

## Exercise for Adults Living with Human Immunodeficiency Virus Infection in the Era of Highly Active Antiretroviral Therapy

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### Abstract

Human Immunodeficiency Virus (HIV) infection is now considered a chronic, long-term disease, potentially affecting all body systems and causing disturbances in functional status. Beside the immune system, the cardiovascular, neuromuscular, and musculoskeletal systems are three of the body systems most affected by HIV and/or its treatment. With these systems affected, mobility and functional activities can be limited in people with this chronic infection. Aerobic and resistive exercise programs have improved bodily function, Health Related Quality of Life (HRQoL), and increased participation in daily life activities of individuals living with HIV. Rehabilitation professionals involved in the treatment of people living with HIV infection must consider exercise prescription or promotion of an active lifestyle as part of their routine clinical evaluation and management. The purpose of this review is twofold: 1) provide rehabilitation clinicians a summary of the effects of exercise on the cardiovascular, neuromuscular, and musculoskeletal systems of adults infected with HIV and 2) discuss the short and long-term benefits of regular aerobic and/or resistive exercise in this population.

**Keywords:** Exercise for adults; HIV infection; Antiretroviral therapy

### HIV and Physiological Impairments

### Introduction

Today, the Human Immunodeficiency Virus (HIV) infection is considered a chronic, episodic, long-term, manageable disease with periods of exacerbation and remission of symptoms [1,2]. The transition from an acute-terminal disease to one that is chronic is the result of advances in treatment since the initial detection of the HIV virus during the early 1980's [1,3,4]. The profile of HIV infection has changed dramatically with the advent of highly active antiretroviral therapies (HAART) [5]; a combination of three or more potent medications that can interrupt the formation of the virus at different points in the lifecycle of the virus and preserve and/or restore immune function [1].

Since the introduction of HAART in the 1990's, people diagnosed with HIV have a greater life expectancy [3,6]. This therapy has significantly decreased morbidity and mortality associated with HIV infection [3,6]. Yet, these therapeutic advances have produced a myriad of health problems and impairments such as muscle wasting [1,7], lipodystrophy [1], and peripheral neuropathies [7] affecting functional activities of daily living and quality of life of these patients [2,3,7]. The purpose of this review are twofold: 1) provide rehabilitation clinicians a summary of the effects of HIV infection on the cardiovascular, neuromuscular, and musculoskeletal systems, and 2) discuss the short and long-term benefits of regular aerobic and/or resistive exercise in this population documented in the last ten years. After reading this review the clinician should: 1) recognize how HIV affects different body systems, 2) recognize physical impairments encountered by individuals diagnosed with HIV, and 3) understand how aerobic and resistive exercise could improve bodily functions and quality of life of these individuals.

The introduction of HAART has increased longevity of individuals living with HIV, but at the same time it has been associated with a new constellation of health problems and physical impairments, such as muscle wasting or sarcopenia and peripheral neuropathies that greatly affect functional activities [2,4,8-11]. Functional limitations and disability within this population is a consequence of the disease itself, and the secondary effects of HAART [2].

Impairments of the cardiovascular and neuromusculoskeletal system affect mobility and participation in daily activities [12]. Lipodystrophy, peripheral neuropathy, myopathies, disturbed balance, unsteady gait, and fatigue are among the most common cardiovascular and neuromusculoskeletal illnesses in adults with HIV [12,13]. Lipodystrophy is a syndrome associated with physical and metabolic changes [12,14] characterized by a reduction in subcutaneous fat in the face, arms, and buttocks (lipoatrophy), an increment in visceral fat and fat accumulation in the back, neck, and chest areas (lipohypertrophy) [2] or both with or without changes in body weight [12]. This syndrome might result in diminished functional capacity [12] and have detrimental effects on the patient's health [14]. For example, lipodystrophy has been associated with dyslipidemia or abnormal lipid metabolism [15], and dyslipidemia has been associated with hyperglycemia, glucose intolerance, and insulin resistance [1]. The occurrence of these metabolic abnormalities, which are known to increase the risk of cardiovascular diseases, have been associated with the use of HAART [1]. In addition, cardiac abnormalities impairing left ventricular function and affecting oxygen delivery to the working muscles have been reported in patients with HIV infection using HAART [1]. Other cardiovascular complications such as myocardial infarction and strokes have also been reported in patients who are receiving HAART [14]. However, the cause and effect relationship between HIV infection, HAART, and the occurrence of these

pathologies remains unclear because of lack of strong empirical evidence [1,2,12].

Peripheral neuropathies primarily affect sensory nerves causing balance impairments and gait difficulties due to numbness, burning sensation, and paresthesias of feet and lower extremities [12]. Neuropathic pain caused by peripheral neuropathy is one of the most recurrent painful conditions in patients with HIV infection [12]. The more frequent type of peripheral neuropathy is the distal symmetric polyneuropathy that usually occurs when CD<sub>4</sub> levels fall to less than 190 cells/mm<sup>3</sup> [16], causing numbness, burning sensation, and paresthesias mostly in the distal sensory nerves [12]. These sensory alterations in the lower extremities are likely to induce balance disturbances and gait deviations that may create impaired gait-related biomechanics [12]; thus, increasing the risk of falls in this population. Hence, unsteady gait and disturbed balance should be considered amongst the most common clinical signs of nervous system deterioration [17-19].

Myopathies are general non-specific disorders of the musculoskeletal system presenting with generalized muscle pain and progressing muscle weakness [1,12]. Myopathies are also related with weakness of proximal muscles [1,7], limited oxygen perfusion in the extremities during exercise, and increased risk of lactic acidosis, fatigue [1,20] breathlessness [7], and diminished muscle function [1]. This condition might appear in any stage of the HIV infection [20], causing pain and slow [12] but progressive muscle weakness [2,20]. Myopathies also induce a higher energy expenditure [2], diminished functional capacity, and impaired glucose uptake [1], all of which limit activities of daily living.

Fatigue is one of the most frequent and debilitating complaints in people diagnosed with HIV [9,11]. The causes of fatigue remain unclear [11] although structural changes within the muscles fibers may contribute to the onset of fatigue [10]. Complications of fatigue related disorders predisposes individuals living with HIV infection to physiological deconditioning, increased activity intolerance, and further restriction of participation in daily activities [1]. Given that people with HIV usually have greater disabilities than the general population, therapeutic interventions for this population must be implemented to address physical impairments, functional limitations, and disturbances associated with the progression of the disease [3,12]. In summary, the combination of these complications predisposes men and women living with HIV to physiological deconditioning, activity intolerance, and further restrictions of participating in daily life activities, social and leisure activities [1]. Therefore, today's treatments for this population should not only take into consideration the immune-physiological aspects of the disease, but also the functional limitations and disabilities associated with the progression of the disease [12].

### Role of Rehabilitation Professionals

Rehabilitation professionals have the ability to impact a vast number of domains including body structure, function and activity, and participation; thus improving quality of life. The goals of rehabilitation in patients with HIV should include maintenance, restoration, and enhancement of their physical and mental health, well-being and quality of life [3]. An important role of the interdisciplinary rehabilitation team should be to implement interventions addressing functional limitations and disability that occurs as consequence of HIV infection and antiretroviral treatment

[12]. Rehabilitation professionals could contribute significantly in the treatment of neuromusculoskeletal system comorbidities such as neuropathies and myopathies by designing and implementing therapeutic interventions to help improve balance, reduce pain, improve gait disorders, and decrease fatigue. As part of the prevention and promotion of health and wellness, rehabilitation professionals could help prevent further physical deterioration and reduce the need for future more intense clinical care and possible institutionalization [21].

### Exercise and HIV

Progressive resistive and aerobic exercise programs have not only effectively improved cardiopulmonary fitness [2,4], strength [2,4], body composition [2,4,22], and decrease fatigue [23], but also have improved quality of life and perception of well being in people living with HIV who participate in regular exercise programs [5,24]. This is an important aspect of health because adults living with HIV face a multitude of stressful life events including deterioration of health status, alienation from others, possible loss of employment, financial insecurity, and impaired expectancy of social roles [25]. These events may potentially have a negative impact at all levels of participation in meaningful life activities. Activities of daily living, and the ability to perform complex roles such as maintaining employment, attending school, and carrying out household activities are within the most affected limitations in society participation [26]. Due to the chronic nature of the disease, and the potential impact of musculoskeletal and cardiovascular impairments on activity performance and participation in daily life activities, a greater number of patients diagnosed with HIV infection are and will be requiring therapeutic exercise interventions [6]. A patient with a higher functional capacity is less prone to long-term disability, institutionalizations, and more likely to have better quality of life [21]. In addition, therapeutic exercise interventions might help reduce the need of more expensive forms of health care [21]. However, in order to treat functional disabilities, rehabilitators must know how to implement exercise interventions to improve functionality and health-related quality of life in patients living with HIV infection [3,6]. Although there are limited guidelines for the prescription of exercise interventions or defined contraindications to exercise for this population [27,28], it is alleged that through specific and individualized aerobic and resistance exercises or therapeutic exercises, these patients can improve their physical fitness, psychological status, and overall quality of life; which will ultimately lead to a better functional capacity and independence [7]. However, rehabilitation professionals are still faced with the challenge of determining the outcomes of exercise interventions on activity performance and participation.

The American College of Sports Medicine (ACSM) provides the following recommendations (Table 1) for exercise prescription in adults living with HIV infection [28,29]. ACSM recommends that aerobic exercises should be performed 3-4 days per week at an intensity of 40-60% of the VO<sub>2</sub> reserve or heart rate reserve for a total of 30-60 minutes per day. They also recommend that strengthening exercises should be performed 2-3 days per week with a resistance that can be lifted 8-10 times involving 10-12 muscle groups in 2-3 sets (80% of 10RM; 60% 1RM) [30,31]. ACSM also suggests that more vigorous exercise could be prescribed for asymptomatic patients but exercise should be supervised if there are HIV/AIDS related comorbidities. This suggestion is based on the possible side effects and interaction among of all medications to manage HIV infection and

comorbidities [29]. For example, high intensity exercise or lack of exercise exposure have shown to decreased adherence to exercise programs [30-33] due to side effects of medications such as nausea and vomiting [30]. Although, some health care providers are timorous in

prescribing exercise for individuals with a diagnosis of HIV/AIDS given initial reports of the possibility of exercise and impairments in immune function [34], more recent data have shown benefits in immune function following exercise [22,35-38].

Type	Modality	Intensity	Duration	Frequency	Goals
Aerobic Endurance	Walking, Jogging, Running, Bicycle, Elliptical trainer	40%-60% VO <sub>2</sub> or heart rate reserve	30-60 min/day 150min/wk	3-5 days/wk	↑ aerobic fitness
Resistance Strength Training	Machine, free weights, resistance bands	60% of 1RM or 80% 10RM	6-8 exercises divided in 2-4 sets with 8-10 repetitions per exercise	2-3 days/wk	↑ strength of major muscles groups such as pectorals, back extensors, latissimus dorsi, elbow flexors, quadriceps, hamstrings, calf muscles.
Flexibility Range of Motion	Static stretching, Yoga, Pilates, Dynamic stretching	Comfortable stretch	Each stretch should be at least 30 seconds	3-5 days/wk before and after aerobic and/or strengthening exercises	Maintain muscle elasticity and range of motion

**Table 1:** Exercise Prescription Summary for Individuals with HIV [30,31].

Studies have demonstrated that aerobic training, resistance training, or the combination of both help improve cardiopulmonary function, increase muscle mass and strength, improve flexibility, reduce depression and anxiety, and improve health related quality of life (HRQoL) in individuals living with HIV [1,3,6,20,22-24]. In addition, it has been demonstrated that progressive resistance and moderate aerobic exercises are safe and beneficial for people living with HIV infection during any stage of the disease [7,13,22]. Progressive resistance training programs have been effective in improving physical fitness and reducing upper and lower limb skinfolds in old adults living with HIV infection without causing significant side effects [22,39]. However, high intensity exercises for prolonged periods of time without an adequate amount of rest potentially increases infection severity and negatively affects immune responses [13,34,36,40]. One study [23] assessed the effectiveness of a 16-week supervised home-based aerobic, progressive aerobic and resistance program on strength, cardiopulmonary fitness, and body composition in 40 women infected with HIV randomized into a control and intervention group. The intervention comprised of cardiopulmonary fitness training in a cycle ergometer and a strengthening component. The intensity for the cardiopulmonary component was established at a 50% of estimated maximal heart rate. The intensity for the strengthening component was established at 60% 1RM for the first two weeks and progressed to 75% thereafter. The program was carried out three times per week for 16 weeks with each session consisting of two hours. A submaximal endurance test in a cycle ergometer was performed to assess cardiopulmonary endurance. Results showed that a combination of aerobic and resistive exercise improves aerobic capacity, endurance, strength and body composition in women infected with HIV [23].

In another randomized controlled trial, the effectiveness of a 24-week supervised aerobic and resistive exercise program in 40 men infected with HIV was assessed [6]. Subjects were randomized into a control group or a supervised aerobic and resistance training program conducted twice a week in a hospital-based facility. The control group participated of an unsupervised walking program whilst the exercise group performed 20 minutes of aerobic exercise using a treadmill, cycle ergometer, stepper or a cross-trainer starting at an intensity of 60% maximum heart rate (MHR) progressing towards 75% MHR as

participants improved cardiorespiratory fitness. The strengthening component consisted of a combination of machines and free weight resistive exercises starting at an intensity of 60% 1RM gradually progressing to 80% 1RM. Results showed that men infected with HIV who participate regularly in a structured and supervised aerobic and strength-training program improve their self-efficacy, cardiovascular fitness and HRQoL [6]. The changes observed in these two studies suggest that exercise interventions might help improve quality of life and body image, and regulate metabolic indexes. Recently it was reported that men and women improved their fitness profile by participating three times a week for 9 months in a community-based exercise program comprising of an aerobic, strengthening, and balance components [22].

## Conclusion

A clear understanding of the effects of HIV infection and HAART will give the rehabilitation professional better tools to manage physical impairments and disabilities in patients who encounter limitations in their activities of daily living. Aerobic and strengthening exercises are an effective intervention to reduce the impact of physical impairments related to HIV infection and secondary effects of HAART that affect quality of life and participation in society. Table 1 compiles the foundations of exercise prescription for this population. However, there is still a need for evidence evaluating the impact of exercise interventions in improving activity performance and participation in meaningful activities in this population. This will require an interdisciplinary approach to better meet the complex needs of individuals living with HIV.

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