

Review

Frailty, Disability and Physical Exercise in the Aging Process and in Chronic Kidney Disease

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Key Words

Frailty • Disability • Physical exercise • Aging • Chronic kidney disease

Abstract

Frailty in the elderly is a state of vulnerability to poor resolution of homeostasis after a stressor event and is a consequence of cumulative decline in many physiological systems during a lifetime. This cumulative decline depletes homeostatic reserves until minor stressor events trigger disproportionate changes in health status. It is usually associated to adverse health outcomes and to one-year mortality risk. Physical exercise has found to be effective in preventing frailty and disability in this population. Chronic kidney disease (CKD) is also a clinical condition where protein energy-wasting, sarcopenia and dynapenia, very common symptoms in the frail elderly, may occur. Moreover elderly and CKD patients are both affected by an impaired physical performance that may be reversed by physical exercise with an improvement of the survival rate. These similarities suggest that frailty may be a common pathway of aging and CKD that may induce disability and that can be prevented by a multidimensional approach in which physical exercise plays an important role.

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Introduction

Chronic kidney disease (CKD) is a growing health problem that prevail in particular in the elderly subjects aged 65 or more [1]. Quality of life is reduced in this population [2] but which causes underlie this condition is still not fully understood. A CKD patient shows not only many cardiovascular risk factors and co-morbidities [3] but also cognitive deficits and

depressive symptoms [4]. Moreover elderly patients population with and without CKD also exhibit the same clinical pattern and CKD and aging process leads both to frailty. Frailty can be prevented and reduce in these two subgroups equally by physical training programs. This paper aims to examine and discuss how and when physical exercise may positively affect frailty and disability both in CKD and elderly patients.

Frailty

Frailty in the aged. Geriatricians have been long aware of a syndrome of multiple coexisting conditions, weakness, immobility, and poor tolerance to physiologic or psychologic stressors [5]. People so affected are often characterized as “frail” and are known to be more vulnerable to poor health outcomes, including disability, social isolation and institutionalization. However, although a number of definitions have been proposed none is considered the gold standard. Most definitions describe a freestanding syndrome marked by loss of function, strength, and physiologic reserve, and by increased vulnerability to sickness and death [6]. They also include declines in mobility, strength, endurance, nutrition and physical activity as the clinical components [7] and others include cognitive impairment and depression [8, 9]. Weakness and fatigue are central to almost all definitions of frailty. Sarcopenia (loss of skeleton muscle mass) and dynamopenia (loss of strength) are key components of the syndrome. Biological markers are associated with frailty. Serum levels of interleukin 6 (IL-6) and C-reactive protein have been found to be elevated in community dwelling frail older adults [10, 11]. The physiologic findings and other features that characterize frailty are not likely to be the result of changes in a single system, but rather of the interaction of several systems resulting in global process. For example the combination of low Insulin Growth Factor 1 (IGF-1) and high IL-6 levels in a cohort of community-dwelling older woman conferred a high risk for progressive disability and death that was greater than the effect of these two factors alone suggesting an additive effect [12]. Muscle mass and strength declines with age, and the trend is even more pronounced in the frailty syndrome [13]. Many studies have shown that exercise is beneficial in older adults along the full spectrum of health status, even in the frailest subset. The benefits include increased mobility, enhanced performance of activities of daily living, improved gait, fewer falls, increased bone mineral density and improvements in well-being [14, 15]. Exercise is likely to benefit even in the frailest of older adults. In a group of nursing homes elderly patients Fiatarone et al. showed that a program of resistance training increased muscle strength more than 100% muscle size in the lower extremities by 3% and gait velocity by 12% [16]. These findings were statistically significant compared with those of a control group, which showed either marginal increase or declines in these areas. Training was also associated with increased mobility and spontaneous physical activity. Even low levels increase muscle strength. Although the perfect prescription for exercise in frail older people is not known, studies have shown benefit from programs of resistance training on as few as 2 days per week [17].

Frailty in CKD. Frailty in CKD also implies decreased body energy and protein reserves and reduced strength [18]. A simple criterion for frailty can be the presence of three or more of the following abnormalities: unintentional weight loss, self-reported exhaustion, measured weakness, slow walking-speed, and low physical activity [19]. Protein energy wasting (PEW) is defined as a loss of somatic and circulating body protein and energy reserves [20]. The term PEW is preferred to protein-energy malnutrition because some causes of PEW are not related to inadequate nutrient intake. Causes of PEW in CKD patients include reduced nutrient intake, losses of nutrients during dialysis, superimposed catabolic illnesses, non specific inflammation, acidemia, catabolic stress from dialysis procedure, low levels or resistance to anabolic hormones such as insulin, IGF-1, increased levels of catabolic hormones as parathyroid hormone and glucagon, blood losses from blood drawing or gastrointestinal bleeding [21] and oxidative stress [22]. Physical activity, in general, is decreased in dialysis patients and tends to decrease with age in both the general population [23] and maintenance hemo dialysis (MHD). Decline in physical activity is greater for MHD

patients with respect to sedentary people without kidney disease [24]. Dialysis patients shows a greater reduction in moderate or vigorous physical activity with aging [25]. Physical inactivity in dialysis patients is associated with lower serum albumin and creatinine levels which are indicative of PEW and small skeletal muscle mass. In contrast, increased levels of physical activity, measured by accelerometry are associated with higher lean body mass in MHD patients [26]. In elderly dialysis patients, reduced frequency of daily physical activity is associated to higher mortality risk [27]. Reduced food intake in advanced CKD is often caused by anorexia that may be caused by uremic state and or inflammation processes. The latter not only stimulates protein degradation and PEW but also suppress appetite [28].

The role of exercise

Although many benefits can be obtained by exercise training in CKD patients [29] the most universally observed improvement is an endurance exercise capacity. Increased strength and physical performance are probably the next most commonly reported improvements [30]. Increased muscle mass with exercise training is described less frequently. This may be due to the less frequent or lower intensity strength training regimens for dialysis patients or their anti-anabolic status [31]. A positive effect on muscle intracellular protein remodelling without hypertrophy seems to be common with exercise training. Many studies investigated exercise training in elderly CKD patients. Their findings are consistent with a general improvement in muscle mass and strength despite the intensity of the training programs. Roshrahan and co-workers found substantially diminished performance in lower extremity function, but relatively preserved upper extremity muscle strength compared with normative values [32]. Specifically, performance on usual gait speed, timed up and go (TUAG) assessment, and six-minutes walking test was at least 30% lower than predicted. After adjustment for demographics and comorbidity, usual gait speed and TUAG were associated with all-cause mortality. These associations were also observed when the subgroup with baseline self-reported mobility disability was excluded. Moreover, lower extremity performance measures more strongly predicted mortality than estimates of kidney function or other common biomarkers. Taken together, these findings suggest that simple objective physical performance measures may be useful for risk stratification of CKD patients not treated with renal replacement therapy and may represent important therapeutic targets in this population.

Conclusions

Chronic kidney disease and common clinical conditions of the elderly people can be interpreted and successfully treated according to a chronic care model in which the disease induced dysfunctional status is more important than the specific disease per se. The condition of frailty in term of risk of developing disability may be the common conceptual framework between aging and CKD. In this setting sarcopenia and PEW explain extensively the impairment of the functional status in both these clinical conditions. Physical exercise training programs have been found to be effective to prevent or even to reduce the risk of disability despite the severity of CKD or the impaired functional status in the aging process.

Disclosure Statement

The authors of this manuscript state that they do not have any conflict of interests and nothing to disclose.

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