Exercise as an Intervention for Frailty

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By 2015, nearly 15% of the US population will be older than 65 years. In 2030, there will be more than 70 million older Americans.\textsuperscript{1} This increase in the elderly population has prompted interest in recent years toward the study of frail older adults. Clinicians use the term frail to describe a person older than 65 years who is vulnerable to any kind of change in health status, such as infection or physical injury.\textsuperscript{2} These individuals are at a high risk for complications during a medical illness and have prolonged recovery times.\textsuperscript{3} An international consensus report in 2006 characterized frail elders as having impairments in mobility, balance, strength, motor processing, cognition, nutrition, endurance (fatigue), and physical activity.\textsuperscript{4}

In 1992, Buchner and Wagner\textsuperscript{5} first proposed a formal definition of frailty as a syndrome of weakness, impaired mobility, balance, and minimal reserve. Using epidemiologic data from the Cardiovascular Health Study (CHS), Fried and colleagues\textsuperscript{2} further characterized individuals with frailty as those who had unintentional weight loss (4.5 kg or more in the past year), fatigue or exercise intolerance, weakness, slowed motor performance, and low physical activity. A person was considered frail if they demonstrated at least 3 of these attributes (Fig. 1) and prefrail if they had 1 or 2 of these characteristics. Fried and colleagues\textsuperscript{2} found that those who were frail had an increased risk of falls, activities of daily living (ADL) disability, hospitalization, and death over a 3-year period. In the Women’s Health and Aging I study, the risk of ADL dependence increased with the number of frailty criteria fulfilled.\textsuperscript{6} At
7 years, mortality in the frail cohort of the CHS was approximately 3 times higher when compared with the nonfrail cohort (43% vs 12%). About 25% of frail subjects in the CHS had only one chronic disease, defined as osteoarthritis, diabetes, hypertension, angina, congestive heart failure, cancer, or pulmonary disease, suggesting that frailty was not always associated with multiple comorbidities. The underlying mechanisms causing the phenotype of frailty remain to be fully elucidated. Buchner and Wagner initially proposed that declines in neurologic processes, musculoskeletal functioning, and energy metabolism were the causes of frailty. Lipsitz later suggested that frailty might be caused by the loss of the ability of the cardiovascular and nervous systems to respond appropriately to stressors caused by age-related changes. Using these concepts, frailty is now thought to be caused by altered function in multiple physiologic systems (including inflammatory, skeletal muscle, endocrine, clotting, and hematologic) and dysregulation of mechanisms between these systems to maintain homeostasis.

With increasing age, there is a well-described decline in voluntary physical activity, which is associated with decreases in several measures of exercise tolerance, including maximal aerobic capacity, muscle strength, and fatigability, leading to an increased risk of frailty. In recent years, increased physical activity or regular exercise training has been proposed as a preventive strategy for frailty and its adverse outcomes because it can target 4 of the frailty criteria: weakness, low physical activity, slowed motor performance, and exercise intolerance. Epidemiologic studies suggest that regular physical activity is associated with a decreased risk of ADL disability in older adults, which is an adverse outcome of frailty. In a large-scale cohort study in Taiwan, Wu and colleagues found that older adults who were physically active, defined as participating in dancing, hiking, jogging, or walking at least twice a week, were less likely to have ADL disabilities at the end of a 3-year period when compared with their sedentary counterparts. These findings were confirmed by the Longitudinal Study of Aging, which found elders who were physically active, defined as walking at least a mile a week, were less likely to develop impairments in their ADL or

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**Fig. 1. Components of frailty.** (Adapted from Fried LP, Xue QL, Cappola AR, et al. Nonlinear multisystem physiologic dysregulation associated with frailty in older women: implications for etiology and treatment. J Gerontol A Biol Sci Med Sci 2009;64(10):1050; with permission.)
instrumental ADLs over a 6-year period, after adjusting for age, gender, comorbidities, and baseline disability.\textsuperscript{11}

This article reviews the literature investigating the utility of aerobic and resistance exercise training as an intervention for frailty in older adults. In addition, areas of future research are addressed, including concerns related to the dissemination of exercise interventions on a widespread scale. Also, guidelines for an “exercise prescription” for frail older adults are briefly outlined.

**AEROBIC OR ENDURANCE EXERCISE TRAINING**

There are 2 mechanisms by which aerobic exercise is thought to alter the frailty phenotype: improvement in the maximal oxygen uptake ($\text{VO}_2\text{max}$) and increased muscle mass. $\text{VO}_2\text{max}$ is defined as the maximum rate of oxygen consumption measured during vigorous exercise and is closely related to submaximal endurance exercise capacity and exercise tolerance.

In an intervention study of 64 frail men and women, a 9-month program of strength training and walking that aimed at reaching 78% of peak heart rate, found an increase in endurance by improving $\text{VO}_2\text{max}$ by 14%.\textsuperscript{12} A small study of healthy, elderly, sedentary women also found that a 12-week regimen of cycle ergometer training improved maximal aerobic capacity by 30% from baseline. This study demonstrated that endurance training increased quadriceps muscle mass by 12%.\textsuperscript{13} Although previous studies have shown that aerobic exercise did not alter muscle size in older adults,\textsuperscript{14–16} a recent cross-sectional study by Sugawara and colleagues\textsuperscript{17} demonstrated that those who undergo aerobic training have a higher percentage of muscle mass in their extremities when compared with their sedentary counterparts.

**RESISTANCE EXERCISE TRAINING**

There is well-documented evidence that muscle strength decreases with advancing age. Muscle strength decreases approximately 12% to 15% per decade after the age of 50 years\textsuperscript{18} in both men and women.\textsuperscript{19} In addition, muscle mass also decreases with increased age. In a cross-sectional study of healthy men of equal mass, muscle mass comprised 24% of total mass in those aged 20 to 29 years but decreased to 13% in subjects aged 70 to 79 years.\textsuperscript{20} Several studies have found that the decline in strength in older adults is associated with this age-related loss of muscle mass.\textsuperscript{21–23} Although resistance exercise training has been shown to increase muscle mass and therefore muscle strength, this response is attenuated in older adults with mobility limitations or other comorbidities. In healthy older men and women, 4 months of resistance training resulted in a 16% to 23% increase in muscle mass compared with a 2.5% to 9% increase in frail or institutionalized older adults.\textsuperscript{24–26} Despite these age-related changes in muscle, resistance exercise training has been found to increase strength in older adults. Multiple studies have demonstrated that these changes can occur even into the ninth decade of life.\textsuperscript{24,27–31} In a systemic review of 41 articles by Latham and colleagues,\textsuperscript{32} resistance exercise training in older adults was associated with gains in strength, and a Cochrane review of 74 studies found similar results.\textsuperscript{33} Both reviews used studies that examined both healthy older adults and frail adults. Fiatarone and colleagues\textsuperscript{25} showed that nursing home residents were able to increase their strength on an average of 97% after 10 weeks of resistance exercise training. Because nursing home residents represent the frailest segment of older adults, this study demonstrates that the intervention is beneficial for even those most severely affected by frailty.
Motor performance in older adults has also been shown to improve after resistance training. In their systemic review, Latham and colleagues\(^\text{32}\) found that resistance exercise training in healthy and frail elders improved gait speed in 14 studies and increased distance covered in the 6-minute walk test in 6 trials. In their respective studies of frail elders living in the nursing home and in the community, Fiatarone and colleagues\(^\text{25}\) and Chandler and colleagues\(^\text{34}\) showed that 10 weeks of resistance training resulted in improved gait speed. There may be a dose-response relationship between resistance exercise and motor performance, because Galvao and Taaffe\(^\text{35}\) found that subjects who did more repetitions of resistance exercise had almost twice the improvement in their 400-m walk time compared with those who did fewer repetitions.

### Combined Aerobic and Resistance Exercise

Given that aerobic or resistance exercise alone has beneficial results and that both types of exercise target specific distinct features of frailty, there has been recent interest in whether an intervention with both components is beneficial for frail older adults. In a randomized controlled trial of elderly subjects who had undergone surgical repair of a femur fracture, a 6-month intervention of aerobic activity and progressive resistance exercise was associated with a mean improvement of 19 m/min in walking speed.\(^\text{36}\) Similar changes in motor function were demonstrated in the Lifestyles Interventions and Independence for Elders (LIFE) study, which found that a 12-month program of walking, resistance exercise, and flexibility training improved scores on the Short Physical Performance Battery test and prevented a decline in the 400-m walk speed in older adults at high risk for disability 1 year after follow-up.\(^\text{37}\)

### Effect of Exercise Interventions on the Adverse Outcomes of Frailty

Several studies have examined the effect of exercise on reducing the risk of falls, a common adverse outcome of frailty. After a single fall, the risk of skilled nursing facility placement in older adults increases 3-fold, after adjustment for cognitive, psychological, social, functional, and medical factors.\(^\text{38}\) In a study examining women undergoing resistance training for 25 weeks, risk of falls was reduced by 57% from baseline.\(^\text{39}\) A meta-analysis of 6 studies by Baker and colleagues\(^\text{40}\) showed that a combined regimen of aerobic, resistance, balance, and flexibility exercises was found to decrease fall risk. A Cochrane review of 111 trials found that a combination of aerobic and resistance exercise reduced the risk of falls by 17% in community-dwelling elders.\(^\text{41}\)

In addition to falls, ADL disability is of major concern in frail individuals because it is associated with higher rates of mortality.\(^\text{42}\) In the systemic review of 41 studies conducted by Latham and colleagues,\(^\text{32}\) resistance exercise training did not decrease the risk of ADL disability in an elderly population. In contrast, a Cochrane review of 121 trials found an association between resistance training and reduced ADL disability.\(^\text{33}\) Neither review stratified their results by the severity of frailty. In a randomized controlled trial of a 6-month home-based program that combined resistance exercise training with balance training and home safety and assistive device evaluations, rates of ADL disability decreased only in those with moderate frailty but not in those with severe frailty. Moderate frailty was defined as the inability to either perform a rapid gait test (requiring >10 seconds to walk a 3-m course) or stand up from a chair with arms folded, and severe frailty was defined as having both characteristics.\(^\text{43,44}\) In contrast, Binder and colleagues\(^\text{45}\) did not find an improvement in the Older American Resources and Services ADL score in a group of mild to moderately frail subjects after a regimen of resistance, balance, and flexibility training. At present, final results of the
FRASI (FRAility, Screening and Intervention) are pending: the study observes the effect of an 8-week exercise regimen on the time of onset of ADL disability in community-dwelling frail elders. Table 1 lists key randomized controlled trials that studied frail older adults.

**EFFECT ON THE PHENOTYPE OF FRAILTY**

Although there have been multiple trials studying the effects of exercise on the various characteristics of frailty and the adverse outcomes of frailty, there have been few studies to determine whether exercise can alter or even reverse frailty status in older adults. In a study conducted with subjects who were frail or at high risk for frailty, a telephone intervention encouraging exercise decreased the proportion of frail elders by 18% at 6 months follow-up. At present, the Frailty Intervention Trial is examining whether a 12-month intervention of aerobic and resistance training can change frailty status in a cohort of already frail older adults.

**ADVERSE OUTCOMES OF EXERCISE**

Adverse outcomes with both aerobic and resistance training, although not uncommon, are rarely life threatening. In a study that examined resistance training in elderly women, most of the adverse outcomes were musculoskeletal complaints. Latham and colleagues found that the risk ratio for adverse events increased to 3.6 in those who underwent 10 weeks of resistance training. However, no reports of death or cardiovascular events were found in a systemic review of 62 trials of resistance exercise. In a randomized controlled trial studying the effect of a 12-month intervention of walking, resistance exercise, and flexibility, similar rates of serious and nonserious adverse events were found for both the intervention and control subjects.

**FUTURE DIRECTIONS**

Clearly, exercise and physical activity are promising interventions for frailty, and several studies are underway to examine their effect. However, there are several related areas that need further investigation before this intervention can be disseminated to frail older adults on a widespread basis. First, adherence to an exercise regimen is key to its beneficial effects, and strategies to overcome this barrier need to be developed before exercise as treatment modality is implemented on a wide scale. Schneider and colleagues found that subjects were interested in exercise for its medical and psychological benefits but had concerns about the time required and their ability to perform adequate exercise. In addition, cognition is a factor that should be considered. A significant proportion of older adults are cognitively impaired, which may affect their ability to properly adhere to a regular exercise regimen. However, if caregivers are involved, cognitive impairment may not be such a barrier. In a randomized clinical trial, subjects with Alzheimer dementia participated in a home-based exercise program of aerobic and resistance exercise under the supervision of their caregivers. At 3 months, the subjects with dementia were more active and had better motor functioning compared with the controls. Almost all the trials reviewed in this article were clinic or facility based. Home-based programs are more accessible and eliminate the barrier of transportation for many elders. In a study that examined a 6-month home-based program that combined resistance and balance training with home safety and assistive device evaluations, there was no improvement in motor performance. However, a later Cochrane review did find that home-based exercise programs reduced the risk of falls in older adults by 23%.
<table>
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<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Fiatarone et al, 1994</td>
<td>Nursing home residents 70 y or older and able to walk 6 m</td>
<td>3 sessions per wk of resistance training of lower extremities for 10 wk vs regular recreational activities</td>
<td>Mean improvement in muscle strength of lower extremities was 97% for intervention group compared with 12% for control group</td>
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<td>Chandler et al, 1998</td>
<td>Community-dwelling adults 65 y and older and unable to climb stairs without a handrail</td>
<td>3 sessions per wk of progressive resistance training of lower extremities with stair stepping and chair rises for 10 wk vs normal activities</td>
<td>Mean improvement in muscle strength of lower extremities was 10%–13% for intervention group compared with 1% improvement to 3% decline in control group</td>
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<td>Binder et al, 2002</td>
<td>Community-dwelling adults 78 y and older who had 2 of the following criteria: modified PPT score 18–32, $\text{Vo}_2\text{max}$ 10–18 mL/kg/min, or difficulty with either 1 ADL or 2 IADLs</td>
<td>3 sessions per wk of resistance training of upper and lower extremities; aerobic training with walking, cycling, or rowing; and flexibility/balance training for 9 mo vs flexibility exercises</td>
<td>Mean improvement in lower extremity strength was 19%–23% for intervention group compared with 5% improvement to 5% decline in control group</td>
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<td>Mean $\text{Vo}_2\text{max}$ improved 13% for intervention group compared with 2.6% decline in control group</td>
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<td>Gill et al, 2002</td>
<td>Community-dwelling adults 75 y and older who required more than 10 s to walk 3 m and/or unable to stand up from a chair with arms folded</td>
<td>Average of 16 sessions in the home of resistance training of upper and lower extremities, flexibility and balance exercises, and home safety and assistive device evaluations for 6 mo vs education program</td>
<td>66% improvement in disability scores for those with moderate frailty but no significant improvement for those with severe frailty in intervention group, using control group as baseline</td>
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*Abbreviations: IADLs, instrumental activities of daily living; PPT, Physical Performance Test.*
Also, whether these exercise interventions would require supervision by a rehabilitation professional or could be conducted in the community is still unclear. If supervision is necessary, this adds to the cost of the intervention. Future and ongoing trials should include an analysis of the costs and benefits of a physical activity intervention.

SUMMARY: AN EXERCISE “PRESCRIPTION”

Although more investigation is still needed, most studies suggest that clinicians should recommend regular physical activity or exercise training to frail older adults. The current guidelines from the US Department of Health and Human Services state that all adults older than 65 years should participate in 150 minutes (ie, 2.5 hours) of moderate aerobic exercise per week. Although most trials studied resistance exercise training, frail older adults are encouraged to start with an aerobic activity, such as walking, as it is more accessible. If possible, resistance exercise training should be added. Depending on the degree of frailty, supervision may or may not be required. For individuals with severe frailty, evaluation by a rehabilitation professional is recommended.

Most evidence shows that regular physical activity or exercise is beneficial for older adults who are frail or at high risk of frailty. Studies have shown that the number of adverse events is minimal and the gains of regular exercise clearly outweigh the risks. Although there are still several areas related to the intervention that require further investigation, regular physical activity or exercise is highly recommended for older adults as a means to modify frailty and its adverse outcomes.

REFERENCES


