev. 2016;3:CD005523. Published 2016 Mar 23. doi:10.1002/14651858.CD005523.pub3

211. Dohrn IM, Hagströmer M, Hellénius ML, Ståhle A. Short- and Long-Term Effects of Balance Training on Physical Activity in Older Adults With Osteoporosis: A Randomized Controlled Trial. J Geriatr Phys Ther. 2017;40(2):102-111. doi:10.1519/JPT.0000000000000077

212. Paulo TRS, Rossi FE, Viezel J, et al. The impact of an exercise program on quality of life in older breast cancer survivors undergoing aromatase inhibitor therapy: a randomized controlled trial. Health Qual Life Outcomes. 2019;17(1):17. Published 2019 Jan 18. doi:10.1186/s12955-019-1090-4

213. Odynets T, Briskin Y, Todorova V. Effects of Different Exercise Interventions on Quality of Life in Breast Cancer Patients: A Randomized Controlled Trial. Integr Cancer Ther. 2019;18:1534735419880598. doi:10.1177/1534735419880598

214. López-Torres Hidalgo J; DEP-EXERCISE Group. Effectiveness of physical exercise in the treatment of depression in older adults as an alternative to antidepressant drugs in primary care. BMC Psychiatry. 2019;19(1):21. Published 2019 Jan 14. doi:10.1186/s12888-018-1982-6

215. Kaushal N, Desjardins-Crépeau L, Langlois F, Bherer L. The Effects of Multi-Component Exercise Training on Cognitive Functioning and Health-Related Quality of Life in Older Adults. Int J Behav Med. 2018;25(6):617-625. doi:10.1007/s12529-018-9733-0

216. Kekäläinen T, Kokko K, Sipilä S, Walker S. Effects of a 9-month resistance training intervention on quality of life, sense of coherence, and depressive symptoms in older adults: randomized controlled trial. Qual Life Res. 2018;27(2):455-465. doi:10.1007/s11136-017-1733-z

217. Pedersen MT, Vorup J, Nistrup A, et al. Effect of team sports and resistance training on physical function, quality of life, and motivation in older adults. Scand J Med Sci Sports. 2017;27(8):852-864. doi:10.1111/sms.12823

218. Neumann S, Meidert U, Barberà-Guillem R, Poveda-Puente R, Becker H. Effects of an Exergame Software for Older Adults on Fitness, Activities of Daily Living Performance, and Quality of Life. Games Health J. 2018;7(5):341-346. doi:10.1089/g4h.2017.0079

219. Bjerk M, Brovold T, Skelton DA, Bergland A. A falls prevention programme to improve quality of life, physical function and falls efficacy in older people receiving home help services: study protocol for a randomised controlled trial. BMC Health Serv Res. 2017;17(1):559. Published 2017 Aug 14. doi:10.1186/s12913-017-2516-5

220. Chittrakul J, Siviroj P, Sungkarat S, Sapbamrer R. Multi-System Physical Exercise Intervention for Fall Prevention and Quality of Life in Pre-Frail Older Adults: A Randomized Controlled Trial. Int J Environ Res Public Health. 2020;17(9):3102. Published 2020 Apr 29. doi:10.3390/ijerph17093102