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Does exercise program of endurance and strength improve health-related quality of life in persons living with HIV-related distal symmetrical polyneuropathy? A randomized controlled trial

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Abstract

Background The most common HIV neurological comorbidity, Distal Symmetrical Peripheral Neuropathy (DSPN), is characterized by severe symptoms and reduced quality of life. Exercise has consistently been mentioned as one of the non-pharmacological therapies for the rehabilitation of individuals with HIV, but little is known about an exercise program to recommend to people living with HIV (PLWHIV)-related DSPN. The purpose of this study was to investigate the effectiveness of aerobic (AE) or progressive resisted exercise (PRE) on quality of life (QOL) in a person living with HIV-related DSPN.

Method A randomized controlled trial was conducted with 136 persons living with HIV-related Neuropathy, including 6 domains of QOL within WHOQOL-BREF, 45 in the AE (used ergometer), 44 in the PRE (used quadriceps bench), and 47 in the control group (CG). The outcome measures (QOL) data were analyzed using the inferential statistic of Friedman for within-group with post hoc analysis of Wilcoxon signed Test. A Kruskal–Wallis test was carried out for between-groups with post hoc analysis of Mann–Whitney to find where significant differences exist.

Results The results indicated significant differences within experimental groups in all six domains $p < 0.05$. Similarly, the result indicated significant differences within the CG in Physical, level of independence, and Spirituality/Religions domains ($p = 0.002$, $p = 0.035$, $p = 0.006$). However, the results indicated significant differences between experimental groups and CG.

Conclusion These findings indicated that strength and endurance exercise of moderate intensity have a positive effect on QOL in PLWHIV-related DSPN.

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Keywords HIV-related DSPN · QOL · Rehabilitation · Exercise

Abbreviations

HIV	Human immunodeficiency virus
QOL	Quality of life
DSPN	Distal symmetrical polyneuropathy
PLWHIV	Person living with HIV
AE	Aerobic exercise
PRE	Progressive resisted exercise
BPNS	Brief peripheral neuropathy screening
SPNS	Subjective peripheral neuropathy screen
WHOQOL-BREF	World Health Organization Quality of Life Scale Brief Version
HAART	Highly active antiretroviral therapy

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Introduction

The most frequent neurological complication associated with HIV infection is distal symmetrical polyneuropathy (DSPN). It is associated with disabling pain, tingling sensation, numbness, and reduced quality of life (QOL) [1, 2]. Although the prevalence of DSPN decreased following initiation of highly active antiretroviral therapy (HAAT) in

persons living with HIV (PLWHIV) in resource-limiting settings [3], more than one-third of the virally suppressed participants still had DSPN at their last visit, suggesting that the remaining cases of neuropathy are a legacy effect of early, irreversible, HIV-induced nerve damage [4]. It has been explained that many HIV-related neurological syndromes especially DSPN markedly diminished the QOL. The factors contributing to the diminished QOL in these patients were wrong diagnosis, increasing physical disability, and pain that negatively impacts the QOL [5]. Recently, the QOL of PLWHIV became an important topic across multiple cultures and societies [6]. While HIV-related neurological diseases are associated with reduced QOL scores, enhanced neurological care has a positive impact on HIV/AIDS patients' overall well-being [7].

Exercise mitigates negative psychological states and promotes positive mood, vigor, and well-being in both healthy individuals and individuals with certain chronic diseases [8, 9]. In addition, it has also been documented in the recent literature that physical activities improve psychological well-being, pain, physical functioning, level of independence, and health-related quality of life of PLWHIV [10–12].

On the other hand, illnesses associated with the advancement of HIV infection or toxicity of medications have been reported to have a significant impact on the QOL of PLWHIV-related DSPN. To our knowledge, there is little available evidence on the impact of endurance training compared with strength training on the QOL of PLWHIV-related DSPN, especially in Sub-Saharan Africa. Even though few studies investigated the effect of either aerobic or resistance exercises on the QOL of PLWHIV and people with another form of chronic neuropathy, these results cannot be extrapolated to PLWHIV-related DSPN. Besides, it is also not known if the exercise regimen will improve the QOL domains of PLWHIV-related DSPN. Therefore, this study was conducted to compare the impact of endurance and strength exercise programs on various domains of QOL in PLWHIV-related DSPN.

Methodology

Subjects

This multi-center study recruited participants using a convenience sampling method. The participants comprise indigent recipients of medical care in four outpatient HIV clinics in Kano metropolis, Nigeria. The participants received detailed information about the study procedure and the risks that may be associated with exercise regimens. The participants also signed informed consent before the commencement of the study. The inclusion criteria were (1) an HIV diagnosis with a history of CD4 + counts of greater or equals to 200 cells/mm^3, on first-line antiretroviral therapy for a minimum of 6 months, with lower extremity peripheral neuropathy syndrome, (2) male and female participants who walked independently and having age 18–50 years, (3) participants with brief peripheral neuropathy screening (BPNS) score of ≥ 2, who were able to complete a 6-min walk distance (6MWD) test. Participants diagnosed with neuropathy not related to the HIV or related to central nervous system and/or pulmonary system were excluded (i.e., patients with AIDS dementia complex, encephalopathy).

Sample size estimation

The sample size (N) was determined using Cohen table [13] at alpha $\alpha = 0.05$ and degree of freedom $(\mu) = k - 1$, where k is the number of groups, with effect size $f = 0.32$. From the previous study [14] and power (w) 80%, sample size $n = 34$. The sample size (N) 102 was sufficient for this study, and the authors increased the desired sample size to 165 participants to make room for attrition. Randomization was conducted using a computer-generated random allocation sequence schedule conducted by a physiotherapist who is not involved in the research and has experience in research. During the enrollment, 11 participants failed the 6MWD test and the remaining 154 participants were randomly allocated into the AE group, PRE group, and the control group (see Fig. 1). To eliminate bias, the assessment of outcome was performed by experienced assessors who were blinded to the type of intervention as well as the intervention groups of the participants. Participants were also instructed not to disclose their intervention groups to the assessors.

Instrumentations

Subjective peripheral neuropathy scale (SPNS)

This was used as a self-administered checklist for the presence of DSPN. The participants were asked to tick Yes/No in the box provided in front of each question. The tool has ten questions rated as follows; if symptoms have been present in the past, but not since the last visit, "currently absent" was marked. If the symptom has never been present, "always been normal" was marked. The participant with a score of 1–3/10 was marked as mild symptoms, the participant with a score of 4–6/10 was marked moderate symptoms, and a score of 7–10 was marked severe symptoms. This comprised muscular cramping, numbness, tingling sensation, inability to tell hot from cold especially when bathing, burning or aching pain, and sharp, stabbing, shooting or sudden electric shock-like pain and allodynia during sleep was also checked. It checks for foot sensation patterns when walking and if the skin becomes so dry it cracks, and participants with severe symptoms were selected to participate in the study [15].

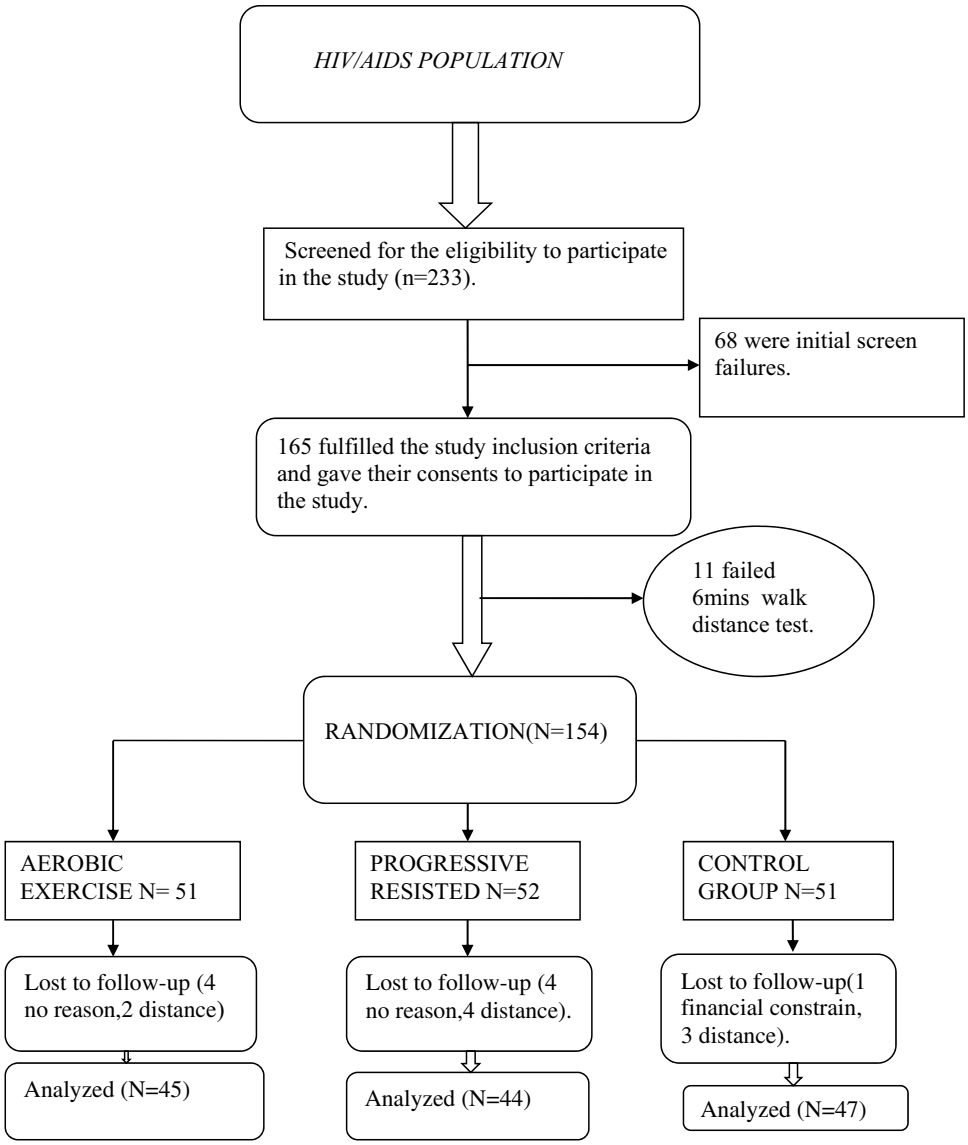

Fig. 1 Flow chart of the study

The aid clinical trial group (ACTG) brief peripheral neuropathy screening (BPNS) tool

This questionnaire was used to confirm the presence of DSPN. This tool is recommended because it has been widely used in clinical trials and can be administered by non-neurologists following minimal training, and encompasses both clinical signs and symptoms suggestive of neuropathy. The intensity of three symptoms which covers the following: 'pain, aching, or burning'; 'pins and needles' (paresthesias); and 'numbness' were assessed. Each of these three different symptoms was rated either as never occurring or occurring. If present at the time of data collection, the severity of the symptoms was scored on a scale of 1 (mild) to 10 (most severe). The subjective neuropathy grade was determined by using the symptom with the highest score between 1 and 10. The symptoms of the participants were scored as follows: from 1 to 3 equaled a clinical grade of 1, a symptom scored from 4 to 6 equaled a clinical grade of 2, and symptom scored from 7 to 10 equaled a clinical grade of 3. These were then categorized into three groups. A grade of 1 illustrated a mild DSPN, 2 moderate DSPN, and 3 severe DSPN. The location of symptoms was also measured depending on where it was, either none = 0, feet only = 1, extend to ankle = 2, extend to above ankle but not to the knee = 3, extend to knee = 4, extend to above knee = 5. Vibration perception was checked using a 128HZ tuning fork, where the participant was placed in a comfortable sitting position on the chair. The examiner compressed the ends of a 128-Hz tuning fork just hard enough to touch each other. Then, the vibrating tuning fork was placed on a bony prominence on the participant's wrist to be sure that he/she can recognize the vibration or "buzzing" quality of the tuning fork. The tuning fork was compressed just hard enough again till the

sides touched, and immediately placed gently but firmly on top of the distal interphalangeal (DIP) joint of one great toe and began counting the seconds. The participant was asked when the "buzzing" stopped. It was repeated for the other great toe, and then the seconds was recorded to determine the severity with score of 0 = felt > 10 s (normal), 1 = felt 6–10 s (mild loss), 2 = felt < 5 s (moderate loss), 3 = not felt (severe loss), and 8 = unable/did not evaluate. The deep tendon reflex was assessed on Achilles tendon using a reflex hammer with the participant seated; the examiner used one hand to press upward on the ball of the foot and dorsiflexed the participant's ankle to 90 degrees. The examiner struck the Achilles tendon and the tendon reflex was felt by the examiner's hand as plantar flexion of the foot, appearing after a slight delay from the time the Achilles tendon was struck. Reinforcement was used by having the participant clenched his/her fist before classifying the reflex as absent with score of 0 = absent, 1 = hypoactive, 2 = normal deep tendon reflexes, 3 = hyperactive, 4 = clonus, and 8 = unable to or did not assess. This is a valid neuropathy screening tool for use in the context of HIV infection and is simple enough to be applicable in poor resourced settings [16].

Outcome measures

World Health Organization quality of life scale brief version (WHOQOL-BREF)

The WHOQOL-BREF is a self-administered questionnaire that was used in assessing participants' QOL. The WHOQOL-BREF provides a valid and reliable alternative to the assessment of domain profiles using the WHOQOL-100 [17]. It consists of parts A and B. Part A assessed demographic characteristics of the participant that covered age, gender, the level of education, marital status, health status, HIV serostatus, year first tested positive, expected year the participant was infected, and how participant thought he/she was infected. The participant circled or wrote the answer. Part B assessed participants' QOL and contained 31 items with each item using a 5-point Likert scale. A score of 1 indicated a low mark (negative perceptions), and 5 indicated a high mark (positive perceptions). These items were distributed in six domains of QOL are as follows: physical health, psychological health, level of independence, social relationships, environment, and spirituality/religion/personal beliefs. The physical health domain measured pain and discomfort, energy and fatigue, and sleep and rest of the participant. The psychological health domain measured positive feelings, thinking, learning, memory and concentration, self-esteem, body image and appearance, and negative feelings of the participant. The level of the Independence domain measured mobility, daily life activities, dependence on medications or treatments, and work capacity of the participant. The social relationships domain measured personal relationships, social support, and sexual activity of the participant. The environment domain measured physical safety and security, home environment, financial resources, health and social care, accessibility and quality, opportunities for acquiring new information and skills, participation in and opportunities for recreation and leisure activities, and physical environment (pollution, noise, traffic, climate, and transport) of the participant. The spirituality/religion/personal beliefs domain measured forgiveness and blame, concerns about the future, and death and dying of the participant [18].

Intervention

Aerobic exercise (AE)

The participants of this group underwent AE while receiving Voluntary Counselling and Treatment's routine services. The subjects were instructed to sit on the seat of stationary bicycle Tunturi E6 Heart Control Ergometer (TUNTURI, USA) with both feet placed on the pedals and held in place with rubber straps. This exercise was divided into 3 phases, the warm-up phase, an exercise phase, and a cool-down phase. During the warm-up phase, the subject pedaled the bicycle for 5 min without any resistance, followed by the exercise phase during which the subject pedaled with low resistance 17 watts. The resistance was gradually increased until the desired intensity of 50% maximum heart rate reserve (HRmax) was attained using the estimated HRmax reserve (206.9—(0.67 × age) [19]. The exercise phase lasted for 20 min and then was followed by a cool-down in which the subjects cycled resistance-free for 5 min. The intensity was increased in the first 2 weeks to level up at 65%HRmax reserve throughout the remaining part of the training period. The frequency of the exercise was 3 times a week and the duration of the exercise was 30 min per session and was explained to the participants and the procedure was adopted from the American College of Sports Medicine [20]. To ensure moderate intensity was not exceeded (50–65% of the age-predicted maximum heart rate), the heart rate displayed on the monitor of the ergometer was used.

Progressive resisted exercise (PRE)

The participants of this group underwent PRE while receiving Voluntary Counselling and Treatment's routine services. The PRE program commenced with 5 min of warm-up which entailed bilateral static stretching of the quadriceps, hamstrings, tibialis anterior, and gastrocnemius muscles. This was followed by the use of the quadriceps bench for PRE and lasted for 20 min. The initial intensity of exercise was set at 50% of 1-repetition maximum (1-RM) or the

maximal amount of weight that the participant could lift once through a full range of motion. The 1-RM was measured at the first exercise session and every other week with the absolute load adjusted to maintain the relative intensity of the training effect for the first 6 weeks. During this period, the participants performed 2 sets of 10 repetitions of 5 min for each muscle group listed above with resting intervals of 3 to 5 s between repetitions. This was followed by a cool-down phase of 5 min of dynamic stretching for the relevant muscles of the lower limb. After 6 weeks, the relative intensity of the exercise was increased to 65% of the 1-RM and participants performed 3 sets of 10 repetitions for 5 min for each muscle group with resting intervals of 2 to 3 s between repetitions as prescribed by the American College of Sports Medicine [20]. 5 min walking cool-down ended the session. The frequency of exercise was 3 times/week for 12 weeks.

A non-exercise control group (CG)

Participants in this group were instructed not to undertake any vigorous physical activity during the 12 weeks of the study. After 12 weeks of receiving Voluntary Counselling and Treatment's routine care which includes a wide range of social and medical services for health and medical care of the participants in this group. Thereafter, the participants were allowed to participate in either AE or PRE program for 12 weeks as stipulated by the ethical criteria.

Measurements were recorded at baseline, 6 weeks, and 12 weeks post-intervention. The research assistants at both exercise sites monitored physiologic parameters (oxygen saturation rate, heart rate, and blood pressure) to ensure safe interventions. The participants reported a perceived exertion rate through the BORG scale at the mid- and end-point of each session [21].

Exercise adherence

The adherence of the exercises was determined using attendance and completion rates of the participants. Adherence to the exercises was expressed as the percentage of exercise sessions completed over the stated period (36 training sessions = 100% attendance). Participants who completed 29(80%) out of 36(100%) possible sessions were considered adherers. An attendance rate of 95% for the exercise sessions was achieved.

Data analysis

Demographic and outcome data are presented as M ± SD or frequency and percentage where appropriate. QOL measures were presented as change from baseline, 6 weeks, and 12 weeks. Outcome measures were not normally distributed, and thus non-parametric statistics were used for within- and between-groups. A Friedman test was carried out to determine differences within the group in QOL across baseline, 6 weeks, and 12 weeks. Post hoc analysis using the Wilcoxon Signed Rank Test was performed where the differences exist. Kruskall–Wallis determined the differences between groups at baseline, 6 weeks, and 12 weeks. Post hoc analysis using Mann–Whitney U test was used to find any significant difference in QOL at baseline, 6 weeks, and 12 weeks, between AE and PRE, AE and CG, and PRE and CG, and between completers group and lost to follow-up group. All statistical analyses were performed at a probability level of 0.05 and 95% confidence interval using Statistical Package for the Social Science (SPSS) (Version 21.0, SPSS Inc., Chicago IL, USA).

Results

Demographic characteristics of the participants

Baseline assessments were completed with 154 participants (51 in the AE, 52 in the PRE, and 51 in the CG). ANOVA showed no significant difference between the groups ($p > 0.05$) as regard to age, height, and weight. Moreover, Kruskall–Wallis showed no significant difference between groups ($p > 0.05$) as regard to gender. In contrast, Kruskall–Wallis indicated significant differences ($p < 0.05$) as regard to level of education and health status (Table1).

A comparison was made between demographic characteristics of completers and those that are lost to follow-up. *T* test showed no significant difference between the two groups ($p > 0.05$) in respect of age ($t = 0.18$, $p = 0.0811$), weight ($t = 0.39$, $p = 0.0601$), and height ($t = 0.56$, $p = 0.801$). In addition, Mann–Whitney *U* test revealed no significant difference between groups with regard to gender ($\chi^2 = 0.58$, $p = 0.576$) and marital status ($\chi^2 = 6.51$, $p = 0.737$). In contrast, the test revealed significant differences in respect to level of education ($\chi^2 = 1.51$, $p < 0.05$) and health status ($\chi^2 = 1.103$, $p < 0.05$).

Differences in QOL domain scores within groups and between groups

Baseline assessments were completed with 154 participants (51 in the AE, 52 in the PRE, and 51 in the CG). The experimental and the control groups were similar in baseline measures. After the 12 weeks, reassessments were done for 88.3% ($N = 136$) participants with 45 from the AE, 44 from PRE, and 47 from CG while 11.7% ($N = 18$) (Fig. 1).

Table 1 Socio-demographic status of the respondents

Variables	$N=136$ M (SD)	Group 1-45 M (SD)	Group 2-44 M (SD)	Group 3-47 M (SD)	F	p value
Age (years)	36.79 (8.23)	38.29 (8.06)	35.98 (8.53)	36.13 (8.10)	1.114	0.331
Weight (Kg)	68.42 (16.39)	64.07 (16.00)	70.96 (15.81)	70.20 (16.16.21)	2.437	0.091
Height (cm)	1.67 (0.11)	1.67 (0.11)	1.67 (0.11)	1.67 (0.12)	0.042	0.0959
	Categories ($N=136$)	Group 1 N (%)	Group 2 N (%)	Group 3 N (%)	χ^2	p value
Gender	Male	18 (40)	20 (45.5)	18 (38.3)	0.51	0.773
	Female	27 (60)	24 (54.5)	29 (61.7)		
Level of education	Not at all	5 (11.1)	4 (9.1)	25 (53.2)	1.603	0.001*
	Primary	7 (15.6)	4 (9.1)	16 (34.0)		
	Secondary	24 (53.3)	24 (54.5)	1 (2.1)		
	Tertiary	9 (20.0)	12 (27.3)	5 (10.6)		
Health status	Very poor	1 (2.2)	16 (36.4)	11 (23.4)	1.012	0.001*
	Poor	10 (22.2)	24 (54.5)	33 (70.2)		
	Neither poor nor good	33 (73.3)	4 (9.1)	3 (6.4)		
	Good	1 (2.2)				

Group1 aerobic exercise group, *group2* progressive resisted exercise group, group3 = control group, *M(SD)* mean ± standard deviation, *N* combined samples, *F* ANOVA, χ^2 Chi square of Kruskal wallis

*Significant at $p<0.05$

Differences in QOL domain scores within groups across baseline, 6 weeks, and 12 weeks

A Friedman test was carried out to determine differences within the group in QOL domain scores (Table 2).

Physical health domain

A Friedman test indicated significant differences across baseline, 6 weeks, and 12 weeks in the AE group, PRE group, and CG ($p<0.05$). Post hoc analysis using Wilcoxon

Table 2 Differences within groups on QOL domains across Baseline, 6 weeks, and 12 weeks post-interventions

Variables	Study groups	n	Baseline Mdn (IQR)	6 weeks Mdn (IQR)	12 weeks Mdn (IQR)	χ^2	p value
Physical health	AE	45	10.0 (4.0)	12.0 (3.0)	15.0 (2.5)	15.0 (2.5)	< 0.001*
	PRE	44	9.0 (3.0)	11.0 (3.0)	14.0 (3.0)	82.245	< 0.001*
	CG	47	10.0 (4.0)	10.0 (4.0)	10.0 (2.0)	14.000	< 0.001*
Psycological	Aerobic	45	10.0 (3.0)	11.2 (0.2)	14.4 (2.4)	79.585	< 0.001*
	PRE	44	10.0 (2.4)	11.2 (0.2)	13.0 (2.4)	2.90	< 0.001*
	CG	47	10.0 (2.0)	10.0 (0.2)	10.0 (2.2)	0.636	0.0725
Level of independence	Aerobic	45	10.0 (3.0)	12.0 (4.0)	14.0 (2.5)	73.578	< 0.001*
	PRE	44	10.0 (4.0)	12.0 (3.0)	14.5 (2.75)	82.582	< 0.001*
	CG	47	10.0 (1.0)	10.0 (2.0)	10.0 (1.0)	7.125	0.028*
Social relationship	Aerobic	45	10.0 (4.0)	12.0 (4.0)	14.0 (3.0)	59.277	< 0.001*
	PRE	44	10.0 (3.0)	10.0 (3.75)	12.0 (4.0)	64.371	< 0.001*
	CG	47	10.0 (3.0)	10.0 (3.0)	10.0 (3.0)	2.436	0.296
Environment	AEROBIC	45	11.0 (2.0)	13.0 (2.0)	14.5 (2.5)	64.767	< 0.001*
	PRE	44	10.5 (2.0)	11.0 (2.0)	13.5 (2.0)	67.121	< 0.001*
	CG	47	10.5 (2.0)	11.0 (2.0)	11.0 (2.0)	5.692	0.58
Spirituality/religion	Aerobic	45	9.0 (2.0)	11.0 (3.0)	15.0 (4.0)	80.369	< 0.001*
	PRE	44	9.0 (2.0)	10.0 (2.0)	12.0 (3.0)	64.750	< 0.001*
	CG	47	9.0 (2.0)	10.0 (2.0)	10.0 (3.0)	29.068	< 0.001*

χ^2 Chi square of fried man test, n sample size in a group, *Mdn (IQR)* median inter quartile range, *AE* aerobic exercise group, *PRE* progressive resisted exercise group, *CG* control group

*Significant at $p<0.05$

Signed Rank Test revealed significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.72$, $r = 0.72$, $r = 0.86$) in the AE group. Similarly, there were significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.77$, $r = 0.87$, $r = 0.86$) in the PRE group. However, there was a significant difference with a moderate effect size between baseline and 12 weeks ($p = 0.002$, $r = 0.46$) in the CG.

Psychological domain

A Friedman test indicated significant differences across baseline, 6 weeks, and 12 weeks in AE and PRE groups ($p < 0.05$). Post hoc analysis using Wilcoxon Signed Rank Test revealed significant differences with moderate to large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.58$, $r = 0.87$, $r = 0.81$) in the AE group. Similarly, there were significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks ($p < 0.001$, $r = 0.71$, $r = 0.85$, $r = 0.80$) in the PRE group. However, there was no significant difference across CG ($p > 0.05$).

Level of independence domain

The Friedman test indicated significant differences across baseline, 6 weeks, and 12 weeks in the AE, PRE, and CG groups ($p < 0.05$). Post hoc analysis using Wilcoxon Signed Rank Test revealed significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.65$, $r = 0.86$, $r = 0.81$) in the AE group. Similarly, there were significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.81$, $r = 0.88$, $r = 0.84$) in the PRE group. However, there were significant differences with small effect sizes between baseline and 12 weeks ($p = 0.046$, $r = 0.29$) and between 6 and 12 weeks ($p = 0.035$, $r = 0.31$) in the CG.

Social relationship domain

The Friedman test indicated significant differences across baseline, 6 weeks, and 12 weeks in the AE and PRE groups ($p < 0.05$). However, there was no significant difference in CG. Post hoc analysis using Wilcoxon Signed Rank Test revealed significant differences with moderate to large effect sizes between baseline and 6 weeks, baseline and 12 weeks, 6 weeks and 12 weeks ($p < 0.001$, $r = 0.58$, $r = 0.76$, $r = 0.72$) in the AE group. Similarly, there were significant differences with moderate to large effect sizes between baseline and 6 weeks, baseline and 12 weeks, 6 weeks and 12 weeks ($p < 0.001$, $r = 0.59$, $r = 0.79$, $r = 0.76$) in the PRE group.

Environmental domain

A Friedman test indicated significant differences across baseline, 6 weeks, and 12 weeks in the AE and PRE groups ($p < 0.05$). Post hoc analysis using Wilcoxon Signed Rank Test revealed significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.70$, $r = 0.82$, $r = 0.78$) in the AE group. Similarly, there were significant differences with moderate to large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.55$, $r = 0.82$, $r = 0.80$) in the PRE group.

Spirituality/religion domain

A Friedman test indicated significant differences across baseline, 6 weeks, and 12 weeks in the AE, PRE, and CG groups ($p < 0.05$). Post hoc analysis using Wilcoxon Signed Rank Test revealed significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks, 6 weeks and 12 weeks ($p < 0.001$, $r = 0.76$, $r = 0.87$, $r = 0.82$) in the AE group. Similarly, there were significant differences with large effect sizes between baseline and 6 weeks, baseline and 12 weeks, and 6 weeks and 12 weeks ($p < 0.001$, $r = 0.63$, $r = 0.81$. $r = 0.73$) in the PRE group. However, there were significant differences with moderate to large effect sizes between baseline and 6 weeks, baseline and 12 weeks, 6 weeks and 12 weeks ($p = 0.006$, $r = 0.40$, $p < 0.001$, $r = 0.70$, $r = 0.62$) in the CG.

Differences in QOL domain scores between groups

Kruskall–Wallis U test was carried out to determine differences in QOL domain scores between groups at baseline, 6 weeks, and 12 weeks (Table 3).

Physical health domains

The test revealed statistically significant differences between groups at 12 weeks post-intervention ($p < 0.05$). Post hoc analysis using Mann–Whitney *U* test revealed significant differences with large effect sizes between the AE group and CG and between PRE group and CG ($p < 0.001$, $r = 0.76$, $r = 0.73$) at 12 weeks.

Psychological domain

The test revealed statistically significant differences between groups at 6 weeks and 12 weeks post-intervention ($p < 0.05$). Post hoc analysis using Mann–Whitney *U* test revealed

Table 3 Differences between groups on QOL domains at baseline, 6 weeks, and 12 weeks post-intervention

Variables	Time period	AE (n)	AE		PRE		CG		*p* value
			Mdn (IQR)	PRE (n)	Mdn (IQR)	CG (n)	Mdn (IQR)	χ^2	
Physical health	Baseline	45	10.0 (4.0)	44	9.0 (3.0)	47	10.0 (4.0)	3.909	0.142
	6 weeks	45	12.0 (3.0)	44	11.0 (3.0)	47	10.0 (4.0)	9.735	0.08
	12 weeks	45	15.0 (2.5)	44	14.0 (3.0)	47	10.0 (2.0)	69.196	< 0.001*
Psychological	Baseline	45	10.0 (3.0)	44	10.0 (2.4)	47	10.0 (2.0)	1.293	0.524
	6 weeks	45	11.2 (0.2)	44	11.2 (0.2)	47	10.2 (0.2)	17.848	< 0.001*
	12 weeks	45	14.4 (2.4)	44	13.0 (2.4)	47	10.0 (2.2)	71.180	< 0.001*
Level of independence	Baseline	45	10.0 (3.0)	44	10.0 (3.0)	47	10.0 (1.0)	0.066	0.967
	6 weeks	45	12.0 (3.0)	44	12.0 (3.0)	47	12.0 (3.0)	24.145	< 0.001*
	12 weeks	45	14.0 (2.5)	44	14.5 (2.75)	47	10.0 (1.0)	81.193	< 0.001*
Social relationship	Baseline	45	10.0 (4.0)	44	10.0 (4.0)	47	10.0 (3.0)	3.895	0.143
	6 weeks	45	12.0 (4.0)	44	10.0 (3.75)	47	10.0 (3.0)	21.301	< 0.001*
	12 weeks	45	14.0 (3.0)	44	12.0 (4.0)	47	10.0 (3.0)	47.042	< 0.001*
Environment	Baseline	45	11.0 (2.0)	44	10.0 (2.0)	47	10.5 (2.0)	5.877	0.053
	6 weeks	45	13.0 (2.0)	44	11.0 (2.0)	47	11.0 (2.0)	32.782	< 0.001*
	12 weeks	45	14.5 (2.5)	44	13.5 (2.0)	47	11.0 (2.0)	33.80	< 0.001*
Spirituality/religion	Baseline	45	9.0 (2.0)	44	9.0 (2.0)	47	9.0 (2.0)	2.440	0.295
	6 weeks	45	11.0 (3.0)	44	10.0 (2.0)	47	10.0 (2.0)	19.848	0.607
	12 weeks	45	15.0 (4.0)	44	12.0 (3.0)	47	10.0 (3.0)	48.856	< 0.001*

AE (n) sample size in the aerobic exercise group, *PRE (n)* sample size in the progressive resisted exercise group, *CG (n)* sample size in the control group, *Mdn (IQR)* median interquartile range, χ^2 Chi-square of Kruskall-Wallis test

*Significant at $p < 0.05$

significant differences with moderate effect sizes at 6 weeks between the AE group and CG ($p < 0.001$, $r = 0.41$), and between PRE group and CG ($p = 0.002$, $r = 0.33$). Similarly, there were significant differences with small to large effect sizes at 12 weeks between AE and PRE groups ($p = 0.042$, $r = 0.22$), AE group and CG ($p < 0.001$, $r = 0.74$), and PRE and CG ($p < 0.001$, $r = 0.76$).

Level of independence domain

The test revealed statistically significant differences between groups at 6 weeks and 12 weeks ($p < 0.05$). Post hoc analysis using Mann–Whitney *U* test revealed significant differences with moderate effect sizes at 6 weeks between the AE group and CG ($p < 0.001$, $r = 0.43$), and between PRE group and CG ($p < 0.001$, $r = 0.45$). Similarly, there were significant differences with large effect sizes at 12 weeks post-intervention between the AE group and CG ($p < 0.001$, $r = 0.82$), and between the PRE group and CG ($p < 0.001$, $r = 0.80$).

Social relationship domain

The test revealed statistically significant differences between groups at 6 weeks and 12 weeks ($p < 0.05$). Post hoc analysis using Mann–Whitney *U* test revealed that there were significant differences with small effect sizes at 6 weeks between AE and PRE groups ($p = 0.004$, $r = 0.21$) and moderate effect size between the AE group and CG ($p < 0.001$, $r = 0.48$). Similarly, there were significant differences with large effect sizes at 12 weeks post-intervention between the AE group and CG ($p < 0.001$, $r = 0.66$), and between PRE group and CG ($p < 0.001$, $r = 0.55$).

Environment domain

The test revealed statistically significant differences between groups at 6 weeks and 12 weeks post-intervention ($p < 0.05$). Post hoc analysis using Mann–Whitney *U* test revealed significant differences with moderate effect sizes at 6 weeks between AE and PRE ($p < 0.001$, $r = 0.42$), and between AE group and CG ($p < 0.001$, $r = 0.55$). Similarly, there were significant differences with moderate effect size at 12 weeks between AE and PRE groups ($p = 0.002$, $r = 0.33$), with large effect sizes between AE group and CG ($p < 0.001$, $r = 0.73$) and between PRE group and CG control ($p < 0.001$, $r = 0.62$), respectively.

Spirituality/religion domain

The test revealed statistically significant differences between groups at 12 weeks ($p < 0.05$). Post hoc analysis using Mann–Whitney *U* test revealed significant differences with

moderate effect size between AE and PRE groups ($p < 0.001$, $r = 0.49$), and with large effect size between AE group and CG ($p < 0.001$, $r = 0.68$), respectively.

Differences in QOL domain scores at baseline between completers and those that are lost to follow-up

A Mann–Whitney *U* test was carried out to find significant difference between completers and those that are lost to follow-up at baseline. The test revealed no significant difference between the two groups (Table 4).

Discussions

This study examined the effect of endurance and strength training program on QOL of PLWHIV-related DSPN. The results indicated significant differences between the groups in health status and level of education on socio-demographic characteristics. There were no strong reasons as to why the level of education and health status significantly differed among groups because all participants were randomized. In addition, this disparity may not have also affected the results of the study (whatsoever) because all the questionnaires were translated to local language as well as using an interpreter that is not part of the study to explain to those that could not read. The results of the present study showed that the groups were similar at baseline in the outcome measure and indicated significant differences from 6 weeks onward. The demonstrated improvements developed in a relatively short period and the exercise regimen of moderate intensity was well tolerated, safe, and beneficial to patients with HIV-related DSPN. This is line with the study of Stringer [22] on the effects of exercise training on aerobic fitness, immune indices, and QOL in PLWHIV, which observed improvement in the variable QOL following 6 weeks of exercise training. Endurance and strength training significantly improved QOL (all domains) when compared to the control group as measured using the WHOQOL-BREF scale in the present study.

The results from the previous studies indicated that exercise of moderate intensity has been proven to improve activity limitation and participation restrictions commonly among PLWHIV [23]. Mutimura and co-workers [24] concluded that regular physical activities help to promote self-esteem and confidence in health, improve psychosocial constructs of well-being, help to alleviate feelings of isolation, and improve QOL of PLWHIV on HAART.

The results of the present study also indicated significant improvement in the experimental groups at 6 weeks and 12 weeks. Statistically significant differences were observed between the AE group and CG, and between PRE and CG in all six domains of QOL. Similarly, statistically significant differences were also indicated between the AE and PRE in some domains with small effect size [Psychological (at 12 weeks), social relationship (at 6 weeks), environmental (at 6 weeks and 12 weeks), and spirituality/religion (at 12 weeks)]. The AE has the largest overall ranking that corresponds to the highest score in all domains. Though the significant differences observed between the experimental groups indicated small effect sizes, this does not mean that the differences have any practical significant especially in research with a large sample size like ours.

The results of this study are in line with the previous studies of Maharaj and Chetty [25] on the rehabilitation program for the quality of life for individuals on HAART. The results indicated significant improvements in all domains of QOL in cycling and treadmill walking training groups compared to the control group using the short-form health survey (SF-36). In their study, Anandh et al. [26] examined the effect of PRE on HR-QOL in PLWHIV. In the study, participants exercised for 30 min on alternate days (3 days per week) for three months and concluded that PRE improves QOL of PLWHIV using the Medical Outcome Study-HIV Health Survey (MOS-HIVHS). Galantino and colleagues [27] examined the effect of endurance training and Tai chi

Table 4 Differences between completers and lost to follow-up groups on QOL domains at baseline

Variables	Time period	Completers (n)	Completers Mdn (IQR)	Lost to follow-up (n)	Lost to follow-up Mdn (IQR)	U	*p* value
Physical health	Baseline	136	10 (3.0)	18	10 (3.0)	1005.500	0.215
Psychological	Baseline	136	10 (2.4)	18	10 (2.0)	894.500	0.061
Level of independence	Baseline	136	10 (3.0)	18	10 (3.0)	982.500	0.168
Social relationship	Baseline	136	10 (3.0)	18	10 (3.0)	800.000	0.016
Environment	Baseline	136	10.5 (2.0)	18	10 (2.0)	805.500	0.17
Spirituality/religion	Baseline	136	9 (2.0)	18	9 (2.0)	1012.500	0.224

Completers (n) sample size of the completers group, *Lost to follow-up (n)* sample size of the lost to follow-up group, *CG (n)* sample size in the control group, *Mdn (IQR)* median interquartile range, *U* Mann–Whitney *U* test

*Significant at $p < 0.05$

on functional outcomes and QOL for PLWHIV. The two experimental groups exercised for 8 weeks twice per week, while the control was a non-exercise control group. Both exercise groups improved in the overall QOL compared to control using the MOS-HIV scale. Similar to our findings was a study of Mkandla and co-workers [28] which indicated that a supervised progressive resisted exercise resulted in a positive effect on QOL among PLWHIV-related DSPN. All these findings are agreement with results of the current study in which significant improvement was found in all the domains of QOL by the use of moderate-intensity exercises at 6 and 12 weeks of intervention.

The result of the present study indicates significant differences in physical health, level of independence, and religion/spiritual domains within the CG. This effect could have been because some participants were used to trekking down to the clinic, and trekking has been proven to have a positive effect on the physical health and level of independence of individuals [29]. However, the improvement of the religious/spiritual domains in the CG could have been due to the strong belief of the people from the northern part of Nigeria where it is believed that life and death are from God. Our findings are in agreement with previous literature [30] which indicated that religious/spiritual domains are among the most important cultural factors that give meaning to human values, behaviors, and life experiences.

In addition, studies were also conducted on the religious commitment and health status of healthy individuals [31], and on the beliefs and attitudes of hospital inpatients about faith healing and prayer [32]. These studies indicated that 94% of patients regarded their spiritual health and physical health as equally important. In another study, Maugans and Wadland [33] also surveyed physicians and patients and found that more than 90% of the participants believed in a higher being. Moreover, a review by Mueller and co-workers [34] on religious involvement, spirituality, and medicine and implications for clinical practice concluded that the majority of patients have a spiritual life and regard their spiritual health and physical health as equally important and may also have greater spiritual needs during illnesses. Furthermore, the study also explained that there was a significant and growing direct relationship between religious involvement, spirituality, and positive health outcomes including mortality, physical illnesses, mental illness, QOL, and coping with illness (including terminal illness).

Conclusion

Despite the withdrawal of the most toxic drugs from recommended HAAT regimens, HIV-related DSPN remains a common neurological complication of HIV disease. Thus, it is important to have strategies as complementary/alternative therapies to improve QOL of PWHIV-related DSPN. Exercise regimens designed to improve QOL domains were well tolerated and improved all QOL domains in the intervention groups compared to CG. Therefore, exercise therapy is currently a promising option as a complementary therapy in the rehabilitation of PLWHIV-related DSPN.

Limitations

One of the limitations of the present study is the inability to use some diagnostic tools like EMG or nerve conduction study to determine the actual pathology of PLWHIV-related DSPN. This was due to the lack of standard diagnostic equipment in the environment where the study was conducted. Though the Brief Peripheral Neuropathy Screen questionnaire is a tool with validity and reliability for the diagnosis of HIV-related DSPN, the research findings may not be actually generalizable to PLWHIV-related DSPN due to the use of non-probability sampling. Participants should be followed up post-intervention to assess whether the level of physical activities increased following the exercise training. Other limitations of the present study were using only QOL as an outcome measure, some participants were used to trekking down to the clinic and trekking has been proven to have a positive effect on the physical health and level of independence of individuals, and also the long-term effect of the exercise was not assessed.

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Compliance with ethical standards

Conflict of interest The authors declare that they do not have any financial or personal relationship(s) which may have inappropriately influenced the study.

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