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EXERCISE AS THERAPEUTIC AGENT TO IMPROVE INTRINSIC CAPACITY IN OLDER ADULTS

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ABSTRACT

Frailty has emerged as one of the most relevant clinical syndromes, due to its direct relationship with adverse health effects such as physical and functional decline and institutionalization. Physical inactivity has been argued to be a key factor contributing to the onset of muscle mass and function decline (i.e. sarcopenia), which in turn appears to be a vital aspect related to frailty. Deterioration in muscular strength and mass, cardiovascular resistance and balance leads to a decrease in daily life activities, a higher risk of falling and a loss of independence, among other consequences. The effects of exercise are potentially similar to those that can be achieved with medication and are even better, with barely any adverse effects when aiming to prevent cardiovascular disease, decrease the risk of death, prevent diabetes and obesity and improve muscular function and quality of life. Multi-component physical exercise programs and, in particular, strength training are the most effective interventions for delaying disability and other adverse events. Likewise, their use has been proven in other fields which are frequently associated with this syndrome such as falls, cognitive deterioration and depression.

Keywords: frailty, multi-component exercise, resistance training, intrinsic capacity

EJERCICIO FÍSICO COMO AGENTE TERAPÉUTICO PARA LA MEJORA DE LA CAPACIDAD INTRÍNSECA EN PERSONAS MAYORES

RESUMEN

La fragilidad se ha convertido en uno de los síndromes clínicos más relevantes y es un buen predictor de eventos adversos de salud como reducción de la capacidad física y funcional y la institucionalización. Para reducir la fragilidad hay que actuar sobre su principal factor de riesgo, la inactividad. La inactividad es un elemento nuclear en el desarrollo de la fragilidad, puesto que es esencial para determinar el estado cardiovascular, la resistencia insulínica y el deterioro musculo-esquelético (sarcopenia), al tiempo que contribuye al deterioro cognitivo y la depresión. El entrenamiento de fuerza y los programas multi-componente, en particular, cada vez tienen más resultados favorables en este grupo poblacional y sus efectos son más destacados en otros dominios del síndrome, como las caídas y el deterioro cognitivo.

Palabras clave: fragilidad, entrenamiento multi-componente, entrenamiento de fuerza, capacidad intrínseca

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From a clinical point of view, frailty has emerged as one of the most relevant clinical syndromes. This term relates to a distinctive aging-related health state in which multiple body systems gradually lose their in-built reserves resulting in decreased physiological reserves (Fried et al., 2001; Rodríguez-Mañas et al., 2013). Over the last few years, it has attracted increasing interest due to its direct relationship with adverse health effects such as physical and functional decline and institutionalization (Kojima, 2018), disability, hospitalization, worse quality of life, morbidity and increased mortality (Buckinx et al., 2016). Accordingly, an important conceptual idea for frailty is that the focus should be on functionality and not on the diagnosis of the disease for older patients. Thus, improving or maintaining function becomes the supreme mission for medical care of older people. In addition, it has been shown that the best strategy is to prevent functional decline instead of trying to recover function once this has been lost (Espeland et al., 2007).

Sarcopenia is a hallmark sign of frailty syndrome, which results in loss of muscle strength, poor mobility and balance and, consequently, an increased risk of falls, adverse health outcomes, dependency, institutionalization and death (Fiatarone et al., 1990). Sarcopenia has not only been related with substantial reorganization in the neuromuscular system and the central nervous system, but it is also associated with numerous factors, many of which are biological mechanisms contributory of aging, such as low-grade chronic inflammation (Fan, Kou, Yang, & Chen, 2016), decline in mitochondrial function and biogenesis (Jackson, 2016), reduced satellite cell numbers that impair regenerative capacity (Aagaard, Suetta, Caserotti, Magnusson, & Kjaer, 2010), apoptosis activation and decline in hormones that are important in muscle mass maintenance (i.e. IGF-1, DHEA, Testosterone and Estrogens) (Fiuza-Luces et al., 2018; Harridge & Lazarus, 2017).

Physical function measures (i.e. including several variables as gait speed, balance, mobility and muscle strength) are currently being proposed as biomarker of healthy-aging in humans, predictive of adverse health events, disability, and mortality, as well as, being commonly used as functional outcomes for clinical trials (Justice et al., 2016). Thus, multimorbidity, including cardiovascular diseases, is not the most important factor modulating individual domains of intrinsic capacity (i.e. cognition and mental health, sensory, metabolic rate of energy utilization and mobility domain and muscle strength) responsible of functional decline and diminished ability to perform activities of daily living. Moreover, physical performance measures, such as gait speed, predict mortality in older adults better than chronic diseases (e.g. hypertension), and preservation of functional capacity might be the focus of clinicians in the management of cardiovascular diseases (Odden, Peralta, Haan, & Covinsky, 2012). For these reasons, functional ability, retaining autonomy and independence as people age is the cornerstone of healthy aging, a term established by the World Health Organization in its first world report on aging and health (Beard et al., 2016).

Physical inactivity has been argued as a key factor contributing to the onset of muscle mass and function decline (i.e. sarcopenia), which in turn appears to be a vital aspect related to frailty (Cadore et al., 2014; Izquierdo, Rodriguez-Mañas, & Sinclair, 2016b). Deterioration in muscular strength and mass, cardiovascular resistance and balance leads to a decrease in daily life activities, a higher risk of falling and a loss of independence, among other consequences. Physical inactivity and a sedentary lifestyle are one of the primary factors in the loss and deterioration of muscular function.

The effects of exercise are potentially similar to those that can be achieved with medication and are even better, with barely any adverse effects when aiming to prevent cardiovascular disease, decrease the risk of death, prevent diabetes and obesity, and improve muscular function and quality of life (Cadore & Izquierdo, 2015; Fiuza-Luces et al., 2018). Multi-component physical exercise programs and, in particular, strength training are the most effective interventions for delaying disability and other adverse events. Likewise, their use has been proven in other fields which are frequently associated with this syndrome such as falls, cognitive deterioration and depression (Cadore et al., 2014; Lazarus, Izquierdo, Higginson, & Harridge, 2018). Multi-component physical exercise programs are fundamental to maintaining mobility, musculoskeletal function and optimal function of other body systems: neurological, cardiovascular, respiratory, and endocrine. Recently, it has been reported that an in-hospital, individualized multi-component exercise intervention including low-intensity resistance training exercises performed during a short period (mean, 5 days) provides a significant benefit over usual care and can help to reverse the functional decline associated with acute hospitalization in older adults (Martinez-Velilla et al., 2018). As a consequence, it is worth promoting healthy and dignified ageing by helping countries to make their health systems more efficient to implement pilot programs that can interact directly with frail older patients, aiming to measure the response to multi-component sport exercise programs for tackling late-life disability. One of these pilot programs, the *Vivifrail Project* (an EU-funded Project as part of the Erasmus+ program) (Izquierdo et al., 2017) with rapid screening for frailty and sarcopenia, tries to provide training on how to promote and prescribe physical exercise in older adults to maintain a level of function that provides them with the highest degree of autonomy possible (http://www.vivifrail.com) (Izquierdo et al., 2016a, 2016b).

Dose-response heterogeneity is not unique to pharmaceutical therapies. In the era of precision medicine, interindividual variability in the magnitude of response to supervised exercise training (subject-by-training interaction; 'individual response') has received increasing scientific interest. An individual´s interaction of physiological, molecular (i.e. genetic, epigenetic, transcriptomic and metabolic factors) and environmental factors are being determined as the mediators of the lack of a response to exercise in some participants. Exercise and medical researchers have recognized the substantial variability in patient response to physical exercise interventions and have sought to understand these differences. Several reports pertain to 'average data', and there is a wide interindividual variability in response to exercise training, which has mainly been explored in endurance-based studies. A physiological non-response to exercise in one outcome is not equal to a non-response in all outcomes. For instance, some individuals show improvements with exercise training (e.g. decrease in fasting glucose) and are considered responders while some other might not have such response (e.g. no change or even increases) and are considered non-responders. Individual variability has been reported mainly with regards to fitness-related variables, and in response to moderate-intensity endurance ('aerobic') (Bonafiglia et al., 2016), resistance (strength), or high-intensity interval training (Álvarez, Ramírez-Campillo, Ramírez-Vélez, & Izquierdo, 2017a, 2017b), and in different age groups such as children, adults, or older populations. This is an exciting time for physicians who wish to combat the increasingly recognized impact of non-communicable diseases in our societies, based on the broad-based benefits of exercise. However, a new era in the precision of the exercise prescription should also consider a priori both, the molecular mechanisms and predictors of the heterogeneity of an individual´s exercise response as well as the optimal exercise intervention being the most time-efficient but eliciting a fewer proportion of non-responder participants.

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