Can Progressive Resistive Exercise Improve Weight, Limb Girth, and Strength of Individuals With HIV Disease?

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<LEAP> highlights the findings and application of Cochrane reviews and other evidence pertinent to the practice of physical therapy. The Cochrane Library is a respected source of reliable evidence related to health care. Cochrane systematic reviews explore the evidence for and against the effectiveness and appropriateness of interventions—medications, surgery, education, nutrition, exercise—and the evidence for and against the use of diagnostic tests for specific conditions. Cochrane reviews are designed to facilitate the decisions of clinicians, patients, and others in health care by providing a careful review and interpretation of research studies published in the scientific literature.

Each article in this PTJ series summarizes a Cochrane review or other scientific evidence on a single topic and presents clinical scenarios based on real patients or programs to illustrate how the results of the review can be used to directly inform clinical decisions. This article focuses on an adult patient with human immunodeficiency virus (HIV) disease. Could a physical therapist–guided progressive resistive exercise (PRE) program improve body weight, body composition, and strength in an individual with HIV disease?

Human immunodeficiency virus (HIV) disease is caused by infection with the HIV retrovirus. If untreated, HIV infection results in progressive immune suppression and subsequent opportunistic infections that are the cause of death in most cases of untreated HIV disease. Advanced HIV disease is known as acquired immunodeficiency syndrome (AIDS). Advances in medical treatment with highly active antiretroviral therapy (HAART) and prevention efforts have led to substantial declines in new cases and AIDS-related deaths since the late 1990s. Many patients who access and adhere to long-term use of HAART can achieve a normal life expectancy. However, the complexity of the disease and potential side effects of HAART make successful disease management a challenge for many individuals. Increased longevity in the HAART era has been mirrored by an increase in comorbidities and episodic disability experienced by some individuals. Disability associated with HIV disease can be exacerbated or ameliorated by extrinsic factors such as social support and stigma and by intrinsic factors such as coping strategies and lifestyle choices.

Human immunodeficiency virus wasting syndrome is an involuntary loss of body weight of more than 10% of baseline weight associated with HIV infection. HIV-associated lipodystrophy is a metabolic disorder associated with morphological alterations, including loss of peripheral subcutaneous fat (lipodystrophy), accumulation of central visceral (intra-abdominal) fat, and fat in the dorsal cervical thoracic region (lipohypertrophy). Metabolic changes include dyslipidemia, glucose intolerance, insulin resistance, hypertension, and altered adipocyte function. HIV-associated lipodystrophy is associated with HAART regimens that include nucleoside reverse transcriptase inhibitors and protease inhibitors, although other mechanisms may be involved.

As a result of the comorbidities associated with HIV disease and related phenomena such as loss of lean muscle mass and pain, individuals often attenuate their activities, which may further reduce activity tolerance and quality of life. Exercise may be used to address many of the impairments and changes in body composition that are sometimes seen in individuals with HIV disease. Progressive resistance exercise (PRE) involves strengthening of muscle through the overload principle via activities such as isotonic or isometric exercise and typically involves weight training. In contrast, aerobic exercise—such as walking, jogging, stair climbing, or swimming—is primarily used for cardiopulmonary benefits. Both forms of exercise (PRE and aerobic) may have beneficial effects on general health and fitness, functional capacity, and psychological outcomes.

O’Brien et al7 performed a Cochrane systematic review to determine the effects of PRE in adults (18 years of age or older) living with HIV disease (Table). They included randomized controlled trials published up to August 2003 that compared PRE or a combination of PRE and other exercise with either no PRE or another exercise or treatment modality.
defined as a regimen containing physical resistive activity performed at least 3 times per week for at least 6 weeks. Interventions could include, but were not limited to, weight training and isotonic and isometric strengthening exercises. The following outcomes were considered: weight, body composition, strength, immunological and virological indicators, cardiopulmonary measures, psychological measures, and safety.

The review included 7 trials involving a total of 294 participants. Six of the 7 trials included only men, and 1 trial included only women. The ages of the participants ranged from 18 to 66 years, and CD4 counts ranged from less than 100/mm³ to greater than 1,000/mm³. In trials published after 1995, most of the participants were undergoing HAART. Five trials assessed PRE alone, and 2 trials assessed PRE combined with aerobic exercise. Five trials included a nonexercise control group. The PRE interventions in the trials included a combination of resistance training of major muscle groups in the upper and lower body for approximately 20 to 25 minutes, ranging from 1 to 5 sets of 4 to 18 repetitions 3 times per week for 6 to 16 weeks. Exercise intensity ranged from 50% to 90% of a 1-repetition maximum (1-RM) or minimum-maximum setting of a hydraulic resistance training unit. Aerobic intensity, included in some of the studies of PRE, ranged from 60% to 70% of maximum oxygen consumption or 60% to 80% of submaximal heart rate.

Take-Home Message
Based upon 2 trials that compared PRE or a combination of PRE and aerobic exercise with no exercise, there was also a significant benefit favoring PRE in increasing body weight (WMD=3.54 kg; 95% CI=2.21, 4.87). Based upon 2 trials that compared PRE or a combination of PRE and aerobic exercise with no exercise, PRE also resulted in a clinically relevant improvement in mean arm and leg girth (WMD=7.91 cm; 95% CI=2.18, 13.65). The review authors considered improvements in body weight and limb girth to be of clinical importance.

Progressive resistive exercise also may result in clinically important improvements in cardiopulmonary fitness, and, based upon the results of individual studies, PRE with or without aerobic exercise also may improve strength and psychological status. Based upon a lack of reported adverse events attributed to exercise within the individual studies as well as the stability of CD4 count and viral load, PRE with or without aerobic exercise also appears safe. Importantly, these results were limited to those who continued to exercise and for whom there were adequate follow-up data.

Limitations of the review include the small size of included trials, heterogeneity in the tested interventions and the reported outcomes, and high withdrawal and nonadherence rates. In addition, longer-term effects (beyond 16 weeks) remain unknown. Although O’Brien et al have not updated their Cochrane review with literature published after August 2003, 3 additional trials published since that time and described by O’Brien et al in AIDS Care do not alter the main conclusions of the earlier review.12

Case #22: Applying Evidence to a Patient With HIV
Can a PRE program benefit this patient?
“Mr Lindy” is a 45-year-old man diagnosed with HIV in 2005. He has been stable and on HAART for 6 years but has experienced changes in body mass (associated with wasting syndrome and lipodystrophy) and generalized weakness. Prior to his diagnosis, he lifted weights and jogged 3 or 4 times per week. Social activities include coaching his son’s soccer games and volunteering with the local homeless shelter. He is employed full-time as a construction worker, and his job duties require significant lifting, carrying, and physical exertion. He is right-handed and has no prior history of trauma or surgery.

Mr Lindy was seen for physical therapy as he was recovering from a pulmonary infection in 2005. The current referral is related to his complaint of generalized weakness. Upon initial examination, Mr Lindy’s height was 175 cm (5 ft 9 in), and he weighed 72.6 kg (160 lb). His waist-to-hip ratio was 1.2. This value is indicative of truncal obesity and corresponds with his diagnosis of lipodystrophy.13 There was mild buccal fat loss observed in his face and a visible loss of subcutaneous fat and muscle mass in the extremities.14 The baseline examination revealed that Mr Lindy’s strength was 4/5 throughout and that his neurological status was unremarkable. Knee range of motion (flexion and extension) was within normal limits. Flexibility testing revealed hamstring muscle tightness bilaterally (65° knee with 90/90 test). Grip strength was 43.1 kg (95 lb) on the right and 39.9 kg (88 lb) on the left. Handheld dynamometry for the quadriceps muscles was 47.6 kg (105 lb) bilaterally. Single-repetition
Table.
Progressive Resistive Exercises for Patients With Human Immunodeficiency Virus Disease: Summary of Cochrane Review

- 7 randomized controlled trials from 1990 to 2001 (search date 1980–August 2003); study duration ranged from 6 to 16 weeks; ages of the 294 participants ranged from 18 to 66 years.

- Participants were diagnosed with HIV disease; CD4 counts ranged from <100 to >1,000 cells/mm³. Two studies reported that most participants were undergoing antiretroviral treatment. Due to the evolution of antiretroviral therapies over the years that the studies were conducted, there was variance in the forms of antiretroviral therapy across studies. Because antiretroviral therapy has been in use as a life-sustaining treatment since 1985, it is plausible that most participants in all reviewed studies were undergoing antiretroviral therapy.

- Studies compared PRE with no PRE or another intervention. Some studies included aerobic exercise or other interventions (testosterone, whey protein supplements, metformin, oxandrolone) as part of the PRE program.

- PRE programs involved resistance exercise at least 3 times per week for at least 6 weeks.

- All trials used randomization, with only 4 describing the randomization process. No studies were double-blinded because the intervention was exercise. Blinding of testers was described in 2 studies. One study did not report on participants who withdrew or were nonadherent. Five studies reported that comparison groups were similar at baseline.

- 6 meta-analyses were performed for outcome measures that included immunological status, cardiopulmonary status, weight, and extremity girth. The meta-analyses yielded evidence for increases in weight and extremity girth, with possible trends toward improved CD4 counts and maximal heart rate. Findings were limited to individuals who continued to exercise.

- Body weight: mean difference was 4.24 kg (95% CI = 1.82, 6.66), favoring PRE, in a meta-analysis of 2 studies that compared PRE with a nonexercise control intervention. Mean difference was 3.54 kg (95% CI = 2.21, 4.85), favoring PRE, in a meta-analysis of 3 studies that compared PRE or combined PRE and aerobic exercise with a nonexercise control intervention.

- Mean arm and leg girth: mean difference was 7.91 cm (95% CI = 2.18, 13.65) favoring PRE, in a meta-analysis of 2 studies that compared PRE or combined PRE and aerobic exercise with a nonexercise control intervention.

- CD4 count: mean difference was 48.32 cells/mm³ (95% CI = 95% CI = −2.28, 9.25), with a possible trend toward favoring PRE, in a meta-analysis of 3 studies that compared PRE or combined PRE and aerobic exercise with a nonexercise control intervention. Mean difference was 31.96 cells/mm³ (95% CI = 95% CI = 29.34, 23.48), with a possible trend toward favoring PRE, in a meta-analysis of 2 studies that compared combined PRE and aerobic exercise with a nonexercise control intervention.

- Maximum heart rate: mean difference was −13.02 bpm (95% CI = −26.67, 0.64), with a trend toward favoring PRE, in a meta-analysis of 2 studies that compared PRE or combined PRE and aerobic exercise with a nonexercise control intervention.

- Individual studies showed favorable effects on strength, psychological status, and body composition.

  Strength: although all 7 studies reported strength outcomes, a meta-analysis was not performed for any strength measurements because of differences in strength outcome measurements and types of participants. Six of the 7 individual studies reported significant increases in strength outcome measures.

  Psychological status: 1 of the 3 individual studies reported significantly favorable changes in health-related quality of life in the PRE intervention group. Another of the 3 individual studies showed higher positive mood and lower negative mood.

  Body composition: 6 individual studies reported a variety of body composition outcomes and showed improvements in the PRE or combined PRE and aerobic group. The variables included lean body mass, muscle area, muscle volume, fat free mass, and body cell mass.

- Across studies, PREs appeared to be safe for individuals with HIV disease who are medically stable.

- Limitations: the results of the review were based on a small number of studies with small sample sizes of mostly male participants between 18 and 66 years of age. There were often high withdrawal or nonadherence rates. There was variance in the parameters of the interventions, participants, and outcome measures. Inability to blind participants may have resulted in a Hawthorne effect. Long-term effects (beyond 16 weeks) remain unclear.

* PRE = progressive resistive exercise, 95% CI = 95% confidence interval, HIV = human immunodeficiency virus.

How did the physical therapist apply the results of the Cochrane systematic review to Mr. Lindy?

Both Mr. Lindy’s infectious disease physician and his physical therapist questioned whether he would be a good candidate for a PRE program because of his HIV-related comorbidities. For individuals with HIV disease, it is important to establish exercise guidelines through the trajectory of treatment because changes in strength and functional status due to the emergence of comorbidities may occur. Mr. Lindy fits the description of the type of patients enrolled in some of the studies included in the 2004 Cochrane review. Using the PICOT (Patient, Intervention, Comparison, Outcome) format, the clinicians asked the question: "In a 45-year-old man with wasting syndrome, HIV-associated lipodystrophy, and com-

maximum strength test was 54.4 kg (120 lb) for the chest press and 68.9 kg (152 lb) for the leg press. Mid-arm muscle circumference was 34.5 cm bilaterally, and mid-thigh muscle circumference was 46 cm bilaterally. The patient’s Lower Extremity Functional Scale (LEFS) score was 66/80, which suggests mild loss of function (LEFS score range = 0–80; full function = 80).
plaints of generalized weakness, will a PRE regimen (as compared with a nonexercise regimen) be beneficial for improving strength and body composition? They determined that 3 of the 7 studies reviewed by O’Brien et al7 included patients with wasting syndrome. One study in the meta-analysis of body weight included participants with wasting syndrome.15 The review does not specifically describe whether participants with lipodystrophy were included in the reviewed studies.7

Mr Lindy was prescribed an outpatient PRE program 3 times per week for 4 weeks. The PRE program utilized free weights and machines for all major muscle groups. He performed 3 sets of 10 to 15 repetitions of each of the 9 different exercises (chest press, overhead shoulder press, upright rowing, biceps muscle curls, triceps muscle extension, knee extension, knee flexion, leg press, and calf raises). Resistance was increased by appropriate increments for any given exercise if he was able to complete 15 repetitions. He completed 11 of 12 PRE sessions. The exercise sessions also included flexibility exercises for his tight hamstring muscles.

How well do the outcomes of the intervention provided to Mr Lindy match those suggested by the systematic review?

Mr Lindy completed 11 of the 12 prescribed sessions. Upon re-examination following the exercise sessions, his hamstring muscle flexibility remained unchanged. Overall strength improved to 5/5. Mr Lindy increased his body weight by 3.1 kg (to 75.7 kg), which is consistent with the body-weight gains in groups that performed PRE (weight gains in PRE groups ranged from 1.7 to 3.2 kg).7 His waist-to-hip ratio improved to 0.95, indicative of a reduction in truncal obesity. Mid-arm muscle circumference improved by 5 cm (to 39.5 cm bilaterally); mid-thigh muscle circumference improved by 4.9 cm (to 53.9 cm bilaterally), which is consistent with the reported girth gains (ranging from 3.5 to 5.19 cm) in groups that performed PRE.7 Grip strength improved to 47.6 kg (105 lb) on the right and 44.9 kg (99 lb) on the left. Hand-held dynamometry measurements for the quadriceps muscles improved to 54.4 kg (120 lb) bilaterally. Single-repetition maximum test values improved to 61.2 kg (135 lb) for the chest press and to 77.1 kg (170 lb) for the leg press. Mr Lindy’s strength gains are consistent with findings of some of the individual studies in the review; however, direct comparisons cannot be made because of the variability in strength outcome measures in the studies included in the review. Mr Lindy’s LEFS score improved to 76/80, surpassing the minimal detectable change score of 9 for this instrument,16 thus indicating clinical improvement in lower extremity function in this patient.

Can you apply the results of the systematic review to your patients?

The results of this study apply to adults living with HIV disease who are medically stable to perform exercise. However, several of the studies included in the review were conducted prior to 1995 (ie, prior to the era of triple-combination antiretroviral therapy). Thus, more research is needed to further elucidate the effects of PRE on individuals such as Mr Lindy who have lipodystrophy and are currently undergoing triple combination antiretroviral therapy. However, we observed that Mr Lindy’s weight and limb girth improvements were consistent with the results reported in the review. Types of therapeutic exercise used in trials in the review included gradual stretching and strengthening or resistance exercises. The results apply to patients in home-based and supervised exercise programs. In addition, a 2010 Cochrane review of the effects of aerobic exercise for adults living with HIV disease showed that performing aerobic exercise (or a combination of aerobic exercise and PRE) for at least 20 minutes, at least 3 times per week for at least 5 weeks, appears to be safe and may improve fitness, body composition, and well-being.17 The results of the review of aerobic exercise also apply to patients like Mr Lindy. Although the focus of this LEAP article was on PRE, the inclusion of combined PRE and aerobic programs in the Cochrane review of PRE and the conclusions of the Cochrane review on aerobic exercise in this population suggest that aerobic exercise should be considered in the plan of care for patients like Mr Lindy.

What can be advised based on the results of this systematic review?

The Cochrane review demonstrates that targeted PRE may result in improvement in body composition and strength in patients with HIV disease.7 A more recent review by the same authors in AIDS Care that included 3 more recent trials also reached the same conclusion.11 Current evidence indicates structured PRE or aerobic exercise programs are beneficial and safe for individuals with HIV disease who are medically stable.7,17 Further research is needed to explore exercise prescription factors such as intensity and duration and to further clarify the effects of exercise on strength, function, and quality of life. Emerging research in the treatment of HIV episodic disability should include contemporary models of care that proactively target HIV-related disabilities.12
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