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Exercise Therapy for Acquired Immune Deficiency Syndrome (AIDS) Patients

Jeanne M. Grace

Abstract

Background: Highly active antiretroviral therapy (HAART) has reduced mortality and morbidity in HIV-infected patients and transformed HIV infection from an acute to a chronic disease, not only increasing the life expectancy but also adding to the potential side effects associated with drug therapy. Exercise has been fused as an important adjuvant therapy and can play a valuable role in the management of health in HIV/AIDS patients.

Methods: EBSCOhost, Science Citation Index, CINAHL database, PsycINFO, Cochrane Database of Systematic Reviews, Physiotherapy Evidence Database, and SPORTDiscus were searched between 1996 and May 2016. Searches of published and unpublished abstracts were conducted, as well as a hand search of reference lists and tables of contents of relevant journals and books were conducted. A total of 60 studies met the inclusion criteria.

Results: Most studies failed to indicate the optimum type (mode), intensity, frequency, and duration of aerobic exercise (AE), progressive resistive exercise (PRE), and a combination of AE and PRE (CARE) prescribed to HIV-infected individuals in relation to the different clinical stages of the disease.

Conclusion: The findings provide information that clarifies the optimal mode, duration, frequency, and intensity of AE, PRE, and CARE prescribed to the different clinical stages of HIV patients. The exercises recommended have the potential to benefit HIV patients and should be adopted by clinical exercise therapists.

Keywords: aerobic exercise, CD4 count, highly active antiretroviral therapy, immunodeficiency, progressive resistive exercise
1. Introduction

Medical advances in the treatment of the HIV disease with highly active antiretroviral therapy (HAART) converted HIV infection into a chronic condition that has been related to several comorbidities [1], disability, impairment in daily activities, and decreased exercise capacity [2, 3]. Increased longevity in the HAART era has dramatically reduced mortality and morbidity of HIV-infected patients [4, 5]. Although HAART has dramatically reduced the prevalence of the wasting syndrome and immunosuppression in HIV patients [6], HAART is associated with anthropometric and metabolic conditions including insulin resistance, dyslipidemia, and abnormal distribution of body fat [5, 7, 8].

Exercise is a key management strategy employed by rehabilitation health professionals for health promotion and rehabilitation of patients with HIV/AIDS [9, 10]. Exercise has the potential to ameliorate a range of side effects associated with HIV infection, as well as the cardiometabolic and morphological complications (i.e., mitochondrial dysfunction, inflammation, and oxidative stress) that may accompany HAART. A large body of scientific evidence suggests that exercise can delay the progression of the disease, improve quality of life [11, 12], improve aerobic capacity [3, 9, 13], improve functional ability [14], have beneficial effects on insulin resistance and diabetes [15], improve oxidative stress [13, 16], improve muscle strength [9, 17], improve lipid profile [13, 18], and reduce the risk of cardiovascular disease [1, 19] in people with HIV infection. Of importance is that exercise is generally regarded as safe and there is no evidence to suggest that regular exercise will suppress immune function in asymptomatic and symptomatic individuals with HIV/AIDS [10, 20]. Exercise training, however, apparently confers no beneficial effect on HIV status and viral load [20, 21].

Exercise studies in HIV/AIDS patients indicate that aerobic exercise (AE) [19, 20] and progressive resistive exercise (PRE) [22] improve various health indices in HIV-infected patients with a combination of aerobic and progressive resistive exercise (CARE) more effective than applying only one component [10]. CARE has recently been employed and recommended by the American College of Sports Medicine [23].

2. HIV disease stages and classification

It is of critical importance to recognize HIV disease stages and classification systems not only for tracking and monitoring the HIV epidemic but also for providing clinicians and patients with important information about the clinical management of the disease. Clinical exercise therapists should therefore consider the HIV disease stages as well as the varying needs during each stage in order to adjust the exercise prescription (Ex Rx) accordingly. Two major classification systems currently are in use: The World Health Organization Clinical Staging and Disease Classification System and the US Centres for Disease Control and Prevention (CDC) classification system [24]. The WHO Clinical Staging and Disease Classification System are used in resource-constrained settings without access to CD4 cell count measurements or other diagnostic and laboratory testing methods whereas the CDC disease staging system assesses
the severity of HIV disease by CD4 cell counts and by the presence of specific HIV-related conditions. The CDC disease staging system should be used because it incorporates the CD4 cell count categories; knowledge of which is important for the clinical exercise therapist because this may dictate changes in Ex Rx.

The CDC categorization of HIV/AIDS is based on the lowest documented CD4 cell count and on previously diagnosed HIV-related conditions (Table 1).

<table>
<thead>
<tr>
<th>CD4 cell count categories</th>
<th>Clinical categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) ≥500 cells/μL</td>
<td>A1</td>
</tr>
<tr>
<td>(2) 200–499 cells/μL</td>
<td>A2</td>
</tr>
<tr>
<td>(3) &lt;200 cells/μL</td>
<td>A3</td>
</tr>
<tr>
<td>A</td>
<td>Asymptomatic, acute HIV, or PGL</td>
</tr>
<tr>
<td>B*</td>
<td>Symptomatic conditions, not A or C</td>
</tr>
<tr>
<td>C#</td>
<td>AIDS-indicator conditions</td>
</tr>
</tbody>
</table>

Abbreviations: PGL = persistent generalized lymphadenopathy

* Category B Symptomatic Conditions - Consult the AIDS Education and Training Centre [24].
# Category C AIDS-Indicator Conditions - Consult the AIDS Education and Training Centre [24].

Note: Reprinted with permission from AETC.

Table 1. CDC classification system for HIV-infected adults and adolescents [24].

For example, if a patient had a condition that once met the criteria for category B but now is asymptomatic, the patient would remain in category B. Additionally, categorization is based on specific conditions, as indicated by the AIDS Education and Training Centre [24]. Patients in categories A3, B3, and C1-C3 are considered to have AIDS [24]. The AIDS Education and Training Centre (AETC) can be referred to for a detailed account of the symptomatic conditions for the different clinical categories [24].

3. Pre-exercise evaluation/testing

HIV/AIDS individuals should be screened for the presence, signs, symptoms, and/or risk factors suggestive of cardiovascular, pulmonary, or metabolic diseases, as well as other conditions (e.g., orthopedic limitations, pregnancy) that require special attention to (i) aid in
the development of a safe and effective Ex Rx and (ii) optimize safety during exercise testing [23]. Regardless of stage of disease progression, all HIV-infected individuals should consult with their physician and obtain medical clearance prior to participating in an exercise program. Once cleared to exercise, it is recommended that the patient consult a clinical exercise therapist for advice and guidelines on an exercise program tailored to the individual’s physical function, health status, exercise response, and stated goals.

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Time point/Frequency</th>
</tr>
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<tbody>
<tr>
<td>CD4 Count</td>
<td>√ Every 2 years after ART initiation, or if virologic suppression is achieved, or if CD4 count &lt;300 cells/mm³ every 12 months; √ every 3 months after ART initiation.</td>
</tr>
<tr>
<td>Fasting Lipid profile</td>
<td>√ If abnormal at last measurement, √ if normal at baseline, annually</td>
</tr>
<tr>
<td>Fasting Glucose or Hemoglobin A1C</td>
<td>√ If abnormal at last measurement, √ if normal at baseline, annually</td>
</tr>
</tbody>
</table>

- If ART initiation occurs soon after HIV diagnosis and entry into care, repeat baseline laboratory testing is not necessary.
- ART is indicated for all HIV-infected individuals and should be started as soon as possible. However, if ART initiation is delayed, patients should be retained in care, with periodic monitoring as noted above.
- Consult the National Lipid Association’s recommendations for management of patients with dyslipidemia.

Table 2. Laboratory monitoring schedule for HIV-infected patients before and after initiation of antiretroviral therapy\(^a\) [37].
A comprehensive pre-exercise test evaluation for HIV-infected individuals includes (i) medical history, (ii) physical examination, and (iii) HIV-related laboratory tests. The physician should provide medical information (e.g., stage of disease, CD4 count, HAART, and other medications used, history of symptoms, and recent illness), whereas the clinical exercise therapist can acquire exercise-related medical information by using the Canadian Physician Clearance Form (ePARmed-X+) [25] as a positive response is expected when using the Canadian Activity Readiness Questionnaire for Everyone (PAR-Q+) [26]. The PARmed-X+ is a form developed for use by physicians and clinical exercise therapists to assist in addressing medical concerns regarding physical activity participation that were identified by the PAR-Q+.

Health-related quality of life (HRQOL) has emerged as an important topic in the treatment of HIV infection, with HIV-infected patients generally demonstrating a HRQOL that is lower than that of the general population [11, 27]. Clinical exercise therapists should use the Multidimensional Quality of Life Questionnaire for Persons with HIV (MQOLHIV) to monitor HRQOL for patients living with HIV disease [28]. HRQOL has become increasingly important with the goals of therapy now, including improvement of HRQOL, in addition to reduction of symptoms, virus suppression, and extension of survival. Repeated assessment can be used to track changes in functional status over time; monitor, assess, and optimize treatment effects and enhance communication between patient and provider with the potential to improve the health care process and overall survival [28]. With physical training regarded as a non-pharmacological treatment, use of HRQOL will be helpful to monitor and improve adherence [29] because the development of side effects can worsen HRQOL and lead to treatment non-adherence [30].

Regardless of the disease status of HIV-infected individuals, it is important to assess their current fitness level prior to developing an exercise program [31]. Despite the lower functional capacities of HIV-infected individuals [11], the standard physical fitness tests applicable to the apparently healthy populations can be applied [31]. BP and ECG are monitored during exercise testing due to the increased prevalence of cardiovascular impairments and cardiac dysfunction [23].

Components of the physical examination conducted by the clinical exercise therapist should include the following:

1. **Body composition**: It includes body weight, body mass index (BMI), skin fold measurement of subcutaneous fat (fat percentage), standard circumference sites (thigh, calf, arm, chest, waist, and hip), waist-to-hip ratio (WHR) [21, 23], muscle mass, lean body mass [32], and self-reported body shape changes [33]. Perceived body image can be measured with the Body Image Scale (BIS) that is a 12-item, disease-specific, valid and reliable tool that measures perceived body image along five dimensions (comfort, competence, appearance, predictability, and existential self). Each item utilizes a five point visual analogue scale and scores range from 12 to 60 (higher scores reflect poorer body image) [34].

2. **Physical capacity**: The modified Bruce protocol or submaximal YMCA cycle ergometer test is used to determine cardiorespiratory fitness [23]. For assessing muscular strength, six-repetition maximum (6 RM) or 10 RM protocol may be more appropriate because the
affected population is generally untrained [31]. A grip strength dynamometer can be used to determine the maximum isometric strength of the hand and forearm muscles [17].

3. Neuromuscular function: Gait analysis and balance test (e.g., Stork stand) should be conducted because peripheral neuropathy, which can be a consequence of fast hyperlactatemia at rest which many people living with HIV/AIDS present, is a common symptom of HIV infection [31, 35].

4. Functional capacity: The Lower Extremity Functional Scale (LEFS) can be used as a measure of patients’ initial function, ongoing progress, and outcome, as well as used to set functional goals [36].

3.1. Laboratory tests

To assist the clinical exercise therapist, it is recommended that a physician conduct the following laboratory tests for HIV-infected individuals:

1. Cardiometabolic: It is fasting blood lipids (total cholesterol, LDL-C, HDL-C, and triglycerides), fasting glucose or hemoglobin A1c (HbA1C), and CD4 cell count when diagnosed with HIV as well as prior to the start of HAART [10, 21]. Table 2 indicates the laboratory monitoring schedule for HIV-infected patients before and after initiation of antiretroviral therapy [37].

2. Bone mineral density (BMD): The literature recommends that for all HIV-infected postmenopausal women and men aged > 50 years, BMD should be tested and, if the results of the test do not warrant medical treatment, the test should be repeated every 2–5 years, depending on the proximity to thresholds for therapy [38].

3. Electrocardiography: Due to the increased risk of heart disease, a resting 12-lead electrocardiogram is recommended [31].

4. Special considerations prior to prescribing an exercise program

Clinical exercise therapists should consider various factors (e.g., clinical/treatment characteristics) when prescribing an exercise program for HIV-infected individuals. HIV-infected individuals adapt readily to exercise training and therefore can the general FITT principle of Ex Rx for apparently healthy adults applied to those carrying HIV [23, 39]. Additional drug-related physical, psychological, and physiological side effects including lethargy, nausea, vomiting, diarrhea, headaches, fever, muscle pain, occasional dizziness, peripheral neuropathy, fatigue, anemia, mitochondrial toxicity, depression, and myopathy must be considered [37]. In particular, the following symptoms, adverse effects, and comorbidity should be taken into account:
4.1. HIV/AIDS wasting syndrome

It is a syndrome of unintentional weight loss that occurs with advanced HIV infection. It is defined as an involuntary weight loss of greater than 10% from baseline body weight during the previous 12 months or a 5% loss of weight during the previous 6 months [40].

4.2. Lipodystrophy

It is as an all-encompassing term used to describe a metabolic complication of fat loss, fat gain, or a combination of fat loss and gain, which is associated with some antiretroviral (ARV) therapies given to HIV-infected individuals [41]. Lipatrophy is the loss of subcutaneous fat, particularly evident in the face, buttocks, and limbs. Lipohypertrophy is the accumulation of visceral and central fat in the abdomen, dorsocervical region (“buffalo hump”), or breasts. Fat redistribution is an all-encompassing term used to describe lipohypertrophy, lipoatrophy, and/or mixed syndrome in HIV-infected individuals [42, 43].

4.3. Dyslipidemia

HAART is associated with hypercholesterolemia, increases in LDL-C, hypertriglyceridemia, and lowered HDL-C [2, 44].

4.4. Diabetes

HAART adversely affects insulin sensitivity and glucose tolerance [45, 46]. Clinical exercise therapists should also distinguish between the three subgroups of patients with diabetes: those with pre-existing diabetes who contract HIV; those who have diabetes at onset of HIV infection; and others who develop hyperglycemia after commencing HAART. These subgroups need to be managed differently. Pre-existing type 2 diabetes mellitus may continue to be managed, after diagnosis of HIV, with the same drug therapy that was being used prior to detection of HIV [46]. It is important to counsel these patients about a possible deterioration in metabolic function, and the chances of drug interactions between oral antidiabetic drugs and HAART. Patients diagnosed with diabetes and HIV together may be treated according to guidelines for uninfected individuals. Patients developing diabetes after HAART may benefit from insulin, because it is a safe and effective method of treatment [46].

4.5. BMD

Initiation of ART is associated with a 2–6% decrease in BMD over the first 2 years [47]. HIV-infected individuals receiving protease-inhibitor-based HAART (up to 30%) are more likely to display significant bone demineralization [48].

4.6. Cardiometabolic disease (CMD) risk

The incidence of CMD increases in HIV-infected individuals, and HAART is associated with an increase in both peripheral and coronary artery disease [49, 50]. Risk factors such as hyperlipidemia [44], oxidative stress [51], impaired glucose tolerance, and increased insulin
resistance [45], accumulation of visceral fat [52], inflammation secondary to HIV [53], and the effects of some antiretroviral drugs all contribute to the risk of developing CMD [54].

5. Program prescription

Exercise training is well established as an important non-pharmacological therapy for HIV-infected individuals and one of the key approached being explored to deal with the complications and symptoms of HIV/AIDS [9, 55]. The primary goals (depending on the stage of the disease) for prescribing exercise to HIV-infected patients are to improve HRQOL, physical, and physiological, functional, and neuromuscular function capacity, decrease the risk of CMD, and promote long-term exercise compliance. It is therefore advised to include both short- and long-term individualized goals based on the subjective and objective findings in the patient’s assessment. In addition to the symptoms, adverse effects, and comorbidity considerations mentioned previously, clinical exercise therapists should take into account the individual’s: (i) physical function; (ii) functional limitations and likes/dislikes; (iii) health status; (iv) availability of equipment and time available to train; (v) exercise dose response (desired goal, type of exercise, and intensity, duration, and frequency of training); and (vi) coordination among members of the multidisciplinary team [10, 23]. HIV/AIDS is a progressive disease; therefore, clinical exercise therapists should frequently reassess the patient’s physical, physiological, functional, and neuromuscular capacity (at least every 6–8 weeks) to determine whether the exercise program is still meeting the individual needs and goals of the patient. As mentioned earlier, HIV-infected individuals adapt readily to exercise training, and therefore, the general FITT principle of Ex Rx for apparently healthy adults can be applied to those carrying HIV [23, 39]. An Ex Rx is the process whereby the recommended exercise regimen is designed in a systematic and individualized manner in terms of the Frequency (How Often?), Intensity (How Hard?), Time (How Long?), and Type/Mode (What Kind?), or the FITT principle of Ex Rx [56].

5.1. Frequency

Frequency refers to how often an individual engages in an activity, usually the number of days per week [56]. Most HIV studies have used a three times weekly intervention for both the aerobic exercise (AE) and progressive resistive exercise (PRE) component [12, 13, 57] with success three/four times per week [31], a few studies have reported positive results twice weekly [39, 58]. Table 3 indicates the specific frequency of the AE and PRE component according to the different clinical categories with the corresponding CD4 cell count for each category [55]; for example, HIV-infected individuals in clinical category A1 (asymptomatic, acute HIV, or persistent generalized lymphadenopathy with ≥500 cells/μL) (Table 1) and clinical category A2 (asymptomatic, acute HIV, or persistent generalized lymphadenopathy with 200–499 cells/μL) (Table 1) can perform PRE three times per week and aerobic AE five times per week whereas clinical category C HIV-infected individuals (AIDS indicator conditions with <200 cells/μL) (Table 1) can perform PRE twice per week and AE three times per week (Table 3) [55]. There should be a rest day between the PRE sessions and, if time constraints are present, separate resistive programs into upper and lower body workouts.
It is recommended to complete flexibility exercises during the warm-up and cool-down of an exercise session. Neuromuscular exercises can be performed two to three times per week by those HIV-infected individuals who are severely debilitated from the disease, typically those from the Centres for disease control clinical categories A3, B3, and C1-C3 (Table 1).

5.2. Intensity

Intensity is the level of exertion experienced during the activity. Individuals can monitor their rate of perceived exertion (RPE) with Borg’s RPE scale that subjectively rates exercise intensity from 6 to 20 with 6 corresponding to “no exertion at all” and 20 corresponding to “maximal exertion” [59]. A person can also use a definitive scale by tracking heart rate. For the aerobic component, a 40–60% exercise intensity of VO$_2$R (difference between VO$_2$max and resting VO$_2$) or heart rate reserve (HRR) [31] or 50–85% of HR$_{max}$ [10] is recommended to HIV-positive individuals.

The recommended exercise intensity for the PRE component is 50–90% of one-repetition maximum (IRM) [12]; 60% of IRM [23] with an intensity of 35–50% of 6–10RM for patients from the Centres for disease control clinical categories A3, B3, and C1–C3 (Table 3) [55]. The specific intensities of the PRE component according to the different clinical categories with the corresponding CD4 cell count for each category are displayed in (Table 3) [55].

![Table 3](https://example.com/table3.png)

**Table 3.** Recommended FITT framework for the frequency, intensity, time, and type of aerobic exercise (AE) and progressive resistive exercise (PRE) for different HIV clinical categories [55].
5.3. Time

Time refers to the duration of an exercise session [56] and depends on the intensity as well as the goal of the exercise. AE performed at a higher intensity performed for a shorter duration produces the same results as exercise done at a moderate intensity for a longer duration. A duration of 45 min for the AE component [12] or 30–60 min [23] including a 5–10 min warm-up and cool-down is recommended. The duration of the AE component for patients from the Centres for disease control clinical categories A3, B3, and C1–C3 is 20–30 min (Table 3) [55].

The recommended duration of the PRE component is 30–90 min with a volume of three sets of eight reps [12], two sets of eight to ten repetitions [31], or 30 min to complete two to three sets of 10–12 exercises [23]. One to two sets of eight to ten repetitions are recommended for patients from the Centres for disease control clinical categories A3, B3, and C1–C3 (Table 3) [55].

The duration of the flexibility component is 5–10 min with a volume of three sets of 20–30 s. Similarly, the duration of the neuromuscular component is 5–10 min with the volume determined by the specific neuromuscular exercise.

5.4. Types (modes) of exercise

Types of activity include aerobic, balance, flexibility, and resistance (or strength) training which help patients achieve different health goals [56]. In HIV-infected individuals, the appropriate exercise mode depends on the patient’s functional impairments, preference, and safety issues regarding the stage of the disease [12, 60].

5.4.1. AE

Aerobic exercise is safe to perform (even at high intensities) and may lead to significant improvements in selected outcomes of cardiovascular fitness, body composition, and psychological status in HIV-infected individuals [19]. Individual studies have shown an improvement in VO2max and other measures of fitness [10, 13], improvement in body composition (decreases in fat percentage, increases in leg muscle area and abdominal fat loss), [13, 21] reduced anxiety, stress, and depressive mood [22], improvement in QOL [11], as well as improvement in lipid profile [8] and glucose tolerance [21]. Crossover effects have also been reported whereby aerobic exercise may lead to improved strength [3, 19]. Type or mode of AE to improve the cardiovascular system includes running, walking, swimming, aerobics classes, circuit training, and cycling [55].

5.4.2. PRE

Progressive resistive exercise is safe and effective in medically stable adults living with HIV [22, 32]. PRE can increase body weight and peripheral girth, and reverse muscular atrophy [61]. Training effects include an increase in strength [17, 61], improvements in body composition (increasing BMI and lean body mass) [17, 62], and improvements in psychological status and
QOL [10], insulin sensitivity [63], and lipid profile [64]. PRE that stresses the muscular system includes weights, cables/pulleys/resistance bands, body weight, and plyometrics [31, 55].

5.4.3. Combined aerobic and resistive exercise (CARE)

The combination of the two exercise modalities, AE and PRE, is recommended by the American College of Sports Medicine [23] and seems not only to be safe but well tolerated by HIV-infected individuals. A combination of aerobic and progressive resistive exercise (CARE) appears to be more effective than applying only one component [10]. Research studies have shown an improvement in \( \text{VO}_{2\text{max}} \) and other measures of fitness [3, 10, 13], functional capacity [10, 14], improvement in body composition (decreases in fat percentage, increases in abdominal fat loss, BMI, and lean body mass) [8, 13, 57], increases in viral load and cell counts for TCD4+/TCD8 [13], improvement in QOL [8, 9, 11] and mood state [61], as well as improvement in lipid profile [13] and glucose tolerance [21].

6. Special considerations during exercise training

For asymptomatic HIV-infected individuals, the ACSM’s guidelines regarding contraindications for exercise applicable to healthy individuals should apply as there are no current guidelines for individuals with HIV/AIDS [23].

It is important that HIV-infected individuals report increased feelings of tiredness or exhaustion (minor increases in feelings of fatigue should not be a reason for exercise discontinuation), lower gastrointestinal distress (especially diarrhea), shortness of breath, or a sense of increased effort in performing activities of daily living [31]. Dizziness, swollen joints, or vomiting preclude exercise participation [23].

The exercise sessions of symptomatic individuals with HIV/AIDS or those diagnosed with comorbidities should be supervised [23].

7. Conclusion

Evidence-based research indicates that AE, PRE, and a combination thereof by HIV-infected individuals are safe and positively influences the cardiometabolic and morphological complications that may accompany HAART as well as a range of side effects associated with the HIV disease itself. The current exercise guidelines available in the literature are generalized and they do not consider the specific clinical stages with significant gaps in knowledge as to the minimal and optimal duration, frequency, mode, and intensity of exercise needed to produce beneficial changes in HIV patients. Most of the studies referred to have not approached the exercise program from a dose-response perspective or from the perspective of validating commonly used exercise prescriptions for HIV-infected individuals. The research provides
information that clarifies the optimal mode, duration, frequency, and intensity of AE and PRE prescribed to the different clinical stages of HIV patients. Clinical exercise therapists should adopt the recommended guidelines that will benefit HIV patients.

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