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Physical exercise, body composition, cholesterol, and triglycerides in the HIV patient: a meta-analysis

Renan Germano[1], Gustavo C. Fernandes[1], Tabatah H. G. Santos[2], Luiz H. S. Nali[3], Carolina N. França[3], Lucas M, Neves[1, 3, 4]

[1]Especialista em Treinamento de força - Escola de Educação Física e Esporte da Universidade de São Paulo – Laboratório de treinamento de força. [2] Graduanda em Educação Física – Universidade Santo Amaro – Unisa. [3]Docente Mestrado em Ciências da Saúde – Universidade Santo Amaro – Unisa.[4] Pesquisador do Programa de Transtorno Bipolar (PROMAN) do Instituto de Psiquiatria do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo – Ipq – HCUSP.

ABSTRACT

OBJECTIVE

To verify if the physical exercise is effective for improving body composition, total cholesterol and triglycerides in HIV patients.

METHODS

The present study is a systematic review with meta-analysis in order to investigate the effects of strength and / or aerobic exercise programs on HIV-positive individuals on body composition, total cholesterol and triglycerides. It is registered on the PROSPERO platform (International prospective register of systematic reviews) under number CRD42016043451. The PICOS research strategy was adopted, selecting the main MeSH terms for the search on Embase, Pubmed and Web of Science platforms. The results were tabulated, selected according to their relevance and classified in relation to the risk of bias.

RESULTS

10 studies were selected. Although several studies individually pointed to the improvement in the investigated variables, meta-analytical statistics did not show significance for the variables of body composition (body and visceral fat, BMI, WHR, lean mass) and total cholesterol, but in the triglycerides variable there was a significant change with a large effect size (TE) (TE1.36 [0.28, 2.44].

CONCLUSIONS

The strength exercise and the aerobic exercise, performed in an isolated or combined are effective for significantly improving the triglycerides variable in patients with the HIV virus under the treatment of highly active antiretroviral therapies.

DESCRIPTORS

Resistance training. Anthropometry. Immune system. Acquired immunodeficiency syndrome.

Corresponding author:
Lucas Melo Neves
Universidade de Santo Amaro, Universidade de Santo Amaro - Campus I.
Sala Mestrado Ciências da Saúde – Prédio F1
Rua Professor Enéas de Siqueira Neto, 340
Jardim das Imbuias
04829300 - São Paulo, SP - Brasil
E-mail: lmneves@prof.unisa.br
ORCID ID: 0000-0003-2426-9736

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INTRODUCTION

The human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS) is a serious public health challenge worldwide, despite widespread efforts to control the disease[1]. In the absence of a cure currently, treatment is carried out with antiretroviral therapy - ART (antiretroviral therapy, from English - ART)[2] and highly active antiretroviral therapy (from English - HAART)[3], which have prolonged the lives of carriers of the virus.

As a result of these therapies, changes in body composition and metabolic disorders of patients with HIV undergoing drug treatment are common[4-6], such as generalized obesity and changes in the distribution of body fat[7], dyslipidemia8 and lipodystrophy[9]. Such changes are associated with the risk of cardiovascular events[8,10], since the increase in visceral adipocytes is important in determining aspects relevant to health, such as obesity and overweight, highlighting the visceral adipose tissue as an important factor in increasing blood pressure, heart attack myocardium and insulin resistance[11].

Due to this problem, a strategy to avoid the increase of such adipocytes is to perform physical exercise, such as aerobic exercises that can contribute to the reduction of central and trunk fat[12], improving insulin sensitivity and dyslipidemia[13], strength exercises, that can increase lean mass, promote weight gain and muscle strength[14]. In addition, the combination of both (strength training and aerobic), indicate improvements in physical fitness and other health indicators[15].

Lindegaard et al[16] verified the effects of physical exercise in HIV patients, pointing to an increase in lean mass and a decrease in body fat, in addition to improvements in the lipid profile. However, Terry et al[17] detected improvements in body composition, but without significant differences for the lipid profile. Dolan and collaborators[18], when evaluating the body composition and lipid profile of 40 HIV female patients, did not detect improvements in body composition after a physical exercise program. Thus, there is no consensus on the effectiveness of exercise in improving body composition in patients with HIV undergoing antiretroviral treatment.

Given the above, the present study aims to verify in the scientific literature the effects of aerobic or strength exercise programs isolated or combined on body composition. In addition, verifying changes in the variables total cholesterol and triglycerides are also objectives of this study. Our hypothesis is that exercise programs will be effective in reducing body fat, total cholesterol, and triglycerides.

METHODOS

Systematic search record

This research was registered in the International prospective register of systematic reviews, PROSPERO platform, under number CRD42016043451: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42016043451.

Eligibility criteria

The studies were eligible for inclusion in this meta-analysis if they met the following criteria: a) HIV patients undergoing drug treatment undergoing ongoing ART (antiretroviral therapy) or HAART (highly active antiretroviral therapy); b) Randomized clinical trials (RCTs) with more than 4 weeks of duration, investigating the effect of isolated or combined aerobic or strength physical exercises (concurrent training); c) body composition measures [total body fat, visceral fat, total lean mass, body mass index (BMI), waist circumference (WC), hip circumference (QC) and waist-to-hip ratio (WHR)] before and after the intervention. In addition, measures of total cholesterol or triglycerides were also analyzed; d) include a non-active control group, such as usual care / usual treatment, control conditions on the waiting list, placebo pills, other social activities without physical exercises; and in peer-reviewed journals in English.

Sources of information and research

The following databases were used: Embase, PubMed and Web of Science and the period of publication adopted was between January 2006 and December 2015.

Search

The 3-step model of evidence-based medicine was adopted for the search: formulation of a clinical question, search for evidence and evaluation of the same19. Then, the search was structured considering the PICOS strategy, which consists of subdividing the study question into the following domains: population (P), intervention (I), control or comparison (C), outcomes or variables (O) and type of study (S), forming the acronym PICOS. In this way, individual searches for these domains are carried out, concatenating them in a final search with the Boolean operator "AND". English subject terms (medical subject headings - MeSH terms) were selected on the MeSH platform (http://www.ncbi.nlm.nih.gov/mesh) as described below. MeSH is the dictionary of vocabularies and synonyms controlled by NLM, used for indexing articles for PubMed. P: acquired immune deficiency syndrome OR acquired immuno-deficiency syndrome OR acquired immuno deficiency syndrome OR acquired immuno-deficiency syndromes OR aids OR human immunodeficiency virus OR human immunodeficiency virus, human OR immunodeficiency viruses, human OR virus, human immunodeficiency OR aids virus OR aids viruses OR virus, AIDS OR hiv; I: strength training OR resistance training OR weight training OR progressive training OR progressive resistance OR aerobic exercise OR aerobic training OR endurance exercise OR endurance training OR cardio training OR cardio exercise OR physical endurance OR physical exercise OR physical exertion OR exercises, physical; C: not used in the present study, aiming at a wider range of searches, not discarding articles with or without some type of comparison. O: fat body OR fat body composition OR body weight OR trunk fat OR visceral fat OR dexa OR abdominal fat OR regional adiposity OR adipose tissue OR fat tissue OR body fat distribution OR distribution, body fat OR fat loss OR weight loss; S: allocation, random OR randomization OR clinical trials, randomized OR randomized clinical trial OR randomized controlled study.

Analysis of the quality of clinical trials and risk of bias in each study

To assess the methodological quality of the studies, we adopted the modified Jadad scale[20], which assigns 1 point to the study description, blinding and loss and exclusion report fields, in addition to 1 additional point for the fields that assess whether the method it was adequate. Studies with a low methodological quality are classified as scoring less than 2 points in total. To analyze the risk of bias in each study, the Cochrane Collaboration tool[21] was used, where the studies are critically evaluated in 7 domains by the authors for different aspects of the risk of bias[22].

Selection of studies

After removing duplicates from different databases, the authors (RG and GC) selected all potentially eligible articles based on titles and abstracts. After obtaining the full texts, the authors applied the eligibility criteria. If there was no consensus, the third author (LMN) evaluated the case and defined its inclusion / exclusion. In all studies, they extracted the number of subjects, the mean and standard deviations of the experimental and control groups to calculate the effect size (ES), standard error of the ES, lower confidence limit for ES, upper confidence limit for ES, Study weight and Study sample size.

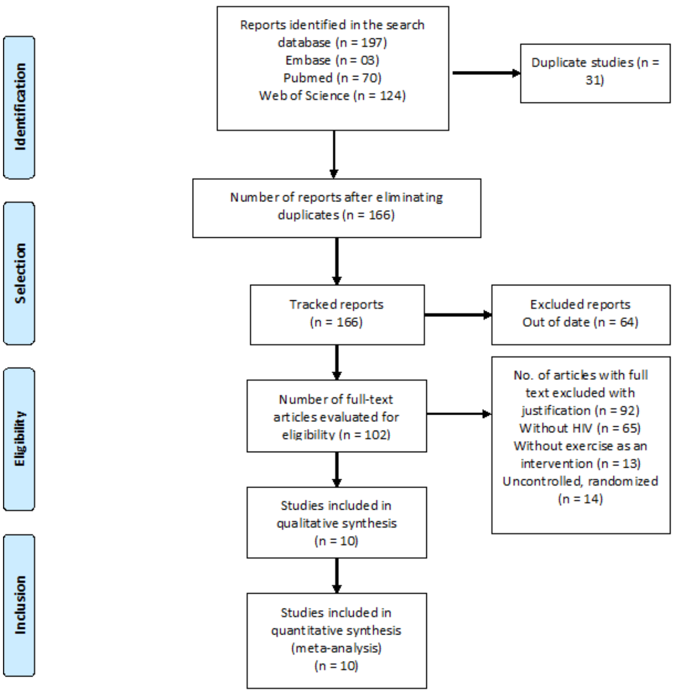
Statistical analysis

All analyzes were conducted using the Comprehensive Meta-analysis software version 2.2 (Biostat Inc., Englewood, NJ, USA). Based on the results, the data were analyzed using random-effect models. The interpretation of the effect size (TE) was: 0 to <0.30 | small, |> 0.30 | for | <0.8 | average and |> 0.80 | wide.

RESULTS

Selection of studies

Below is presented the process of identification, extraction, and selection of studies through the flowchart Consort[23].



Flowchart 1. CONSORT flowchart with systematic selection of studies.

In the initial search, 197 potentially relevant articles were identified. After removing duplicates (31 articles), our research identified 166 potentially relevant articles. Of the remaining 166 articles, 64 studies published before 2006 were excluded. Thus, 102 articles in the full text review stage were accessed, with 92 studies being excluded [samples without HIV (n = 65); studies without exercise as an intervention (n = 13); Uncontrolled or randomized studies (n = 14). Thus, 10 complete peer-reviewed studies that met the eligibility criteria were included in our meta-analysis (16-18, 24-30).

Methodological quality

Table 1 and Figure 1 show the selected studies compiled regarding their methodological quality and their risk of bias, respectively, and classifies aspects of the experimental design of the studies considering: low, uncertain, or high risk of bias.

Table 1. Studies compiled regarding methodological quality and risk of bias.

Study	Was the study described as random? (use of words such as random, random, randomization)	The method was adequate?	The study was described as double-blind?	The method was adequate?	There was a description of losses and exclusions?	TOTAL
Terry L, et al., 2006	Yed	No	No	No	Yes	2
Mitimura E, et al.,2008	Yes					2
Mitimura E, et al.,2008b	Yes	No	No	No	Yes	2
Balasubramanyan A, et al., 2011	Yes	No	No	No	Yes	5
Ogalha C, et al.,2011	Yes	Yes	Yes	Yes	Yes	2
Yarasheski KEC, et al.,2011	Yes	No	No	No	Yes	3
Roos RM, et al., 2014	Yes	Yes	No	No	Yes	4
Dolan SE, et al.2006	Yes	Yes	No	Yes	Yes	3
Hamid M, et al.,2015	Yes	Yes	No	No	Yes	3

Adapted from Jadad[20].

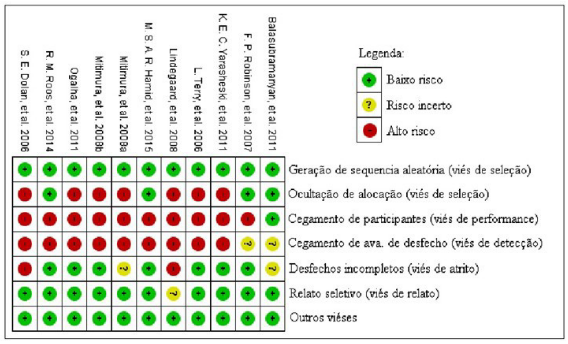


Figure 1. Assessment of the risk of bias in the studies presented by the authors and their respective results.

Table 2 shows the studies of interest compiled regarding the sample (number of subjects and percentage of women), type of intervention (type of training performed in the intervention group, intervention weeks and activities developed by the control group), synthesis of the tests performed (cholesterol and fraction measurements, and body composition - waist and hip circumference and waist-to-hip ratio, BMI, fat percentage, lean mass, and their results.

Table 2. Studies of interest compiled regarding the sample, interventions, tests performed, pre and post values, percentage o f change Total sample (N); standard deviation (sd); measured through skinfolds (CD); measured by dual emission X-ray absorptiometry (DEXA); measured through bioimpedance (BI); maximum oxygen consumption (VO2max); maximum beats per minute (max bpm); weeks.

Authors	N % woman	Age (dp)	Intervention	Variables analyzed	Pre control group	Post control group	%Δ	Pre exercise group	Post exercise group	%Δ
Terry L, *et al*, 2006	30 (30)	37,5 2,1	Experimental: diet + exercise - low fat + 12 wk. aerobic exercise Control: diet - low fat + 12 wk. stretching	Cholesterol	256	251	-2,0	256	243	-5,1
				Body fat (DC)	23	19	-17,4	27	22	-18,5
				BMI	24	23	-4,2	25	24	-4,0
				RCQ	0,94	0,91	-3,2	0,91	0,90	-1,1
				Triglycerides	338	346	2,4	325	296	-8,9
				Cholesterol	220	219,6	-0,2	229,3	223,5	-2,5
Lindegaard B, *et al, 2008*	18 (0)	49,5 (5,1)	Experimental: aerobic training: 16 weeks, 3x weeks, interval (35 min. Duration), intensities between 50 - 100% VO2max. Control: strength training: 16 weeks, 3x weeks, 8 exercises (12 - 8 reps / 50% - 80% / 1-2 min. Interval	Body fat (DEXA)	18,6	15,3	-17,7	19,5	18,5	-5,1
				Lean mass	77,5	79,3	2,3	76,4	77	0,8
				Triglycerides	186	152,3	-18,1	212,5	212,6	0,0
Mutimura E, *et al.*2008ª	97 (60)	37,7 (0,2)	Experimental: aerobic + strength: 6 months, 3x sem., 1.5 hours per training, stretching, 15 min. walking + 45 - 60 min. jogging and running (45% - 75% bpm max), climbing, lumbar and abdomen stabilization. Control: without performing exercises	Circ. Waist	83.1	83.8	0.8	91	83.8	-7.9
				Circ. Hip	93,7	93,9	0,2	92,3	93,4	1,2
				Cholesterol	150,4	152,7	1,5	146,1	147,3	0,8
				Body fat (DC)	29,3	29,1	-0,7	29,4	27,9	-5,1
				BMI	24,4	24,5	0,4	24	23,4	-2,5
									86,6	5,5
				RCQ	0,98	0,98	0,0	0,99	0,89	-10,1
				Trigriceridae	118,6	124,9	5,3	117,8	98,3	-16,6
Mutimura E, *et al. 2008b*	100 (100)	37,7 (0,2)	Experimental: aerobic + strength: 6 months, 3x sem., 1.5 hours per training, stretching, 15 min of walking + 45 - 60 min jogging and running (45% - 75% bpm max), climbing, lumbar and weight stabilization abdomen. Control: without performing exercises	Circ. Waist	92	92,3	0,3	91	83,9	-7,8
				Circ. Hip	93,7	93,9	0,2	92,3	93,4	1,2
				Body fat	29,3	29,1	-0,7	29,4	27,9	-5,1
				BMI	24,5	24,6	0,4	24	23,4	-2,5
Balasubramanyan A, *et al.* 2011	97 (60)	37,7 (0,2)	Experimental: diet + exercise + medication - weight maintenance diet + aerobic exercise programs + strength, 3x wk. lasting between 75 - 90 min. Control: guidance on healthy diet, 1 week food diary with later feedback and a guide on general exercises.	Cholesterol	214,4	195,6	-8,8	207,9	178,4	-14,2
									44,8	11,7
				BMI	26,3	26,9	2,3	27,2	26,7	-1,8
				Triglycerides	313,5	199	-36,5	283,1	135,6	-52,1

Ogalha C, *et al.* 2011	63 (43)	43,1 0,7	Experimental: aerobic + strength + stretching: nutritional monitoring and exercises in a supervised gym, 3x without. for 24 weeks. Control: 1 month of workshops with 1h. duration on the importance of physical activity and nutritional guidance.	Circ. Hip	78,7	78	-0,9	82.0	80,8	-1,5
				Cholesterol	189,8	186,8	-1,6	222,72	203,7	-8,5
				Body fat (DC)	20,1	21,5	7,0	21,5	19,9	-7,4
				BMI	23	22,7	-1,3	22,9	22,3	-2,6
				Lean mass	54,2	56	3,3	56,6	59,7	5,5
				RCQ	0,85	0,84	-1,2	0,84	0,85	1,2
				Triglycerides	187,4	204,3	9,0	190,2	172,1	-9,5
Roos RM, *et al.* 2014	84 (79)	39,1 9,6	Experimental: aeróbio: 12 meses, caminhadas leves e moderadas, 30 min., 3 - 5 x por sem. Controle: apoio clínico e monitoramento mensal sobre condições de saúde.	Circ. waist	80	79,9	-0,1	81	81,6	0,7
				Hip Circ	103,5	103	-0,5	104,2	104,7	0,5
				Cholesterol	168,2	160,1	-4,8	166,6	165,9	-0,4
									58,3	6,2
				BMI	25,4	26,8	5,5	25,8	27,4	6,2
									89,7	-5,3
				RCQ	0,77	0,77	0,0	0,78	0,77	-1,3
				Triglycerides	90,3	93	3,0	86,7	88,5	2,1
Dolan SE, *et al.* 2006	40 (100)	41,5 2,1	Experimental: aerobic + strength: 16 weeks, 48 sessions, 2 hours. per session. Control: without performing exercises.	Circ. Waist	99	100	1,0	103,8	103	-0,8
				Cholesterol	162	162	0,0	191	189	-1,0
				Body fat (DEXA)	27,8	27,1	-2,5	28,7	28,5	-0,7
				Visceral fat	111	119	7,2	142	140	-1,4
									51	-1,9
				BMI	28,6	28,5	-0,3	29,3	29,7	1,4
									109	-2,7
				Triglycerides	107	107	0,0	141	147	4,3
Hamid M, *et al.* 2015	29 (0)	41,7 6,2	Experimental: 12 weeks, exercises with Thera-Band. Control: 12 without, similar exercises without Thera-Band.	Body fat (BI)	20,5	21,1	2,9	17,4	16,9	-2,9
					79,9	79,3	-0,8	82,6	83,1	0,6
				Lean mass	18,4	18,3	-0,5	19	19,7	3,7
Yarasheski KEC, *et al.* *2011*	39 (100)	45 (1,4)	Experimental: aerobic + strength + medication - 4 months of Pioglitazone, intervention with 1.5 - 2h. of exercises per day, 3x without. Control: medication: 4 months of Pioglitazone.		189.5	177.9	-6.1	181.7	174	-4.2
				BMI	27,3	27,9	2,2	26,5	25,6	-3,4
				Cholesterol	1,93	2	3,6	1,9	1,75	-7,9
				Body fat						2,9
				Visceral fat						-3,7
					72,7	72,1	-0,8	73,5	74,4	1,2
					203,7	221,4	8,7	186	159,4	-14,3

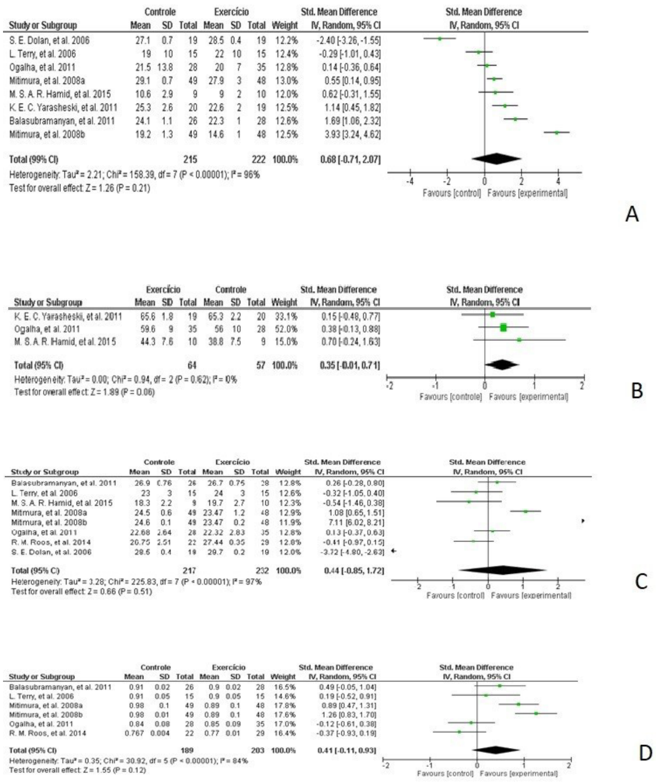


Figure 2. (Forest plot) Body composition variables - Figure 2A: Total body fat; Figure 2B: Lean Mass; Figure 2C: BMI; Figure 2D: Waist-hip ratio-CRQ.

All studies reported body composition variables, with 8 studies using total body fat as a variable (Figure 2A). Totaling 437 patients (215 patients in the control group and 222 patients in the intervention group), there was no significant difference between the groups [TE0.68 (CI: -0.71, 2.07)], with a heterogeneity of 96% (high).

Only 3 studies used lean mass as a variable (Figure 2B). Totaling 121 patients (64 patients in the control group and 57 in the intervention group), there was no significant difference between the interventions [TE0.35 (CI: -0.01, 0.71)], with a heterogeneity of 0% (low).

Eight studies were verified that used BMI as a variable (Figure 2C). Totaling 449 patients (217 patients in the control group and 232 patients in the intervention group), no significant difference was found between the interventions [TE 0.44 (CI: -0.85, 1.72)], with a heterogeneity of 97% (high).

Six studies were verified that used WHR as a variable (Figure 2D). Totaling 392 patients (189 patients in the control group and 203 patients in the intervention group), there was no significant difference between the interventions [TE 0.41 (CI: -0.11, 0.93)], with a heterogeneity of 84% (discharge).

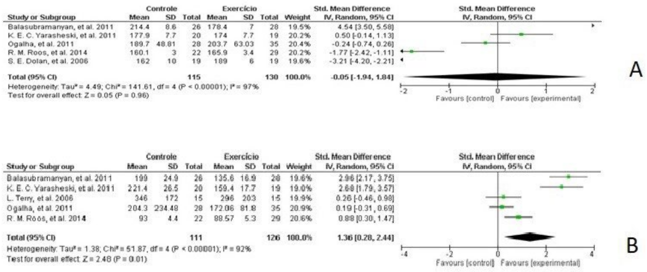


Figure 3. (Forest plot). Variables total cholesterol (Figure 3A) and triglycerides (Figure 3B).

Five studies were found that used total cholesterol as a variable (Figure 3A). Totaling 245 patients (115 patients in the control group and 130 patients in the intervention group), no significant difference was found between the interventions [TE -0.05 (CI: -1.94, 1.84)], with a heterogeneity of 97% (discharge).

Five studies were found that used triglycerides as a variable (Figure 3B). Totaling 237 patients (111 patients in the control group and 126 patients in the intervention group), a significant difference was found between the groups [TE 1.36 (CI: 0.26, 2.44)], with a heterogeneity of 92% (discharge).

DISCUSSION

The present study verified in the scientific literature whether strength training and aerobic training (combined or isolated) promote improvements in body composition, total cholesterol, and triglycerides in HIV patients. It encompassed 10 studies, compiling a sample of 572 participants with an average age of 41.9 years and an average infection time of 8.8 years, of which 62% were women. The interventions were carried out for periods between 12 and 48 weeks, showing no effectiveness in mitigating the increase in fat.

Despite the potential of physical exercise programs to positively alter body composition, there was no significant effect on the variables body fat [TE0.68 (CI: -0.71, 2.07)], lean mass [TE0.35 (CI: -0.01, 0.71)], BMI [TE 0.44 (IC: -0.85, 1.72)], WHR [TE 0.41 (IC: -0.11, 0.93)]. In addition, there was no change in total cholesterol [TE -0.05 (CI: -1.94, 1.84)]. The triglyceride variable showed a significant change of great magnitude (TE> 1) in favor of the intervention group [TE 1.36 (CI: 0.26, 2.44)].

Although most variables have no significant effect on the meta-analytical analysis, some important considerations about the results should be made considering the individual data from these studies. Regarding body fat, Terry, and collaborators[17], Mutimura and collaborators[24] and Ogalha and collaborators[27] found significant decreases in percentage terms, in the order of 18.5%, 5.1%, and 7.4 % respectively, which may reflect clinical improvements. Cavalcanti et al.[31] pointed out that the minimum detectable difference (MDD) for body fat measured by dual emission X-ray absorptiometry[8] is 4.3% or 628 grams for HIV + individuals with lipodystrophy. An MDD means the smallest difference in individual scores that represent true changes that go beyond the standard error of the measurement. Thus, studies that include scores within this range may represent clinical improvements for individuals. In addition, the differences between the results obtained may result from the evaluation method used. Studies that used DEXA to assess body fat[16, 18, 30] showed variations in the range of 20% to 0.7% for this variable. Such variations may result from the type of sample, since in some studies[16-18, 25, 29, 30] it was composed only of men or women, while in the other selected works they were of a mixed sample. Studies indicate that women have a higher proportion of fat mass and a greater amount of fat in the subcutaneous compartments compared to men[32], which may explain part of this difference between studies. Regarding the studies that used the method of summation of skinfold thickness[17, 24, 25], although it is a doubly indirect method for estimating body fat, it is validated and very useful in research or in patient monitoring services. where there is no imaging equipment33.

In fact, Florindo et al.[33], in a study to validate a method of estimating body fat in HIV / AIDS patients by comparing the values provided by DEXA with the sum of the thickness of skinfolds and body circumferences, found positive correlation (r≥0.80) for total subcutaneous fat (by summing the thickness of 7 folds), central subcutaneous fat (summing up the thickness of 4 folds) and subcutaneous limb fat (summing up the thickness of 3 folds) finding also correlation between waist circumference with subcutaneous and total abdomen fat, and waist / hip ratio and the sum of subcutaneous fat folds in the central region with total abdomen fat.

Regarding the waist-to-hip ratio (RCQ), Terry and collaborators[17], Mutimura and collaborators[24, 25], and Roos and collaborators[28], showed decreases of 1.1%, 10.1%, 10.1% and 1.3%, respectively, which are important because WHR has a positive correlation (r≥80) with total abdomen fat, which accumulation may represent an increase in cardiovascular risk in addition to being associated with hyperinsulinemia[34].

As for waist circumference, Mutimura and collaborators[24, 25], and Dolan and collaborators[18], showed significant decreases of 7.9%, 7.8% and 0.8% respectively, while Roos and collaborators[28], showed increases of 0.7%. Regarding BMI, an interesting fact is that the study by Hamid et al.[29], even with increases, has a BMI below that found in other studies[35, 36] and according to the recommendations established by the World Health Organization (WHO)[37].

Regarding the triglyceride variable, there were reductions in favor of the physical exercise group of up to 16%, which is the most relevant finding in this study. The potential for exercise to reduce triglycerides regardless of significant weight change has already been demonstrated in a recent meta-analysis, but the benefits are substantially greater when weight loss occurs[38]. Consequently, although physical exercise alone can be effective in reducing triglycerides, the greatest benefits occur when exercise interventions contribute to weight loss, which indicates that other strategies combined with exercise, such as restriction of dietary energy, can be important, and future studies should verify this issue in patients with the HIV virus. In addition, the use of protease inhibitors decreases the expression of adipocyte markers, which may cause an increase in circulating triglycerides[39].

CONCLUSION

Based on the evidence presented, we point out that strength exercise and aerobic exercise, performed in an isolated or combined manner, were not effective in changing variables related to body composition and total cholesterol in patients with HIV, however an important change was seen in the variable triglycerides.

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