Physical Exercise as Therapy for Frailty

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Longitudinal studies have demonstrated that regular physical exercise extends longevity and reduces the risk of physical disability. A decline in physical activity with aging is associated with a decrease in exercise capacity that predisposes to frailty. The frailty syndrome includes a lowered activity level, poor exercise tolerance, and loss of lean body and muscle mass. From age 50 to 70 years, a 30% reduction in strength can occur, with muscle strength losses being most dramatic after age 70 years, mostly due to loss of muscle volume (sarcopenia). Frail lean and obese older adults are less capable of tolerating the stress of medical illness, hospitalization, and immobility. The population of older adults at risk for frailty is expected to increase due to the expected increase in adults aged 65 years and older. Frailty increases the risk of morbidity and mortality; it is not only preventable but also treatable with exercise.

Specific exercise training yields specific results. Exercise may be an effective strategy to prevent frailty as it can target specific components of frailty. Poor exercise tolerance is related to aerobic endurance. Aerobic endurance training can significantly improve peak oxygen consumption (VO$_{2peak}$) [1]. The loss of lean body and muscle mass is related to strength. Resistance training can significantly improve muscle strength and gait speed in older adults with an increase in fat-free mass.

Because both aerobic and resistance training target specific components of frailty, studies combining aerobic and resistance training provide promising evidence for effectively treating frailty. The Lifestyle Intervention and Independence for Elders Pilot trial [2] and the Frailty Intervention Trial [3] examined whether multifactorial interventions including endurance exercise, strength, and balance could improve mobility and reduce frailty. These studies found clinically meaningful improvements in physical performance, which was assessed using the Short Physical Performance Battery and gait speed [2], and a reduction in the prevalence of frailty [3].

We have shown that combined aerobic and resistance exercise improved scores in VO$_{2peak}$ and modified the physical performance test in
frail obese older adults, which were additive to the effects of diet-induced weight loss [4]. We have also shown that in frail older men and women resistance training combined with diet reduced fat-free mass loss during voluntary weight loss and still increased both upper- and lower-extremity muscle strength [5].

At the molecular level, exercise reduces frailty by decreasing muscle inflammation, increasing anabolism, and increasing muscle protein synthesis. Aging and physical inactivity are associated with increased levels of chronic inflammation. Inflammatory cytokines, e.g. tumor necrosis factor (TNF)-α and interleukin-6 (IL-6), have direct catabolic effects on skeletal muscle by suppressing muscle protein synthesis or by inhibiting the anabolic effects of insulin-like growth factor-1 (IGF-1). High concentrations of TNF-α or IL-6 are associated with lower muscle mass or strength and mobility disability, and high IL-6 and low IGF-1 levels contribute synergistically to impaired mobility. We have found that 12 weeks of exercise (aerobic and resistance) but not 12 weeks of weight loss decreased IL-6 and TNF-α and increased mechanogrowth factor mRNA of skeletal muscles, which was associated with positive effects on the functional status [6].

Table 1. Exercise recommendations for frail older adults

| Aerobic exercise | Moderate-to-vigorous activity enough to raise the pulse rate to 70–80% of the maximum heart rate Activity performed for a minimum of 20–30 min at least 3 days per week |
| Resistance exercise | The progressive resistance program should involve all major muscle groups of the upper and lower extremities and trunk One set of 8–10 different exercises, with 10–15 repetitions per set, performed 2–3 nonconsecutive days per week Moderate-/high-intensity training is recommended, in which moderate intensity is 5 or 6 on a scale from 0 to 10 |
| Flexibility and balance exercise | Stretching to the point of tightness and holding the position for a few seconds Flexibility activities are performed on all days that aerobic or muscle strengthening activity is performed Balance training exercise 2–3 times per week |

The exercise program should be individualized according to an older individual’s medical conditions and disability. The program should start at a low-to-moderate intensity, duration, and frequency to promote compliance and minimize musculoskeletal injuries.
More studies are needed to determine what exercises are best suited, effective, and safe for frail older adults. Based on the available evidence, an individualized multicomponent exercise program that includes aerobic activity, strength exercises, flexibility, and balance (table 1) is recommended to treat frailty. Frailty is not a contraindication to prescribing physical activity. Rather, frailty may be one of the most important indications for exercise.

References