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ASSOCIAÇÃO ENTRE ATIVIDADE FÍSICA E SÍNDROME LIPODISTRÓFICA EM PACIENTES COM HIV/AIDS

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Orientadora: Profª. Drª. Sandra Costa Fuchs

PORTO ALEGRE, 2010

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SUMÁRIO

APRESENTAÇÃO

O artigo 1 apresenta uma revisão sistemática da literatura a fim de determinar a prevalência de atividade física em indivíduos infectados pelo HIV. Nossa hipótese era que esses indivíduos, devido ao quadro infeccioso e comorbidades, fossem menos ativos que a população em geral. Para testar tal hipótese pretendíamos calcular uma medida sumarizada de prevalência, através de metanálise, e comparar com dados para a população geral. Contudo, a variabilidade de métodos de aferição de atividade física, escassez de artigos sobre o tema e qualidade metodológica insuficiente dos artigos encontrados não permitiu a realização de metanálise, sendo apresentada uma revisão sistemática qualitativa.

O artigo 2 apresenta estudo metodológico sobre a análise de dados para quantificação de atividade física, medida por acelerômetro. Essa questão de pesquisa tornou-se relevante face a necessidade que tomarem-se decisões, na ausência de orientações padronizadas em diretrizes nacionais ou internacionais sobre uso do equipamento e suas repercussões na análise e interpretação dos dados.

O artigo 3 descreve a prevalência de atividade física entre os indivíduos participantes desse estudo, haja vista a conclusão do artigo de revisão sistemática. A mensuração de atividade física foi feita por meio de questionário e, em subamostra, por medida direta com uso de acelerômetro. A coleta de dados foi feita em amostra representativa da população e utilizaram-se métodos adequados para estudos populacionais.

O artigo 4 analisou a associação entre atividade física e síndrome lipodistrófica do HIV, com ênfase em hipertrofia e alterações metabólicas no perfil lipídico e glicêmico. Essa comorbidade tem ganhado importância e destaque nos últimos anos, mas há poucos artigos avaliando essa associação.

INTRODUÇÃO

A infecção pelo vírus HIV e a AIDS constitui problema de saúde pública devido ao número de casos notificados, à expectativa prolongada pelo tratamento e ao impacto social e econômico nos países atingidos devido à doença e suas complicações. Segundo dados da Organização Mundial de Saúde, a estimativa mundial de pessoas infectadas pelo HIV ou doentes de AIDS ao final de 2008 era de 33,4 (30,6 – 36,1) milhões entre adultos e crianças. A América Latina é o terceiro continente em número de casos de AIDS[1]. No Brasil, segundo dados do Ministério da Saúde, a taxa de incidência em 2008 era de 18,2 casos por 100 mil habitantes. Desde 1980 até novembro de 2009 foram notificados 544.846 casos de AIDS, mais de 200 mil óbitos, e estima-se que existam 700 mil portadores do HIV no país[1, 2]. Somente no Rio Grande do Sul, até novembro de 2009, havia 52.245 casos de AIDS notificados[2].

Com o advento da terapia antirretroviral potente (TARV), o perfil epidemiológico da infecção pelo HIV, que ocasionava doença aguda e com sobrevida reduzida, passou a ser o de doença crônica, tornando os indivíduos infectados em risco de desenvolver doenças não transmissíveis, em particular as cardiovasculares. Além disso, reverteram os efeitos imunossupressores inerentes a história natural da doença[3, 4].

Entre os efeitos adversos atribuídos ao tratamento antirretroviral e também a própria infecção, destacam-se os associados à redistribuição anormal de gordura e alterações metabólicas[5, 6]. Na tentativa de prevenir ou minimizar tais efeitos, diversos estudos têm investigado o papel do exercício agudo e, até mesmo, da atividade física. Contudo, frequentemente, os artigos incluem número reduzido de pacientes e limitações metodológicas impossibilitam a extrapolação dos resultados e a investigação de associações.

REVISÃO DA LITERATURA

A infecção pelo HIV e a AIDS

A infecção pelo HIV é clinicamente um processo trifásico, caracterizado por infecção aguda, fase clínica assintomática e fase crônica. A história natural da doença, dependente da imunossupressão, pode ser diretamente avaliada pela diminuição das subpopulações linfocitárias, especificamente de linfócitos CD4+[7]. Os linfócitos CD4+ são o alvo primário da infecção pelo HIV, e seu declínio correlaciona-se com a progressão clínica[8, 9]. A AIDS é a fase da doença na qual ocorrem infecções oportunistas e/ou doenças neoplásicas, com sintomas e complicações graves, ou seja, é a fase na qual ocorrem as manifestações clínicas da falência imunológica. Embora avanços significativos tenham sido feitos no tratamento da AIDS e de suas complicações, ela ainda persiste como doença fatal[10].

Tratamento antirretroviral

O principal objetivo da terapia antirretroviral é diminuir a replicação viral, contribuindo para reduzir a destruição celular, principalmente de células T-CD4+. Tal tratamento possibilita ao paciente, durante determinado período, melhor condição imunológica e menor risco de vir a desenvolver as complicações da doença, proporcionando-lhe melhor prognóstico e qualidade de vida. A terapia antirretroviral atual consiste de cinco classes de medicamentos: inibidores da transcriptase reversa análogos de nucleosídeos (ITRN), inibidores da transcriptase reversa não-análogos de nucleosídeos (ITRNN), inibidores da protease (IP), inibidores de entrada ou de fusão e inibidores de integrase[11].

A terapia com combinações de, pelo menos, três drogas antirretrovirais é conhecida como terapia antirretroviral potente (TARV), ou *highly active antiretroviral therapy* (HAART), causou impacto na história natural da infecção pelo HIV, obtendo-se controle da elevação da carga viral e redução da morbimortalidade pelo HIV em proporção considerável[12, 13].

Contudo, a TARV apresenta efeitos adversos, incluindo alterações metabólicas, como resistência insulínica, síndrome metabólica; ou morfológicas, como lipodistrofia e, em consequência das anormalidades, maior risco de doenças cardiovasculares[6, 14, 15]. Essas alterações foram definidas como síndrome lipodistrófica do HIV, a qual tem sido associada à utilização dos IP e ITRN, mas cuja fisiopatologia ainda não está totalmente elucidada[16-18]. À medida que os portadores de infecção pelo HIV sobrevivem e mantêm-se em tratamento por períodos cada vez mais prolongados, eleva-se o risco de desenvolvimento de doenças não transmissíveis, particularmente doenças cardiovasculares[19].

Além disso, cabe ressaltar que a lipodistrofia, seja causada pela infecção pelo HIV ou pelo uso de TARV, amplia o estigma da doença, já que alguns sinais são visualmente identificáveis, e podem reduzir a adesão ao uso desses medicamentos[20, 21].

Síndrome lipodistrófica do HIV

Redistribuição anormal de gordura:

O uso de TARV está associado a mudanças na distribuição da gordura corporal e alterações do perfil lipídico e glicêmico. Estas alterações foram posteriormente denominadas de síndrome lipodistrófica do HIV (podendo apresentar outras denominações) descrita oficialmente em 1997 pelo *Food and Drug Administration*, órgão norte-americano regulador da liberação e uso de medicamentos[22]. A síndrome lipodistrófica do HIV pode ser melhor caracterizada pela perda de depósitos de gordura periférica (lipoatrofia) e/ou acúmulo de gordura central (lipo-hipertrofia), ou anormalidades metabólicas lipídicas e glicêmicas[23].

Em relação às alterações de composição corporal, os pacientes com AIDS apresentam acúmulo de gordura no tecido subcutâneo, em vísceras abdominais, nas regiões abdominal e cervical (atrás do pescoço, conhecida por gibosidade dorsal), além de ginecomastia e aumento das mamas em mulheres[24, 25]. Contudo, ocorre perda de massa muscular e óssea, com diminuição da gordura nas extremidades superiores e inferiores, tais como braços, pernas, face e glúteos[26]. Não há uma definição única para as diferentes formas de lipoatrofia ou lipo-hipertrofia; por esse motivo, há grandes variações nas taxas de prevalência, oscilando entre 11 e 83%[16, 24, 27]. Entre os fatores associados, destacam-se gênero, idade, classe de antirretroviral e duração do uso de TARV[27]. Não há consenso sobre critérios diagnósticos mais apropriados para detectar lipodistrofia associada ao HIV, mas os mais utilizados são essencialmente clínicos, incluindo o autorrelato do paciente sobre acúmulo de gordura no tronco, perda de tecido adiposo na face ou nos membros, ou pela observação clínica do médico[16, 28].

Recentemente, uma definição de caso foi proposta e validada pelo *Lipodistrophy Case Definition Study Group*, baseada em um estudo caso-controle, que identificou dez variáveis para compor um escore diagnóstico e de gravidade para lipodistrofia: gênero, idade, duração da infecção pelo HIV, estágio da infecção pelo HIV, relação da circunferência cintura/quadril, ânion *gap*, nível sérico de colesterol HDL, gordura em membros inferiores, relação de gordura tronco/membros, relação de gordura intra-abdomina/abdominal superficial. Juntamente com exames de imagem, como

DEXA (*dual-energy X-ray absorptiometry scan*) ou tomografia computadorizada, obtiveram sensibilidade de 79% e especificidade de 80% para o diagnóstico de lipodistrofia[29]. Entretanto, os exames de imagem apresentam alto custo e difícil acesso para pacientes da rede pública, inviabilizando seu uso como método diagnóstico.

Além disso, alguns autores determinaram que a lipoatrofia ocorre mais precocemente do que a lipo-hipertrofia[30] e a lipoatrofia nem sempre está associada ao aumento de gordural visceral[31, 32].

Entre os mecanismos fisiopatológicos propostos para explicar a síndrome lipodistrófica do HIV estão a disfunção mitocondrial, que leva à apoptose de células adiposas, sendo a explicação causal da lipoatrofia, geralmente associada ao uso de ITRN; a inativação de fatores de transcrição adipogênica, que aumenta os níveis glicêmicos e gera resistência à insulina (mais associada ao uso de IP); e a influência de citocinas pró-inflamatórias, como o fator alfa de necrose tumoral, na lipogênese e lipólise corporal[24, 27, 33].

Alterações metabólicas:

A lipodistrofia associada ao HIV ocasiona distribuição anormal de gordura corporal e alterações metabólicas, como: resistência à insulina, elevação dos níveis de triglicerídeos, colesterol total e lipoproteína de baixa densidade (LDL), redução dos níveis de lipoproteína de alta densidade (HDL), e hiperglicemia ou diabetes[16, 24, 34]. Essas alterações estão fortemente associadas ao aumento de risco cardiovascular, tanto na população em geral como nos indivíduos infectados pelo HIV, e apresentam semelhanças com as detectadas na síndrome metabólica. Aproximadamente um terço dos pacientes infectados pelo HIV, nos Estados Unidos, apresenta síndrome metabólica, o que aumenta em duas vezes a chance de um evento cardiovascular como infarto agudo do miocárdio ou acidente vascular cerebral[35]. É importante destacar a associação da síndrome metabólica com doença cardiovascular, aumentando a mortalidade geral em cerca de 1,5 vezes e a cardiovascular em cerca de 2,5 vezes[36].

O *Frankfurt Cohort Study* realizou estudo retrospectivo com 4.993 indivíduos infectados pelo HIV e em uso de TARV, e verificou aumento na taxa de incidência de infarto agudo do miocárdio de 0,86/1.000 pacientes-ano, entre 1983 e 1986, para 3,41/1.000 pacientes-ano entre 1995 e 1998, período pós introdução da TARV[37]. Outro trabalho, *The Data Collection on Adverse Events of anti-HIV Drugs (DAD) study group*, acompanhou 23.468 pacientes, dos quais 0,5% tiveram infarto agudo do miocárdio associado ao uso de TARV[38].

O tratamento da síndrome lipodistrófica inclui mudanças no estilo de vida, como baixa ingestão calórica, aumento da atividade física, redução do consumo de álcool e cessação do tabagismo. Entretanto, essas mudanças isoladas nem sempre afetam os níveis lipídicos. Estudo de intervenção nutricional com 83 indivíduos infectados pelo HIV em início de tratamento concluiu, após 12 meses de acompanhamento, que o grupo com intervenção dietoterápica apresentou menor percentual de dislipidemia quando comparado ao grupo controle, com redução da ingestão de calorias e gorduras, e redução dos níveis de triglicerídeos[39]. Em alguns pacientes, há necessidade de alteração no esquema terapêutico, mas é necessário avaliar a relação risco-benefício[40]. Também tem sido discutida a utilização de hormônios androgênicos, esteróides e de crescimento para reduzir o desenvolvimento da lipodistrofia e restaurar a massa muscular[34, 41]. Fármacos hipoglicemiantes, hipotrigliceridêmicos e hipocolesterolemiantes têm sido utilizados para melhorar o perfil lipídico e glicêmico dos indivíduos infectados pelo HIV e em uso de HAART[16].

Exercício e Atividade física

Vários estudos têm sugerido que a atividade física aeróbica é segura e benéfica para adultos que vivem com HIV/AIDS. Além de ter sido associada a maior qualidade de vida[42], pela redução de sintomas depressivos[43, 44], risco cardíaco[45], foi considerada fator protetor para a síndrome de redistribuição de gordura corporal[46, 47]. Também foi verificada redução na carga viral plasmática[48] e sugerida a minimização de efeitos deletérios do estresse oxidativo[49]. Entretanto, tornam-se necessários estudos com maior tamanho amostral e maior poder estatístico para confirmar essas associações[50, 51].

Antes da introdução do TARV, os estudos envolvendo exercício físico e HIV tinham o foco nos sistemas imunológico e cardiovascular. Estudos com pacientes soronegativos mostraram que o exercício moderado parecia aumentar a imunidade, contrastando com o observado em indivíduos maratonistas, que expostos a exercícios de alta intensidade sofriam de imunossupressão temporária e maior prevalência de infecções de trato respiratório superior. A ausência de uma curva dose-resposta no efeito do exercício pode ser real ou explicada por problemas metodológicos nos artigos publicados[52].

Um dos primeiros estudos sobre a influência do exercício físico crônico em pessoas com HIV mostrou aumento das taxas de CD4+ e redução dos escores de ansiedade e depressão em um grupo de homossexuais masculinos, notificados sobre a infecção no decorrer do estudo. Contudo, os dados descritivos são incompletos e não há grupo controle[53]. Com base nesse primeiro trabalho, foi conduzido estudo para verificar se havia diferença entre exercício moderado e exercício vigoroso em pacientes com HIV. Os resultados demonstraram não haver modificação nas taxas de CD4+ e CD8+ entre esses indivíduos, apenas melhora na capacidade funcional atribuível ao exercício[54].

A partir de 1996, com a introdução da TARV, novos estudos avaliaram a influência do exercício físico sobre comorbidades cardiovasculares associadas ao HIV. Apesar de diversos trabalhos experimentais publicados, todos apresentavam limitações de delineamento e amostragem que dificultam a generalização dos resultados para indivíduos infectados pelo HIV[50, 52].

A falta de uma definição que não só caracterizasse atividade física, como "qualquer movimento corporal produzido pela musculatura esquelética que resulte num gasto energético acima dos níveis de repouso"[55], mas que também permitisse classificar os níveis de atividade física, leves (menos que 3 METs), moderadas (3 a 6 METs) e intensas ou vigorosas (acima de 6 METs), levou a criação de instrumentos testados e validados internacionalmente. A unidade MET (equivalente metabólico) corresponde ao gasto energético em repouso (consumo de oxigênio de aproximadamente 3,5ml/kg/min)[55].

Aferição de atividade física

A medida precisa da atividade física é considerada um desafio aos pesquisadores, pois ainda não existe um único método com validade, fidedignidade e facilidade de uso que possa ser empregado em estudos populacionais. Entre os métodos mais frequentemente utilizados estão água duplamente marcada, calorimetria, questionários, frequência cardíaca, podômetros e acelerômetros. De modo simples, pode-se dividir os métodos de aferição de atividade física em duas categorias: métodos objetivos, como os sensores de movimento, e os indiretos, como os questionários.

Resumidamente, a água duplamente marcada consiste na ingestão de água marcada com isótopos de deutério e oxigênio. A medida da concentração desses elementos na urina e no ar expirado permite o cálculo da demanda de energia. O custo elevado, a necessidade de pessoal e equipamentos especializados restringe o uso em estudos populacionais[56].

A calorimetria direta mede a energia despendida através da taxa de calor do corpo perdido para o ambiente e é realizada dentro de câmaras fechadas; a calorimetria indireta é um método não-invasivo que determina as necessidades nutricionais e a taxa de utilização dos substratos energéticos a partir do consumo de oxigênio e da produção de gás carbônico obtidos por análise do ar inspirado e expirado pelos pulmões. Esse método apresenta como desvantagens: custo muito elevado, tempo maior despendido por pesquisadores e sujeitos de estudo, e ambiente artificial que não representa as atividades realizadas na vida diária[57].

A monitoração de frequência cardíaca é considerada um método fácil e acessível; baseia-se na relação entre o gasto energético e a frequência cardíaca. Embora os monitores mensurem com precisão a frequência cardíaca, a sua precisão para a medida de gasto energético é limitada pelo fato de a frequência cardíaca elevar independentemente da atividade física[58].

Há vários questionários padronizados para medir atividade física em indivíduos adultos[59]. A Organização Mundial de Saúde, o Instituto Karolinska, da Suécia, e o Centro de Controle e Prevenção de Doenças, dos Estados Unidos, reuniram especialistas para desenvolverem o *International Physical Activity Questionnaire* (IPAQ) que, em 2000, foi testado e validado em 12 países[60]. Embora possuam vantagens quanto ao custo e abrangência, o uso de questionários apresentam desvantagens pela falta de precisão de estimativas de gasto energético, comparativamente aos métodos diretos[61], e, às vezes, falta de reprodutibilidade.

O podômetro é um sensor de movimento uniaxial que grava movimentos de passos em resposta à aceleração do corpo no eixo vertical, resultando no deslocamento acumulado (número de passos por dia). Apesar de apresentar custo baixo, não mede gasto energético decorrente de atividades sedentárias, exercícios isométricos e movimentos de braços, além dos movimentos realizados nos demais eixos (antero-posterior e médio-lateral)[58].

Os acelerômetros são sensores de movimentos, sensíveis à variação na aceleração do corpo em um ou nos três eixos e, por isso, são capazes de medir objetivamente a frequência, intensidade e duração da atividade física realizada[58]. São capazes de detectar e registrar a magnitude da aceleração[62].

As medidas de atividade física são importantes para determinar quais atividades estão associadas a benefício à saúde e qualidade de vida, e a quantidade ou dose de atividade requerida para influenciar parâmetros de saúde. Recentemente, a Organização Mundial de Saúde criou a Estratégia Global para Promoção da Alimentação Saudável, Atividade Física e Saúde. Com respeito à atividade física, a Estratégia Global recomendou, pelo menos, 30 minutos de atividade física regular, intensa ou de moderada intensidade, na maioria dos dias da semana, mas pelo menos em cinco dias, a fim de prevenir doenças cardiovasculares e diabetes mellitus[63], e melhorar o estado funcional nas diferentes fases do ciclo de vida, especialmente na fase adulta e idosa.

Ainda não existe um teste de referência de atividade física que possa servir de padrão ouro para a construção e validação de instrumentos mais simples e de baixo custo, para uso em estudos populacionais. Enquanto não é desenvolvido um instrumento que atenda a todas as características desejadas, a combinação de diferentes instrumentos pode fornecer dados mais confiáveis e precisos[58].

Prevalência de atividade física na população geral

Os trabalhos sobre prevalência de atividade física em alguns municípios ou regiões do Brasil mostram que parcela representativa da população brasileira seja insuficientemente ativa ou sedentária[64]. Estudo realizado em Pelotas (RS), com 1.961 indivíduos, encontrou prevalência de 80,6% de inatividade física. A inatividade física esteve positivamente associada à idade, gênero feminino, relação estável e tabagismo[65]. Estudo de base populacional realizado em Joaçaba (SC), com 575 indivíduos entre 20 e 59 anos, encontrou prevalência de 57,4% de inatividade física, estando positivamente associada às variáveis: idade superior a 29 anos, índice de massa corporal <18,5 kg/m^2 ou > 29,9 kg/m^2, renda elevada, dificuldade de locomoção e não estar trabalhando ou não ser aposentado[66].

Estudo conduzido em duas regiões brasileiras – nordeste e sudeste – com 11.033 indivíduos constatou que 13% dos indivíduos realizavam, pelo menos, 30 minutos de atividade física no seu tempo de lazer e que apenas 3,3% se exercitam por esse tempo em cinco dias da semana ou mais[67].

Atividade física em pacientes infectados pelo HIV

Há poucos estudos na literatura que verificaram o nível de atividade física em indivíduos infectados pelo HIV. Os estudos identificados geralmente possuíam tamanho amostral reduzido, utilizavam atividade física como uma variável adicional ao estilo de vida, considerada fator de confusão para se verificar associação entre exposição e desfecho. Contudo, não há dados na literatura sobre a influência da atividade física na síndrome lipodistrófica entre população com HIV/AIDS em terapia antirretroviral. A maioria dos trabalhos envolve exercício e seu efeito sobre parâmetros clínicos, aferidos em indivíduos infectados pelo HIV, em uso de TARV.

Justificativa

Desse modo, a justificativa para esta tese leva em conta a atualidade do tema e a lacuna no conhecimento sobre prevalência de atividade física entre indivíduos infectados pelo HIV, e sua associação com o perfil lipídico e distribuição de gordura corporal.

REFERÊNCIAS

1. World Health Organization. Joint United Nations Programme of HIV/AIDS. Report on the Global AIDS Epidemic. 2008. www.who.int/hiv.

2. Brasil. Boletim Epidemiológico DST e AIDS. 2009; www.aids.gov.br.

3. Dourado I, Veras MA, Barreira D, de Brito AM. [AIDS epidemic trends after the introduction of antiretroviral therapy in Brazil]. *Rev Saude Publica.* 2006;40 Suppl:9-17.

4. Barbosa MT, Struchiner CJ. [Impact of antiretroviral therapy on the magnitude of the HIV/AIDS epidemic in Brazil: various scenarios]. *Cad Saude Publica.* 2003;19(2):535-541.

5. Baker R, Kotler D, Carr A, Torres RA. Altered body shape in HIV disease: a side effect of therapy? *AIDS Patient Care STDS.* 1999;13(7):395-402.

6. Carr A, Cooper DA. Adverse effects of antiretroviral therapy. *Lancet.* 21 2000;356(9239):1423-1430.

7. Carr A, Boyle MJ. Managing HIV. Part 2: Phases of disease. 2.1 Primary HIV infection. *Med J Aust.* 1996;164(2):105-106.

8. Bowman CA, Lacey CJ. The investigation of patients with human immunodeficiency virus infection. *Int J STD AIDS.* 1991;2(1):10-16.

9. Cooper DA, Gold J, Maclean P, et al. Acute AIDS retrovirus infection. Definition of a clinical illness associated with seroconversion. *Lancet.* 1985;1(8428):537-540.

10. Fonseca MG, Bastos FI. Twenty-five years of the AIDS epidemic in Brazil: principal epidemiological findings, 1980-2005. *Cad Saude Publica.* 2007;23 Suppl 3:S333-344.

11. Shafer RW, Vuitton DA. Highly active antiretroviral therapy (HAART) for the treatment of infection with human immunodeficiency virus type 1. *Biomed Pharmacother.* 1999;53(2):73-86.

12. Hacker MA, Kaida A, Hogg RS, Bastos FI. The first ten years: achievements and challenges of the Brazilian program of universal access to HIV/AIDS comprehensive management and care, 1996-2006. *Cad Saude Publica.* 2007;23 Suppl 3:S345-359.

13. Honda M, Oka S. Current therapy for human immunodeficiency virus infection and acquired immunodeficiency syndrome. *Int J Hematol.* 2006;84(1):18-22.

14. Carr A. Cardiovascular risk factors in HIV-infected patients. *J Acquir Immune Defic Syndr.* 2003;34 Suppl 1:S73-78.

15. Carr A. Pathogenesis of cardiovascular disease in HIV infection. *Curr Opin HIV AIDS.* 2008;3(3):234-239.

16. Kravcik S. HIV lipodystrophy: a review. *HIV Clin Trials.* 2000;1(3):37-50.

17. Valente AM, Reis AF, Machado DM, Succi RC, Chacra AR. [Metabolic alterations in HIV-associated lipodystrophy syndrome.]. *Arq Bras Endocrinol Metabol.* 2005;49(6):871-881.

18. Bodasing N, Fox R. HIV-associated lipodystrophy syndrome: description and pathogenesis. *J Infect.* 2003;46(3):149-154.

19. Bergersen BM, Sandvik L, Bruun JN, Tonstad S. Elevated Framingham risk score in HIV-positive patients on highly active antiretroviral therapy: results from a Norwegian study of 721 subjects. *Eur J Clin Microbiol Infect Dis.* 2004;23(8):625-630.

20. Duran S, Saves M, Spire B, et al. Failure to maintain long-term adherence to highly active antiretroviral therapy: the role of lipodystrophy. *AIDS.* 2001;15(18):2441-2444.

21. Ammassari A, Antinori A, Cozzi-Lepri A, et al. Relationship between HAART adherence and adipose tissue alterations. *J Acquir Immune Defic Syndr.* 2002;31 Suppl 3:S140-144.

22. Lumpkin M. FDA Public Health Advisory: Reports of diabetes and hyperglycemia in patients receiving protease inhibitors for the treatment of human immunodeficiency virus (HIV).Washington, DC.: US Government Printing Office.; 1997.

23. Engelson ES. HIV lipodystrophy diagnosis and management. Body composition and metabolic alterations: diagnosis and management. *AIDS Read.* 2003;13(4 Suppl):S10-14.

24. Baril JG, Junod P, Leblanc R, et al. HIV-associated lipodystrophy syndrome: A review of clinical aspects. *Can J Infect Dis Med Microbiol.* 2005;16(4):233-243.

25. Carr A, Miller J, Law M, Cooper DA. A syndrome of lipoatrophy, lactic acidaemia and liver dysfunction associated with HIV nucleoside analogue therapy: contribution to protease inhibitor-related lipodystrophy syndrome. *AIDS.* 2000;14(3):F25-32.

26. Dudgeon WD, Phillips KD, Carson JA, Brewer RB, Durstine JL, Hand GA. Counteracting muscle wasting in HIV-infected individuals. *HIV Med.* 2006;7(5):299-310.

27. Carr A. HIV lipodystrophy: risk factors, pathogenesis, diagnosis and management. *AIDS.* 2003;17 Suppl 1:S141-148.

28. Shevitz A, Wanke CA, Falutz J, Kotler DP. Clinical perspectives on HIV-associated lipodystrophy syndrome: an update. *AIDS.* 19 2001;15(15):1917-1930.

29. Carr A, Emery S, Law M, Puls R, Lundgren JD, Powderly WG. An objective case definition of lipodystrophy in HIV-infected adults: a case-control study. *Lancet.* 2003;361(9359):726-735.

30. Grunfeld C, Saag M, Cofrancesco J, Jr., et al. Regional adipose tissue measured by MRI over 5 years in HIV-infected and control participants indicates persistence of HIV-associated lipoatrophy. *AIDS.* ;24(11):1717-1726.

31. Bacchetti P, Gripshover B, Grunfeld C, et al. Fat distribution in men with HIV infection. *J Acquir Immune Defic Syndr.* 2005;40(2):121-131.

32. Fat distribution in women with HIV infection. *J Acquir Immune Defic Syndr.* 2006;42(5):562-571.

33. Bodasing N, Fox R. HIV-associated lipodystrophy syndrome: assessment and management. *J Infect.* 2003;46(2):87-93.

34. Fisher K. Wasting and lipodystrophy in patients infected with HIV: a practical approach in clinical practice. *AIDS Read.* 2001;11(3):132-133, 137-140, 147.

35. Baum MK, Rafie C, Lai S, et al. Coronary Heart Disease (CHD) Risk Factors and Metabolic Syndrome in HIV-Positive Drug Users in Miami. *Am J Infect Dis.* 2006;2(3):173-179.

36. [I Brazilian guidelines on diagnosis and treatment of metabolic syndrome]. *Arq Bras Cardiol.* 2005;84 Suppl 1:1-28.

37. Rickerts V, Brodt H, Staszewski S, Stille W. Incidence of myocardial infarctions in HIV-infected patients between 1983 and 1998: the Frankfurt HIV-cohort study. *Eur J Med Res.* 2000;5(8):329-333.

38. Friis-Moller N, Sabin CA, Weber R, et al. Combination antiretroviral therapy and the risk of myocardial infarction. *N Engl J Med.* 2003;349(21):1993-2003.

39. Lazzaretti RK. *Intervenção nutricional previne alterações do perfil lipídico em indivíduos HIV-Positivo que iniciam terapêutica anti-retroviral : um ensaio clínico randomizado.* Porto Alegre: Programa de Pós-Graduação em Ciências da Saúde: Cardiologia e Ciências Cardiovasculares., Universidade Federal do Rio Grande do Sul. Faculdade de Medicina.; 2007.

40. Sax PE. Strategies for management and treatment of dyslipidemia in HIV/AIDS. *AIDS Care.* 2006;18(2):149-157.

41. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. *Clin Infect Dis.* 2003;36(Suppl 2):S69-78.

42. Clingerman E. Physical activity, social support, and health-related quality of life among persons with HIV disease. *J Community Health Nurs.* 2004;21(3):179-197.

43. Kemppainen JK, Eller LS, Bunch E, et al. Strategies for self-management of HIV-related anxiety. *AIDS Care.* 2006;18(6):597-607.

44. Stringer WW, Berezovskaya M, O'Brien WA, Beck CK, Casaburi R. The effect of exercise training on aerobic fitness, immune indices, and quality of life in HIV+ patients. *Med Sci Sports Exerc.* 1998;30(1):11-16.

45. Lima EM, Gualandro DM, Yu PC, et al. Cardiovascular prevention in HIV patients: results from a successful intervention program. *Atherosclerosis.* 2009;204(1):229-232.

46. Domingo P, Sambeat MA, Perez A, Ordonez J, Rodriguez J, Vazquez G. Fat distribution and metabolic abnormalities in HIV-infected patients on first combination antiretroviral therapy including stavudine or zidovudine: role of physical activity as a protective factor. *Antivir Ther.* 2003;8(3):223-231.

47. Klemack C. Benefits of Exercise for People with HIV/AIDS. 2007; http://www.ncpad.org/, 2009.

48. Bopp CM, Phillips KD, Fulk LJ, Dudgeon WD, Sowell R, Hand GA. Physical activity and immunity in HIV-infected individuals. *AIDS Care.* 2004;16(3):387-393.

49. Deresz LF, Sprinz E, Kramer AS, et al. Regulation of oxidative stress in response to acute aerobic and resistance exercise in HIV-infected subjects: a case-control study. *AIDS Care.* 16:1-8.

50. Nixon S, O'Brien K, Glazier RH, Tynan AM. Aerobic exercise interventions for adults living with HIV/AIDS. *Cochrane Database Syst Rev.* 2005(2):CD001796.

51. O'Brien K, Nixon S, Tynan AM, Glazier RH. Effectiveness of aerobic exercise in adults living with HIV/AIDS: systematic review. *Med Sci Sports Exerc.* 2004;36(10):1659-1666.

52. Terry L. HIV e exercício. *Revista da Sociedade de Cardiologia do Rio Grande do Sul.* 2008;XV(9):1-7.

53. LaPerriere A, Fletcher MA, Antoni MH, Klimas NG, Ironson G, Schneiderman N. Aerobic exercise training in an AIDS risk group. *Int J Sports Med.* 1991;12 Suppl 1:S53-57.

54. Terry L, Sprinz E, Stein R, Medeiros NB, Oliveira J, Ribeiro JP. Exercise training in HIV-1-infected individuals with dyslipidemia and lipodystrophy. *Med Sci Sports Exerc.* 2006;38(3):411-417.

55. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* 1985;100(2):126-131.

56. Stifelman M. Using doubly-labeled water measurements of human energy expenditure to estimate inhalation rates. *Sci Total Environ.* 2007;373(2-3):585-590.

57. Murgatroyd PR, Shetty PS, Prentice AM. Techniques for the measurement of human energy expenditure: a practical guide. *Int J Obes Relat Metab Disord.* 1993;17(10):549-568.

58. Macfarlane DJ, Lee CC, Ho EY, Chan KL, Chan D. Convergent validity of six methods to assess physical activity in daily life. *J Appl Physiol.* 2006;101(5):1328-1334.

59. Warren JM, Ekelund U, Besson H, Mezzani A, Geladas N, Vanhees L. Assessment of physical activity - a review of methodologies with reference to epidemiological research: a report of the exercise physiology section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil.*;17(2):127-139.

60. Amorim PR, de Faria RC, Byrne NM, Hills AP. Physical activity and nutritional status of children of low socioeconomic status. Two interrelated problems: undernutrition and overweight. *Asia Pac J Clin Nutr.* 2006;15(2):217-223.

61. Barros MVG. *Medidas de atividade física: teoria e aplicação em diversos grupos populacionais.* Londrina Midiograf; 2003.

62. Hendelman D, Miller K, Baggett C, Debold E, Freedson P. Validity of accelerometry for the assessment of moderate intensity physical activity in the field. *Med Sci Sports Exerc.* 2000;32(9 Suppl):S442-449.

63. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation.* 2007;116(9):1081-1093.

64. Matsudo V, Matsudo S, Andrade D, et al. Promotion of physical activity in a developing country: the Agita Sao Paulo experience. *Public Health Nutr.* 2002;5(1A):253-261.

65. Dias-da-Costa JS, Hallal PC, Wells JC, et al. Epidemiology of leisure-time physical activity: a population-based study in southern Brazil. *Cad Saude Publica.* 2005;21(1):275-282.

66. Baretta E, Baretta M, Peres KG. [Physical activity and associated factors among adults in Joacaba, Santa Catarina, Brazil]. *Cad Saude Publica.* 2007;23(7):1595-1602.

67. Monteiro CA, Conde WL, Matsudo SM, Matsudo VR, Bonsenor IM, Lotufo PA. A descriptive epidemiology of leisure-time physical activity in Brazil, 1996-1997. *Rev Panam Salud Publica.* 2003;14(4):246-254.

OBJETIVOS

Objetivo geral:

Avaliar a associação entre atividade física e síndrome lipodistrófica em pacientes infectados pelo HIV.

Objetivos específicos:

- Determinar a prevalência de atividade/inatividade física em indivíduos infectados pelo HIV, por meio de revisão sistemática da literatura.
- Avaliar protocolo de análise de atividade física aferida através de acelerômetro e suas implicações.
- Verificar a prevalência de atividade/inatividade física em indivíduos infectados pelo HIV, em atendimento ambulatorial em centro de referência e sua associação com características demográficas, sociais e clínicas.
- Avaliar a associação de atividade física com lipo-hipertrofia e perfil metabólico dos pacientes infectados pelo HIV.

ARTIGO 1

PHYSICAL ACTIVITY AMONG HIV-INFECTED PATIENTS: A SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES.

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Running head: PHYSICAL ACTIVITY AMONG HIV PATIENTS.

ABSTRACT

Background: Several studies have suggested that aerobic physical activity is safe and beneficial for HIV-infected adults.

Objective: To verify the prevalence of physical activity, sedentary lifestyle or lack of physical activity in non-experimental conditions performed by HIV-infected subjects in order to obtain a pooled estimate.

Methods: The electronic search was conducted using Medline and EMBASE bibliographic databases and the platforms of Bireme, Ovid, Science Direct, High Wire and SCIELO from January 1990 to Augusto 2010. Original observational studies were included. Of the 2,585 articles found, 46 met the inclusion criteria. Following data extraction and after reading the manuscripts, 24 were selected for systematic review.

Results: Of the 24 studies, two were prospective cohort studies, eight were prevalence studies, and 14 were cross-sectional studies. The average quality score using the modified Newcastle-Ottawa scale was 2.8±1.5. It was possible to determine the percentage of sedentary lifestyle among HIV-infected individuals in 13 articles. The variation was between 19% and 73.3%, with the level determined by different methods.

Conclusion: There are few well-designed studies with adequate sample size to represent the population of HIV-infected individuals. A pooled estimate could not be calculated due to the differences in design, physical activity measurements, and studied populations.

Descriptors: Motor activity, physical activity, lifestyle, exercise, HIV, AIDS.

INTRODUCTION

Regular physical activity has been recommended as part of the global strategy for prevention of non-transmissible diseases.[1, 2] The current guideline suggests that adults should engage in moderate-to-vigorous physical activity at least 30 minutes a day, five days a week.[1] The guideline aimed at the general population[3] and there is no specific recommendation for HIV-infected individuals, however a systematic review has found that aerobic exercise or its combination with strength training for four weeks, at least three times a week, might be enough for improving cardiorespiratory capacity of HIV-infected individuals.[4] Additional evidences suggest that the effect of long-term endurance exercise can increase CD4, improve functional capacity and quality of life, as well as to reduce the prevalence of depression.[5, 6] Furthermore, moderate-to-vigorous exercise improved cardiorespiratory fitness and promoted weight loss with no detrimental influence on immunological profile or viral load level increase in subjects on antiretroviral treatment.[7-9] Most of these studies were interventions, administered for a short period of time, and some studies had no control group. Therefore, these results do not support long-term benefit; they were conducted on small samples of highly selected participants and could hardly be generalized to the overall population of HIV-infected individuals. Moreover, there is scarce information regarding the level of physical activity performed by HIV-infected individuals. This systematic review aimed to verify the prevalence of physical activity, sedentary lifestyle or lack of physical activity in non-experimental conditions performed by HIV-infected subjects in order to obtain a pooled estimate.

METHODS

Protocol

A standardized record form was designed, pretested, piloted and revised. Characteristics of the study such as year, setting, population and sampling, study design, instrument or equipment used do quantify physical activity were recorded, and the instrument to verify quality of the study was selected.

Eligibility criteria

The eligibility criteria included observational studies that evaluated physical activity performed by HIV-infected adults, published from January 1990 to August 2010, and with no language restriction. Prevalence, cross-sectional, and cohort studies that assessed physical activity using a standardized protocol or equipment were eligible.

Information source and search strategy

The search strategy was performed using Medline and EMBASE bibliographic databases and the platforms of LILACS, Ovid, Science Direct, High Wire and SCIELO. Unpublished studies were investigated in the largest theses and doctoral dissertations database of a Brazilian Agency (CAPES). The searching by hand was conducted in the references of the review papers and in a few non-indexed Medline Brazilian journals. Duplicate publication was checked and, if necessary, the corresponding author was contacted.

Three investigators conducted independent search strategies and the final one included primary descriptors for PubMed: "physical activity" [textword] or "exercise" [MESH] or "motor activity" [MESH] that were intersected with secondary descriptors: "lifestyle" [MESH], "HIV" [MESH], "AIDS" [MESH] using Boolean operators. Even though this review is not focused on “exercise”, this descriptor was included in order to capture all relevant papers that might contain both physical activity and exercise measurement.

Study selection

Screening and eligibility were checked by three independent investigators who read the titles and the abstracts of all articles in order to identify those that met the inclusion criteria or those that could not be clearly excluded. Disagreements were solved by consensus in staff meetings.

Data collection process

Two independent investigators extracted the data using a spreadsheet previously tested and refined. Divergences were resolved by discussion between the reviewers. Selected studies were critically appraised and data were recorded in tabular format allowing comparisons between studies. Three authors were contacted in order to obtain additional information or to clarify some details about the methodology of measurement or physical activity score.

Data items

Information was extracted from each included article on: (1) article identification; (2) characteristics of participants, such as age, gender, HIV or AIDS diagnosis/testing method; (3) design and setting; (4) sample size; (5) physical activity including measurement methods and type, duration and frequency of physical activity in order to classify the level.

Summary Measures

It was anticipated that the report of physical activity might be presented using different formats, so all continuous (mean and SD) or categorical (percentage) data were recorded for type, duration and frequency of physical activity. Individuals physically active could be identified by moderate-to-vigorous physical activity performed during 150 min/week[10], questionnaire or accelerometer; walking at least 10,000 steps/day measured by pedometer[10], or any other standardized definition. Participants who did not achieve such levels could be classified as inactive. A priori, it was planned to aggregate the results of the studies into a summary measure of prevalence rate, and assessing heterogeneity using the comprehensive Meta-Analysis® statistical program.

Quality analysis

The modified Newcastle-Ottawa Scale, derived from quality assessment scales for case-control and cohort studies, was used to assess quality of the study regarding sampling, selection, exposure, and outcome measurements. A star was given for each item completed, resulting in scores ranging from 0 (worst) to 7 (best).[11]

RESULTS

Study selection

The database search identified 2,745 as potentially eligible studies. Six were detected by checking the references of relevant papers and two doctoral dissertations were additionally retrieved. All 2,753 studies were screened by reviewing the title and abstract and 46 needed review of the full-text. The remaining retrieved studies were excluded since they did not meet the eligibility criteria, and the full text of 46 studies was examined by two investigators. The rate of overall agreement between investigators was 95%. Disagreements regarding eligibility or quality of the study were solved in staff meetings. Figure 1 presents the flow diagram to summarize study selection processes that resulted in the inclusion of 24 articles.

[Figure 1 here]

Study characteristics

Of the 2,101 articles screened, 24 were included. Two were cohort studies, eighth were prevalence studies, and 14 were cross-sectional studies. Two articles[12, 13] showed superposition of main and complementary results, and they were handled as a single article for data analysis purpose.

Of the 24 articles included in this systematic review, 14 primarily aimed to determine the prevalence of physical activity or to examine its association with metabolic disorders, abnormal fat distribution, progression of HIV infection or its influence on the immune system. The remaining 10 studies used physical activity to test secondary hypotheses, verifying energy intake and expenditure or the association with lifestyle, coronary heart disease, metabolic syndrome or other outcomes among HIV-infected individuals.

No study reached the maximum score of quality. Most articles were prevalence studies, a few had a control group to compare prevalence rates, most did not present the non-response rate; those were the reasons why the average score was low. The individual study scores and the results are presented in Table 1.

Participants

A total of 4,982 participants were analyzed and their characteristics were described in Table 1. The main inclusion criteria entailed adults aged 18 years or older, who reported having been tested positively for HIV infection and had physical activity assessed. Most studies included men and women. Seven studies enrolled only men, one did not specify how many of the 66 participants were males or females, and gender was not reported in one. Most participants were males (n=3,494), with age ranging between 18 and 81 years, and the mean age ranged from 33 to 47 years.

[Table 1 here]

Physical activity measurement

Most studies adopted standardized instruments (n=13), specific questions (n=10), accelerometer or pedometer (n=3), and a few additionally used laboratory tests, assessing indirect calorimetry, proxies of energy expenditure and peak of oxygen uptake (n=5). The questionnaires used to assess physical activity included the short version of IPAQ (International Physical Activity Questionnaire), Behavior Risk Factor Surveillance Survey (BRFSS-PAQ), Minnesota Leisure Time Physical Activity Questionnaire, Leisure Activity Inventory and Seven-Day Physical Activity Recall, Baecke Questionnaire, Modified

Paffenbarger Questionnaire, Daily Life and Sports Exercise. Data were obtained from face-to-face interviews, administered questionnaires (n=17), self-completed questionnaire (n=2), and the use of diaries (n=2). All instruments used different protocols to classify sedentary and active lifestyle. Physical activity was assessed during periods of time that ranged from one to seven days or for the usual pattern of physical activity.

Sedentary lifestyle or insufficient physical activity

Prevalence rate of sedentary lifestyle or lack of physical activity among HIV-infected individuals was described in 13 articles, ranging from 19.0% to 73.3%.[10, 13-23] The IPAQ identified 81% as physically active, followed by the accelerometer ActiGraph (54%), and the pedometer DigiWalker (17%), while the prevalence of inactivity was higher for the pedometer (83%) and accelerometer (46%) than the IPAQ (19%).[10] The other two studies using the IPAQ either followed the IPAQ general protocol or considered active individuals those who reached the achievement of at least 150 min/wk of moderate-to-vigorous physical activity.[15]

The studies that used the Minnesota Leisure Time Physical Activity Questionnaire considered sedentary patients those who had a total activity metabolic index below than 143 kcal/day.[18] Studies using the Baecke Questionnaire did not outline sedentary behavior or physical inactivity. They only showed the total score as mean and standard deviation, obtained from the instrument scores and the percentage of active individuals in some activities or sports.[24-26]

There were several criteria used for defining lack of physical activity, which were barely comparable. One of the studies defined the exercise behavior based on the answer to the following question: how many times a week do you engage in physical activity? Those who reported never exercising, or exercising less than once a month, once a month or above, or every few weeks, or twice a week were aggregated into non-exercising category.[17] In another study, inactive were those who neither walked for more than 10 minutes at a time, nor performed moderate, vigorous, or strengthening physical activity.[13] In a few studies, the percentage of individuals who performed some types of exercises (running, jogging, weight training) were classified as physically active. For one study, the rate of inactive or sedentary individuals was not described and had to be extracted from the difference on percentages shown in the figures.[19] Ramirez-Marrero et al. defined those participants with energy expenditure below 300 kcal/day as inactive.[20] Shah et al. did not present the cutoff point for physical activity, but this article present the percentage of active individuals separated by gender, thus allowing calculating the overall percentage of inactive subjects.[22] In other study, using the lifestyle questionnaire created by

Nahas, those participants who scored below 27 were classified as poorly physically active.[16] Salyer et al. defined as inactive those who performed ≤ 2 times of physical activity per week.[21] Arendt et al. defined as sedentary participants whose Physical Activity Coefficient was typical daily living activities, household shores, walking to get the bus.[14]

Effects of physical activity undertaken

The effect of physical activity has been established as inversely related to several metabolic disorders, such as high level of triglycerides and insulin resistance,[19] and directly associated with an increase in CD4 T-lymphocyte counts, a slower HIV progression and death with AIDS[17] and High Density Lipoproteins (HDL) level.[22] Some studies suggested that physical activity was related to higher quality of life,[13] and the potential explanation was that healthier body composition was more prevalent among active ones.[20] Arendt et al.[14] attributed the metabolic abnormalities to high-fat diet with low intake of micronutrients and fiber, rather than to the lack of physical activity and energy gain, noting that patients with metabolic syndrome generally were overweight or obese, despite having a satisfactory level of physical activity.

Level of physical activity among HIV-positive and -negative subjects

The comparison between HIV-infected and non-infected subjects regarding levels of physical activity was conducted on five studies.

In two studies, HIV-negative subjects had higher prevalence of physical activity than those HIV-infected, but there was a controversy regarding those on potent highly active antiretroviral therapy (HAART).[27, 28]

The energy expenditure from vigorous physical activity was higher among HIV-negative and untreated HIV-positive individuals than among those on HAART[27]. However, in one study there was no statistically significant between HIV-infected individuals with or without antiretroviral treatment, but when comparison was made between HIV-infected and those without HIV infection, the latter performed regular physical activity more frequently (46% vs. 60%, respectively).[28]A third study detected that HIV-positive patients reported more physical activity than the non-infected ones. However, the comparison group was composed of patients with nonalcoholic fatty liver disease.[29]

The study by Fillipas et al.[15] showed that HIV-positive individuals spent more time in performing vigorous physical activity (P value = 0.034) and physical activity in general (P value = 0.010) than HIV-negative individuals. Similarly, with regard to energy expenditure at each intensity, they showed that HIV-positive patients had higher expenditure in vigorous activities (P value = 0.028), moderate (P value = 0.046) and total (P value = 0.019) than HIV-negative individuals.

Finally, a fifth study did not find differences in the level of physical activity carried out among HIV-infected and non-infected individuals.[17]

DISCUSSION

This systematic review screened 2,745 studies measuring physical activity performed by HIV infected adults. Despite extensive literature search to obtain studies, only a few met the eligibility criteria. Moreover, the studies had low quality score, assessed by the modified Newcastle-Ottawa Scale, in addition to heterogeneity in the methods of physical activity measurement. The absence of a reference test for physical activity assessment of large population-based studies and the diversity of methods to measure physical activity, besides their characteristics, accounted for the heterogeneity that precluded from conducting a meta-analysis. The heterogeneity could also be attributed to different study designs and small sample size, leading to low statistical power.

There were also controversial results with regard to the difference on physical activity levels among HIV-infected and uninfected individuals. However, few studies had a control group for this analysis. While Mohammed et al.[29] and Fillipas et al.[15] rejected the null hypothesis, detecting that HIV-infected individuals had higher levels of physical activity in comparison with uninfected individuals, Smit et al.[27] found that individuals without HIV infection performed physical activity for longer periods than infected ones. Jacobson et al.[28] also reported that the practice of regular physical activity over the past 30 days were higher among individuals without infection, while Mustafa et al.[17] found no difference between the groups.

In order to avoid the variability in the measurement of physical activity, the choice was to analyze the percentage of sedentary lifestyle or physical inactivity as the outcome. There was a great range of variation (19% and 73%), according to the measurement method even measuring the same population.[10] An estimate from the United States for the last decade showed that 45% to 50% of the adult population did not perform physical activity during leisure time.[1] A study conducted between 1996-1997 in two most populous Brazilian regions, Southeast and Northeast, found a prevalence of 87% of sedentary lifestyle.[30] Due to the characteristic of the cross-sectional design, it was not possible to determine whether inactivity or sedentary lifestyle was due to the infection or whether it could be influenced by the antiretroviral treatment. Likewise, the body changes related to HIV lipodystrophy syndrome needed to be investigated in longitudinal studies, to ensure the causality and preventive role of physical activity in the development of those changes.

Thus, with few studies available and their low quality and high heterogeneity, it was not possible to calculate a summary measure by meta-analysis. Further studies are needed with larger population-based samples, using the same instrument, in order to determine the level of physical activity performed and how it works on the clinical parameters of HIV-infected individuals.

In conclusion, there are few well-designed studies with adequate sample size to represent the population of HIV-infected individuals. From the evidence available, it was possible to determine the level and intensity of physical activity performed by HIV-infected patients.

REFERENCES

1. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation.* 28 2007;116:1081-1093.

2. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA.* 1995;273:402-407.

3. Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee Report, 2008. 2008.

4. Nixon S, O'Brien K, Glazier RH, Tynan AM. Aerobic exercise interventions for adults living with HIV/AIDS. *Cochrane Database Syst Rev.* 2005;CD001796.

5. LaPerriere A, Fletcher MA, Antoni MH, Klimas NG, Ironson G, Schneiderman N. Aerobic exercise training in an AIDS risk group. *Int J Sports Med.* 1991;12 Suppl 1:S53-57.

6. Solomon GF. Psychosocial factors, exercise, and immunity: athletes, elderly persons, and AIDS patients. *Int J Sports Med.* 1991;12 Suppl 1:S50-52.

7. Terry L, Sprinz E, Ribeiro JP. Moderate and high intensity exercise training in HIV-1 seropositive individuals: a randomized trial. *Int J Sports Med.* 1999;20:142-146.

8. O'Brien K, Nixon S, Tynan AM, Glazier RH. Effectiveness of aerobic exercise in adults living with HIV/AIDS: systematic review. *Med Sci Sports Exerc.* 2004;36:1659-1666.

9. Rigsby LW, Dishman RK, Jackson AW, Maclean GS, Raven PB. Effects of exercise training on men seropositive for the human immunodeficiency virus-1. *Med Sci Sports Exerc.* 1992;24:6-12.

10. Ramirez-Marrero FA, Rivera-Brown AM, Nazario CM, Rodriguez-Orengo JF, Smit E, Smith BA. Self-reported physical activity in Hispanic adults living with HIV: comparison with accelerometer and pedometer. *J Assoc Nurses AIDS Care.* 2008;19:283-294.

11. Wells GA SB, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.

12. Clingerman E. Physical activity, social support, and health-related quality of life among persons with HIV disease. *J Community Health Nurs.* 2004;21:179-197.

13. Clingerman EM. Participation in physical activity by persons living with HIV disease. *J Assoc Nurses AIDS Care.* 2003;14:59-70.

14. Arendt BM, Aghdassi E, Mohammed SS, et al. Dietary intake and physical activity in a Canadian population sample of male patients with HIV infection and metabolic abnormalities. *Curr HIV Res.* 2008;6:82-90.

15. Fillipas S, Bowtell-Harris CA, Oldmeadow LB, Cicuttini F, Holland AE, Cherry CL. Physical activity uptake in patients with HIV: who does how much? *Int J STD AIDS.* 2008;19:514-518.

16. Eidam CL LA, Guimarães MDC, Oliveira OV. Estilo de vida de pacientes infectados pelo vírus da imunodeficiência humana (HIV) e sua associação com a contagem de linfócitosT CD4+. *Rev Bras Cineantropom Desempenho Hum.* 2006;8:51-57.

17. Mustafa T, Sy FS, Macera CA, et al. Association between exercise and HIV disease progression in a cohort of homosexual men. *Ann Epidemiol.* 1999;9:127-131.

18. Domingo P, Sambeat MA, Perez A, Ordonez J, Rodriguez J, Vazquez G. Fat distribution and metabolic abnormalities in HIV-infected patients on first combination antiretroviral therapy including stavudine or zidovudine: role of physical activity as a protective factor. *Antivir Ther.* 2003;8:223-231.

19. Gavrila A, Tsiodras S, Doweiko J, et al. Exercise and vitamin E intake are independently associated with metabolic abnormalities in human immunodeficiency virus-positive subjects: a cross-sectional study. *Clin Infect Dis.* 15 2003;36:1593-1601.

20. Ramirez-Marrero FA, Smith BA, Melendez-Brau N, Santana-Bagur JL. Physical and leisure activity, body composition, and life satisfaction in HIV-positive Hispanics in Puerto Rico. *J Assoc Nurses AIDS Care.* 2004;15:68-77.

21. Salyer J, Lyon DE, Settle J, Elswick RK, Rackley D. Coronary heart disease risks and lifestyle behaviors in persons with HIV infection. *J Assoc Nurses AIDS Care.* 2006;17:3-17.

22. Shah M, Tierney K, Adams-Huet B, et al. The role of diet, exercise and smoking in dyslipidaemia in HIV-infected patients with lipodystrophy. *HIV Med.* 2005;6:291-298.

23. Kowal J, Overduin LY, Balfour L, Tasca GA, Corace K, Cameron DW. The role of psychological and behavioral variables in quality of life and the experience of bodily pain among persons living with HIV. *J Pain Symptom Manage.* 2008;36:247-258.

24. Florindo AA, de Oliveira Latorre Mdo R, Jaime PC, Segurado AA. Leisure time physical activity prevents accumulation of central fat in HIV/AIDS subjects on highly active antiretroviral therapy. *Int J STD AIDS.* 2007;18:692-696.

25. Florindo AA, Latorre Mdo R, Santos EC, Negrao CE, Azevedo LF, Segurado AA. Validity and reliability of the Baecke questionnaire for the evaluation of habitual physical activity among people living with HIV/AIDS. *Cad Saude Publica.* 2006;22:535-541.

26. Jaime PC, Florindo AA, Latorre Mdo R, Segurado AA. Central obesity and dietary intake in HIV/AIDS patients. *Rev Saude Publica.* 2006;40:634-640.

27. Smit E, Crespo CJ, Semba RD, et al. Physical activity in a cohort of HIV-positive and HIV-negative injection drug users. *AIDS Care.* 2006;18:1040-1045.

28. Jacobson DL, Tang AM, Spiegelman D, et al. Incidence of metabolic syndrome in a cohort of HIV-infected adults and prevalence relative to the US population (National Health and Nutrition Examination Survey). *J Acquir Immune Defic Syndr.* 2006;43:458-466.

29. Mohammed SS, Aghdassi E, Salit IE, et al. HIV-positive patients with nonalcoholic fatty liver disease have a lower body mass index and are more physically active than HIV-negative patients. *J Acquir Immune Defic Syndr.* 2007;45:432-438.

30. Monteiro CA, Conde WL, Matsudo SM, Matsudo VR, Bonsenor IM, Lotufo PA. A descriptive epidemiology of leisure-time physical activity in Brazil, 1996-1997. *Rev Panam Salud Publica.* 2003;14:246-254.

31. Paton NI, Elia M, Jebb SA, Jennings G, Macallan DC, Griffin GE. Total energy expenditure and physical activity measured with the bicarbonate-urea method in patients with human immunodeficiency virus infection. *Clin Sci (Lond).* 1996;91:241-245.

32. Bopp CM, Phillips KD, Fulk LJ, Dudgeon WD, Sowell R, Hand GA. Physical activity and immunity in HIV-infected individuals. *AIDS Care.* 2004;16:387-393.

33. Sutinen J, Yki-Jarvinen H. Increased resting energy expenditure, fat oxidation, and food intake in patients with highly active antiretroviral therapy-associated lipodystrophy. *Am J Physiol Endocrinol Metab.* 2007;292:E687-692.

34. Tsiodras S, Poulia KA, Yannakoulia M, et al. Adherence to Mediterranean diet is favorably associated with metabolic parameters in HIV-positive patients with the highly active antiretroviral therapy-induced metabolic syndrome and lipodystrophy. *Metabolism.* 2009;58:854-859.

35. Tang AM, Forrester JE, Spiegelman D, et al. Heavy injection drug use is associated with lower percent body fat in a multi-ethnic cohort of HIV-positive and HIV-negative drug users from three U.S. cities. *Am J Drug Alcohol Abuse.* 36:78-86.

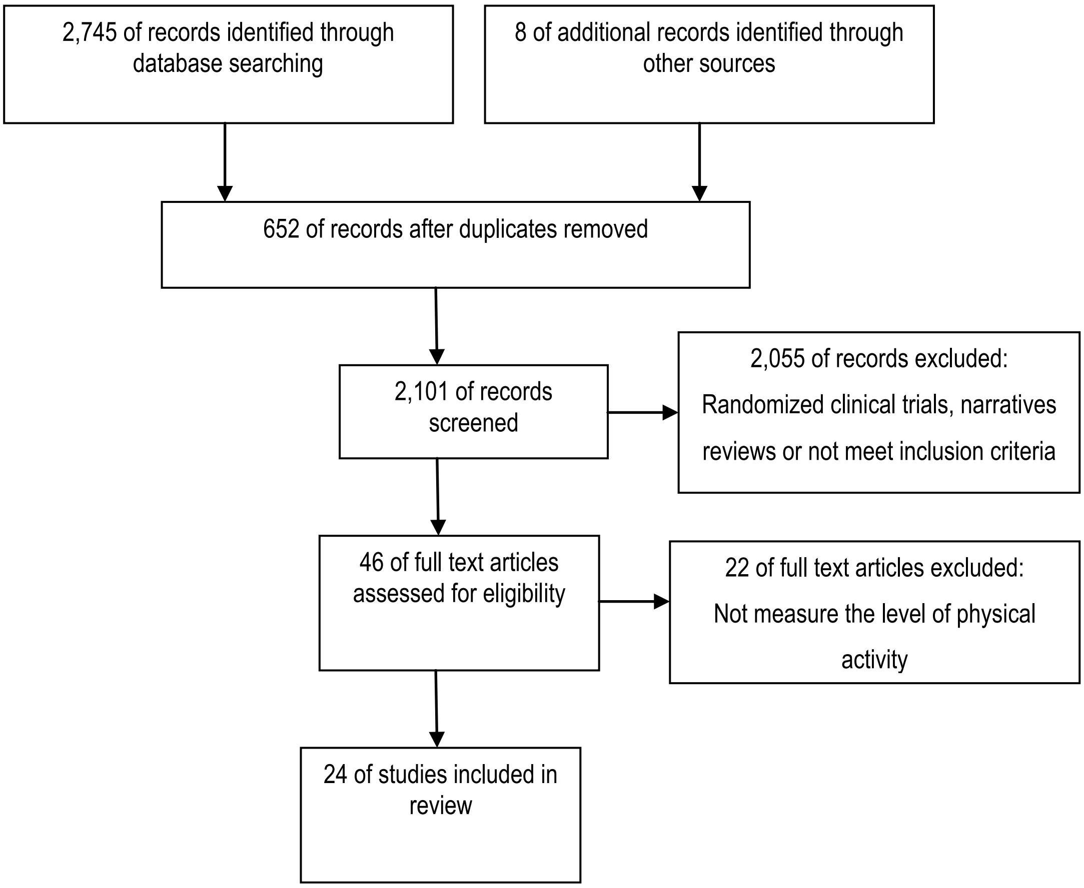

Figure 1: Flowchart of article search and selection for systematic review.

Table 1: Characteristics of observational studies that measurement physical activity in HIV infected patients.

Reference, year of publication	Modified Newcastle-Ottawa score	Population, setting and data collection	Design and sample size	Gender, age - mean ± SD and range	Physical activity instruments and measurements	Physical activity results of the studies	Inactivity prevalence
Paton, 1996.[31]	2	Men with stable infection without opportunistic disease; St George's Hospital, London Not mentioned.	Prevalence study n=10	100% Males, Mean age: 33.5 years (26-45)	Diary of PA, fulfilled by participant for 2 days. Each PA energy expenditure was graded from tables of PA	Level of PA 1.34±0.16 (daily) Level of PA 1.42±0.14 (measured)	-
Mustafa 1999.[17]	5	Homosexual or bisexual living in New York, USA, who took part in a cohort study: The Longitudinal AIDS Impact Project December, 1991.	Cohort study n=415 * 156 HIV+ 259 HIV- * Subsample that had HIV status determined	100% Males, Mean age: HIV+ 35±6.4 (22-55); HIV- 37±9.1 (20-75)	Question: How many times a week do you exercise?	Exercise: Exercising daily: 35% HIV+ vs. 31% HIV- 3-4 times/wk: 36% HIV+ vs. 41% HIV-	Non-exercisers: 29% HIV+ vs. 28% HIV-
Clingerman 2003.[13]	-	Infectious disease clinics and community service for HIV positive patients, Northern Great Lakes region, USA Not mentioned.	Prevalence study n=78	89.7% Males, Mean age 40.4±8.33 years (23-70)	Physical Activity Questionnaire (PAQ, composed of 11 reformatted questions from Module 11 of the BRFSS). This instrument assesses frequency (days per week) and duration (minutes per week) of leisure time and occupationally related physical activity.	Walking for 5 or more days per week for 30 or more minutes per occasion: 53.8%* Moderate PA for 5 or more days per week for 30 or more minutes per occasion: 28.2%* Vigorous PA for 3 or more days per week for 20 or more minutes per occasion: 19.2%* * Some participants fulfilled two categories	Participants who did not walk, did not perform moderate, vigorous, or strengthening PA: 25.6%
Gavrila 2003.[19]	1	Outpatients of the General Clinical Research Center; aged 16 years or older, with documented HIV infection, and on any antiretroviral regimen for at least 6 months; Beth Israel Deaconess Medical Center, Boston, Massachussetts, USA Not mentioned.	Cross-sectional study n=120	89% Males Mean age 43.7±8.0 years	3 Multiple-choice questions with type, intensity, frequency and duration of exercise) Intensity: Mild: walking on level ground/swimming; Moderate: running, aerobic classes, or use of treadmill, stationary bike or cardiovascular machines; Heavy: weight training. Frequency: 0 to 7 sessions/week; Session duration: <15, 15–29, 30–59, 60–89, or ≥90 min Cumulative indexes for either aerobic or total (aerobic and/or resistance) exercise, calculated as number of sessions per week, duration (min) per session	Any exercise: 86% Aerobic exercise: 83% Mild: 39% Moderate/ heavy: 44% Number of sessions per week: 4.4±2.7; Exercise duration: 42±30 minutes Index of aerobic exercise: 349±339 min/week Index of total exercise 478 ±485 min/week	14%

					exercise intensity.		
Domingo 2003.[18]	3	Patients participating of a study on metabolic disturbances associated with HAART; aged 18 or over, have documented HIV-1 infection, being on first highly active antiretroviral therapy, for at least the 6 months, and be under active follow-up. AIDS Clinic, Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, Barcelona, Spain June to August, 2000.	Cross-sectional study n=150	78.7% Males Mean age 39.05±9.05 years (21-69)	Spanish version for Minnesota Leisure Time Physical Activity Questionnaire Sedentary: total activity metabolic index lower than 143 kcal/day Authors did not specified the criteria for physically active. It was assumed it identify those with total activity metabolic index ≥143 kcal/day.	Physically active: 28% (patients on d4T) and 25.3% (patients on AZT)	73.3%
Bopp 2004.[32]	1	Convenience sample of HIV-infected individuals receiving care at the outpatient referring clinic, aged 18 years of age or older, able to read and understand English; Columbia, South Carolina, United States. Not mentioned.	Prevalence study n=66	Male and female, Mean age 39±8 years (18-64)	Mini-motion logger wrist accelerometer on the non-dominant hand of the subject, for three days. Physical activity index: percentage of time units (minutes) that the wrist ActiGraph recorded activity. Mean physical activity: average minutes of physical activity per day over the data collection period. Acceleration index: measure of physical activity intensity.	Average minutes of physical activity: 144 ± 31 minutes per day (range 43-193 min) Average PA index: 84 ± 8.4% Physical activity index averaged: 84 ±8.4% Acceleration index averaged: -0.22	-
Ramirez-Marrero 2004.[20]	2	AIDS Clinical Trial Unit at the University of Puerto Rico, Puerto Rico. Not mentioned.	Prevalence study n=68	63% Males, Mean age 40.4±8years (30-50)	Leisure Activity Inventory and Seven-Day Physical Activity Recall Leisure Activity Inventory: 29 commonly practiced leisure activities in Puerto Rico, with frequency of participation for each activity recorded as 4-point scale (never =0, rarely=1, occasionally = 2, and frequently = 3). Overall score: the sum of each particular activity, ranging between 0 and 87.	Leisure Activity Inventory score: Overall mean: 43.4 ±10.6 Men: 44.0 ±11.9 Women: 42.0 ±12.3 Leisure time (average score) 45.0±10.8 in the active vs.41.1±9.9 in the inactive group. The cutoff point ≥300 kcal/day of physical activity–related energy expenditure was used to identify participants physically active: 58.8% Seven-Day Physical Activity Recall: daily	TV watching (hours per day): 5.4; 4.5±2.4 in the active vs. 5.9 ±2.9 in the inactive group.

					The Seven-Day Physical Activity Recall measure the time spent in moderate, hard, and very hard intensity leisure and occupational activities during the previous 7 days.	average of 1.2 hours	
Shah 2005.[22]	2	Participants should have documented HIV infection; cumulative exposure to protease inhibitors for 6 months or more; and fat redistribution confirmed. Parkland Health and Hospital Systems, HIV Clinics at the University of Texas Southwestern Medical Center, Dallas, USA. Not mentioned.	Cross-sectional study n=51	88% Males Mean age 46.5±8.1 years	Questions about the type and number of hours of light , moderate and intense activity per week Subjects were asked to provide information on the typical number of hours spent doing mild, moderate and heavy aerobic exercise, weight training/lifting and flexibility exercise per week. Mild exercise: walking and light sports. Moderate and heavy exercise: running, hard sports and jogging. Flexibility exercises included stretching and yoga. The total number of hours spent exercising per week was calculated.	Exercise [h/week (% exercising)] Total aerobic: 2.3 ±3.0 (62.2%) for males and 1.3±2.8 (33.3%) for females Moderate/heavy aerobic: 0.5±1.2 (20%) vs. 0 (0%) Weight training/lifting: 1.4±2.3 (44.4%) vs. 0 (0%) Flexibility: 0.2 ±0.6 (11.1%) vs. 0.3 ±0.8 (16.7%) Total exercise: 3.9±4.2 (66.7%) vs.1.7±2.7 (50%)	No exercise: Men: 33.3% Women: 50%
Eidam 2006.[16]	2	Convenience sample of HIV-infected individuals receiving care at the outpatient clinic of infectious disease, aged 18 years or older, be under active follow-up and not be on restricted regimen of freedom from 2 public health care centers, Florianópolis, Santa Catarina, Brazil. October to December, 2002.	Cross-sectional study n=111	61.3% Males Mean age 37 years (21-55)	Instrument to evaluate the lifestyle profile with 3 questions regarding:1) walking or bicycling as the usual transportation mode, 2) physical activity for at least 30 minutes 5 or more days per week, and 3) lifting or stretching exercises. Each question had four options of answer: (never =0, rarely=1, occasionally = 2, and frequently = 3). The PA score ranged from zero to 9 points and 5.4 to 9 were considered satisfactory.	Walking or bicycling as the usual transportation mode: 66,7% Physical activity for at least 30 minutes 5 or more days per week: 76.6% Lifting or stretching exercises:27.0% Overall habitual satisfactory PA: 50.5%	45.5%

Salyer J 2006.[21]	2	Participants were selected from two infectious diseases clinics (one located in an urban area and the other located in a rural area of the same state). They should have documented HIV infection; being able to read and understand English, under follow-up for at least one year, had cumulative exposure to HAART, including a protease inhibitor, and had laboratory measures on the day of data collection. Medical College of Virginia/Virginia Commonwealth University Virginia, USA. May to December, 2002.	Cross-sectional study n=95	83% Males Mean age 41±8.4 years (21-68)	Duke Activity Scale Index (DASI) with 12 items providing an indirect measure of exercise capacity. Physical activity habits were investigated regarding how many days of the week participants performed 30 minutes or more of moderate intensity exercise. Weighted responses (which correspond to the metabolic equivalents for each activity) were computed and summed to produce the DASI score	≤2 times/week: 33.7% ≥3 times/week: 66.3% Participation in strenuous sports: 47% Heavy work around the house: 28% Participate in moderate recreational activity: 27%.	33.3%
Jaime 2006.[26]	3	Participants HIV/AIDS, who had been using HAART with protease inhibitors for at least three years, from a Referral Center for HIV/AIDS, Sao Paulo, São Paulo, Brazil. March to June, 2002.	Cross-sectional study n=223	76.8% Males Mean age 38.9 years (20-59)	Baecke questionnaire investigated habitual PA, for the last 12 months, with 16 questions covering three components: occupational activity, leisure time and locomotion activities Each question was converted to a Likert scale and each block of questions generated a final score for physical activity. The total score for habitual physical activity is obtained by adding occupational physical activity, physical exercise in leisure, leisure and locomotion activity scores.	Prevalence rate for physical activity was not described, neither the average score for the whole population. The final score for participants with central obesity were 2.75±0.7 and 2.88±0.65 for those with no central obesity.	-
Smit 2006.[27]	5	Subjects have participated in a sub-study from the AIDS Linked to Intravenous Experiences (ALIVE) cohort, an ongoing study of HIV-negative and -positive IDUs. For the Alive, participants were recruited in the Baltimore area at several clinics, hospital emergency rooms, homeless shelters and the Street Outreach AIDS Prevention in Unit. Baltimore, Maryland, USA.	Cohort study n=324	67% Males	Modified Paffenbarger questionnaire Self-reported physical activity habits included questions on the number of stairs climbed per day, the number of blocks walked per day, the number of times per week they engaged in regular exercise and strength training and the amount of time spent in various activity levels during weekdays and weekends.	Males: 13.2±0.3 h/week of light; 2.6±0.2 h/week of moderate and 1.1 ±0.2 h/week of vigorous activity. Females: 13.3±0.4 h/week of light; 3.0±0.3 h/week of moderate and 0.3±0.1 h/week of vigorous activity. Regular exercise (times per week): 1.21 HIV+ on HAART vs. 1.23 HIV+ and no treatment vs. 1.37 HIV- Strength exercise (times per week): 0.57 HIV+ on HAART vs. 0.45 HVI+ and no treatment vs. 0.74 HIV-	-

		Not mentioned.			Energy expenditure (kcals) was estimated by multiplying the time spent in each activity by body weight and by the specific MET level for each activity.	Light PA (hours per day): 13.6 HIV+ on HAART vs. 13.0 HIV+ and no treatment vs. 12.7 HIV- Moderate PA (hours per day): 2.74 HIV+ on HAART vs. 2.81 HVI+ and no treatment vs. 3.1 HIV- Vigorous PA (hours per day): 0.57 HIV+ on HAART vs. 1.41 HVI+ and no treatment vs. 1.03 HIV-	
Florindo 2006.[25]	3	Participants were selected among a consecutive sampling at the AIDS clinic, Department of Infectious Diseases of the School of Medicine, University of São Paulo, São Paulo, Brazil October 2001 to June 2002.	Cross-validation study n=30	Mean age 37.2 years (26-49.5)	Baecke questionnaire investigated habitual PA, for the last 12 months, with 16 questions covering three components: occupational activity, leisure time and locomotion activities Each question was converted to a Likert scale and each block of questions generated a final score for physical activity. The total score for habitual physical activity is obtained by adding occupational physical activity, physical exercise in leisure, leisure and locomotion activity scores. The total score for habitual physical activity is obtained by adding occupational physical activity, physical exercise in leisure, leisure and locomotion activity scores.	The first and second PA scores were: Occupational: 2.6±0,5 *vs.* 2.7±0.6 Leisure time: 2.3±0,7 *vs.* 2.4±0.5 Leisure and locomotion: 2.6±0.6 *vs.* 2.7±0.5 Total score = 7.3±1.2 *vs.* 7.5±1.3	-
Jacobson 2006.[28]	5	Participants included HIV-positive adults, aged 18 years or older, living in the greater Boston area or Rhode Island. They were recruited through advertisements on the radio as well as in local newspapers, health clinics, and physician networks. Nutrition for health living (NFHL), Cohort study of volunteers with HIV, comparing seronegative participants of	Cross-sectional analysis of a cohort study n=477	74.6% Males Mean age 42.6 years (25-63)	Questionnaire developed by Sallis et al [33], which measures the usual activity over the past 7 days. In this study participants were asked about moderate or vigorous physical activity and muscle strengthening activities over the past 30 days. Regular exercise as any moderate or vigorous activity	Regular exercise: 50.7% Strength exercise: 34.3%	-

		the National Health and Nutrition Examination Survey (NHANES), United States. Beginning July, 2000.			over the past month. Strength training as any strength training over the past month.		
Florindo 2007.[24]	3	Infectious Disease Clinic, Clinical Hospital of São Paulo, Brazil. Not mentioned.	Prevalence study n=220	76.8% Males (20-59 years)	Baecke Questionnaire, 16 Likert scale questions	PA adequate locomotion 65% (female 70.6%, male 63.3%) Leisure-time exercise 47.3% (female 31.4%, male 52.1%) Modalities Walking: 33.7% - 43.8 and 31.8 Weight training: 20.2% - 18.8 and 20.5 Swimming: 9.6% - 12.5 and 9.1 Other forms: 36.5% - 24.9 and 38.6 Overall score: 8.7 ± 1.3	-
Sutinen 2007.[33]	2	Helsinki Central University Hospital, Finland. Not mentioned.	Prevalence study n=43	79% Males Mean age 41.8±2 years	Questions about PA during the interview and indirect calorimetry	Light (6.9 ±0.8 vs.5.7±2.3 h/wk, HAART+LD+ vs. HAART+LD-, NS) and Strenuous physical activity (2.4 ±0.7 vs. 2.7±0.8 h/wk, respectively, NS) was comparable between the groups.	-
Mohammed 2007.[29]	5	HIV+ and HIV- with hepatic alterations Clinics of the University Health Network. October 2003 to June 2005.	Cross-sectional study n=51	100% Males HIV- 43.1±2.5 years; HIV+ 46.2±1.5 years	Questions about PA performed, duration, intensity and date and time in the last week	HIV+ patients were more physically active than HIV-	-
Kowal 2008.[23]	3	Outpatient clinic at publicly funded university teaching hospital in a urban area. Not mentioned.	Cross-sectional study n=97	84% Males Mean age 39.4±8.7 years	Questions about health behaviors included PA	None 36 (37%) One to three times per week 38 (39%) More than three times per week 23 (24%)	37%
Filipas 2008.[15]	5	Infectious Diseases Unit The Alfred Hospital, Melbourne, Australia. April, 2006.	Cross-sectional study n=261	86.6% Males Mean age 43.3 (18-81)	IPAQ short version, usual week	HIV positives Low: 49 (25.7%) Moderate: 63 (33.0%) High: 79 (41.3%) Walking: 90.1% HIV negatives Low: 24 (34.3%) Moderate: 23 (32.9%) High: 23 (32.9%) Walking: 84.3% Not fulfilled classification: 142 (73.8%) HIV- vs. 46 (65.8%) HIV+ p <0.05	28%

Arendt 2008.[14]	1	Unidentified Between July 2004 and May 2007	Prevalence study n=65	100% Males, Mean age 47±0.9 years	Daily life and sports exercise Recommendations from Canada's Physical Activity Guide and Institute of Medicine (IOM)	Recommendation of ≥ 60 min of mild activity per day 30 to 60 of moderate84.5% Moderate to very strenuous 81%	IOM 41.4% sedentary, 15.5% low active, 27.6% active, 15.5% high active
Ramirez-Marrero 2008.[10]	2	AIDS Clinical Trial Unit at the University of Puerto Rico, Puerto Rico. Not mentioned.	Prevalence study n=58	60.3% Males Mean age 46.5±8.8 years	IPAQ ActiGraph Accelerometer Digiwalker Pedometer	Active individuals IPAQ 81% Accelerometer 54% steps per day: 6,862±2,246 counts per day: 24,9146±10,3592 monitoring hours per day: 14.9±2.7 Pedometer 17% steps per day: 7,418±2,714	IPAQ 19% Accelerometer 46% Pedometer 83%
Tsiodras 2009.[34]	3	Outpatient General Clinical Research Center of Beth Israel Deaconess Medical Center (BIDMC). Not mentioned.	Cross-sectional study n=218	85.3% Males Mean age 44.1±7.9 years	Current exercise was evaluated using 3 multiple-choice questions regarding the type and intensity of exercise, frequency and duration. Cumulative indexes for either aerobic or total exercise were calculated as number of sessions per week x duration in minutes per session x exercise intensity	Exercise (number of sessions/week) Non-fat redistribution group 4.7±2.6 Fat accumulation group: 4.1±2.8 Mixed fat redistribution group: 3.7±.8 Fat wasting group: 5.3±2.3	-
Tang 2010.[35]	4	The Tufts Nutrition Collaborative (TNC) Study. Persons with or without HIV living in three US cities (Baltimore, Boston, Providence). 2005-2007.	Cross-sectional study n=511 54.4% HIV+	65% Males Mean age 42.9±7.4 years	Questions about exercise were determinate from the audio computer-assisted self-interview (ACASI) Regular strength training ≥ once/week Aerobic exercise ≥ once/week	30-40% engaging in regular strength training and 50% engaged in regular aerobic exercise	-
Schuelter-Trevisol 2010.*	4	Outpatient Health Care Center (Secretary of Health, State of Rio Grande do Sul, Brazil). 2006-2008.	Cross-sectional study n=1,240	50.6% Males Mean age 39.1±10.1 Range: 18-78 years	IPAQ ActiGraph Accelerometer	Subjects were considered active if they performed physical activity of moderate-to-vigorous intensity at least 150 minutes a week. Active individuals: IPAQ : 57.7%; Accelerometer: 33.3% Physical activity was associated with gender, age and obesity when measured by the accelerometer.	IPAQ 42.3% Accelerometer 66.7%

* Unpublished

PA = physical activity; IPAQ = International Physical Activity Questionnaire; OR = odds ratio; CI = confidence interval

ARTIGO 2

PHYSICAL ACTIVITY ASSESSED BY ACCELEROMETER AMONG HIV-INFECTED PATIENTS: ANALYTICAL AND METHODOLOGICAL ISSUES.

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Running title: Analytical and methodological issues of accelerometer data.

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ABSTRACT

Purpose: To compare different approaches to analyzing accelerometer-based measurement of physical activity among HIV-infected patients, and to verify whether the days of the week chosen to wear the equipment affect the classification of the subjects as physically active.

Methods: Cross-sectional study of HIV-infected adults. Patients were interviewed using a standardized questionnaire during the routine visit for HIV treatment and used ActiGraph accelerometer during two weekdays and two weekend days. Sedentary activities resulted in less than 100 counts recorded, and moderate to vigorous activities in ≥1952 counts. Participants were categorized as active by doing ≥ 150 minutes of moderate or vigorous activities per week or its equivalent for less than seven days recorded. Mean comparison of the level of activity was determined using Generalized Estimation Equations, with sequential Bonferroni analysis.

Results: In the total, 216 patients were studied; mean age was 39.9 ± 9.6 years; 57.4% were women. Within the weekdays, Friday presented the highest average time in minutes of moderate to vigorous activity. The lowest time spent doing moderate to vigorous physical activity was on Sundays, considered a leisure-time day, statistically different from Saturdays.

Conclusion: The choice of accelerometer wearing days interfered with the analysis of data and, consequently, the results. Even so, there was no statistical difference between the categorization of subjects according to their level of physical activity, which allowed reducing the number of accelerometer wearing days, without impairing the quality information.

Keywords: Accelerometer, Physical Activity, Motor Activity, Objective Monitoring, Measurement.

INTRODUCTION

Physical activity is a complex and multi-determined behavior, difficult to measure or estimate with acceptable accuracy[1]. In population-based studies, physical activity is often measured using standardized instruments[2-4]. Questionnaires and diaries of physical activities usually collect data for the previous or the usual week[5]. Therefore, participants' collaboration is necessary for the completion of the record or to recall the activities carried out[6]. Due to the drawbacks of most instruments[7], direct methods for measuring physical activity, such as motion sensors or accelerometers, have been preferred to the recalled data because the objective measurement meets the assumptions of variability of the monitored group[8, 9].

Accelerometers have been used as the reference test for physical activity monitoring [8, 9], since it is possible to estimate the intensity of physical activity at the exact moment that it is performed. In an ideal scenario, it should be assessed in subjects performing daily activities, for a period long enough to capture the usual pattern, with minimal discomfort[3, 10]. The accelerometer captures physical activity as units of counts, which increase linearly with the amount of movements, accounting for the magnitude of the acceleration, due to the changes of a piezoelectric driver[2]. This measurement of body acceleration is generally defined as the area under the corrected acceleration signal, which is measured over a fixed time interval. The counts are used to express frequency, duration and intensity of physical activity [2, 11, 12].

The accuracy of the accelerometer depends on the movements performed, since the equipment does not gather qualitative information regarding the kind of activity or movements with static hip position. Walking is the key activity measured by accelerometers[13]. However, the accelerometer has its own shortcomings such as high cost, counts not being directly converted to any biological unit, and difficulties to interpret the data[9, 14, 15]. The best method to analyze and interpret the data remains unclear. The aim of this study was to compare different approaches to analyzing accelerometer-based measurement of physical activity among HIV-infected patients, and to verify whether the days of the week chosen to wear the equipment affect the classification of the subjects as physically active.

METHODS

Subjects

This cross-sectional study enrolled HIV-infected male and female patients, aged 18 years or older, between March and October 2008, attending a secondary hospital, which is a reference center for HIV-testing and outpatient treatment for HIV, in Porto Alegre, southern Brazil. Patients under the influence of illicit drugs or alcohol at the time of the interview were excluded, as well as pregnant women and subjects with participation restrictions due to mental disability or restrain of freedom. In addition, individuals unable to complete the information for the accelerometer assessment, living in another city, or incapable to return the equipment to the outpatient clinic, were also excluded. The Institution Review Board approved the protocol and patients signed an informed consent to participate.

Data collection

Patients were interviewed using a standardized questionnaire during the routine visit for HIV treatment. Demographic characteristics (age and gender) and questions pertaining to education (years at school), among other variables, were collected by certified interviewers.

The accelerometers were applied and installed by trained research assistants, who provided instructions for its proper use. Participants should wear the equipment continuously including sleeping hours, starting on the day of the appointment. The equipment recorded data for six days, the records for the first and last days were excluded, so two weekdays plus the whole weekend entered in the analysis. The procedures usually took place on Wednesdays, Thursdays or Fridays, in order to include Saturday and Sunday, and the devices were returned on Mondays, Tuesdays or Wednesdays. The accelerometer was attached to the left side of the patient's waist, and they were recommended to remove the monitor when showering, bathing, or swimming. The time spent in these procedures should be recorded, as well as when traveling by bus or car for more than 10 minutes. At the time of the interview, participants received an instruction sheet containing a brief description of the equipment, details about wearing it, and a contact number for calling, if necessary.

Analysis of accelerometer data

Data were read using Mah Huff version 1.7.0.2., which summarizes the information read from the accelerometer in a Microsoft Office Excel spreadsheet and classified physical activity intensity levels[16]. Accelerometer data was considered valid whether it was recorded at least 3,000 counts during three days. The intensity of physical activity measured by accelerometer counts were categorized according to the Freedsom criteria: sedentary activities (0-99 counts), moderate physical activity (1,952-5,724 counts), vigorous physical activity (5,725-9,497 counts), and very vigorous physical activity (> 9,498 counts)[16]. The accelerometer counts ≥1,952 (moderate physical activity or higher) were further aggregated into one category. Physically active participants were also determined according to the number of days recorded doing moderate to very vigorous physical activities, and the overall duration as ≥ 150 minutes during seven days, or its proportional amount for four days (≥ 86 minutes during two weekdays plus two weekend days), and three days (≥65 minutes during two weekdays plus the average of two weekend days)[17, 18].

Sample size calculation and statistical analysis

The sample size was calculated to detect a correlation coefficient of at least 0.20 among physical activity performed in different days, with 90% power and 95% confidence level, which required at least 215 participants. Epi Info version 3.5.1 (Centers for Disease Control) was used for double data entry. The accelerometer exported data to Microsoft Office Excel. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows v 16; Chicago, IL, USA).

Generalized Estimation Equations with sequential Bonferroni analysis was used to compare mean values of physical activity at each intensity level, and for combinations of weekdays and weekend days wearing the accelerometer, such as Monday and Tuesday, Thursday and Friday or Friday and Monday, in addition to Saturday and Sunday.

RESULTS

A total of 216 patients, out of 266, were enrolled; 50 (10.9%) were excluded due to inappropriate use of equipment or battery failure. Most participants were women (57.4%); mean age was 39.9±9.6 years; 64.8% had up to eight schooling years. Accelerometer data was recorded for Sundays (n=215), Mondays (n=166), Tuesdays (n=65), Thursdays (n=51), Fridays (n=151) and Saturdays (n=216). Figure 1 shows that participants tend to spend more time at sedentary activities and lower time in moderate to vigorous activities on Sundays (Figure 2) than the other days, during the accelerometer monitoring days. Figura 3 shows a scatter plot with a linear relationship between weekdays plus Sunday and weekdays plus Saturday (R^2 linear=0.97; P value <0.001).

No one did very vigorous physical activity and Table 1 shows a reduced time spent in vigorous activities. Sedentary activities increased on Sundays, but the active time was reduced. With regard to the days of the week, individuals were more active on Fridays than Sundays (P value <0.001) or Saturdays (P value=0.06), and had more active days on Saturdays than Sundays (P value <0.001), but there was no statistically significant differences between Thursdays and the other days.

Table 2 shows the time spent in moderate to vigorous activities and the percentage of subjects classified as sedentary or active, according to different criteria to analyze the accelerometer data. There was a statistically significant difference in average of time spent in moderate to vigorous activities, but no difference in the categorization of subjects, regardless of the combination of monitoring days.

DISCUSSION

To the best of our knowledge, this is the first study to examine the accelerometer monitoring days and their combinations to classify HIV infected subjects according to levels of physical activity. We were able to detect that the days wearing accelerometer do matter and affect the average time spent in physical activity. The monitoring days were closely related to the duration and intensity of physical activity. While individuals were more sedentary on Sundays, what might be related to the leisure-time activities[19], for most of the weekdays there was no difference in time spent in sedentary activities, possible due to professional activities with no physical demands.

This study also showed that the choice between Saturday and Sunday or their average to represent the weekend might account for differences in the amount of time, but it did not affect the classification of participants as active ones. In adults, accelerometers are usually wear for a period not lower than three days, so complete information can be gather for two weekdays (working days) and for the weekend (resting and leisure-time days) [1, 20]. In the accelerometer analysis, typically five weekdays contributed with 2/3 of the overall amount of records and the weekend included one, two days or their average to complete the 3/3 of counts used to classify subjects. Since we have detected a statistically significant difference in the average of minutes of moderate to vigorous physical activity performed in the weekend, choosing Sunday, Saturday or their average might account for measurement bias.

On weekdays, there was also variability between the mean physical activities per day, at different intensities. Activity counts were higher on Fridays at moderate-to-vigorous activities than in other weekdays. Besides a true difference in physical activity on each day of the week, there are alternative explanations for these results, which include external influences such as day-to-day environmental changes (climate, temperature), individual’s behavior subject to fluctuations, and safety, that is less likely to be instantaneously affected. Based on these results, the most appropriate alternative is the use of alternate monitoring weekdays among different individuals.

Although in some studies participants wore accelerometer for seven days[9, 19, 21], in epidemiological studies this goal is difficult to achieve without jeopardizing the full data collection. Wearing accelerometer in such relatively long period of time is likely to increase missing or lost data, either by not using the equipment, not recording the information or by problems with the battery charge[20, 22, 23]. Besides wearing the equipment on the body for the whole time, they must record the non-wearing hours and bus or car traveling time. In addition, the seven-day period should be increased in two days in order to disregard the first and the last day. Considering the cost, time and sample size, this recommendation restricts the use of accelerometer in large epidemiological studies and hampers the logistics of the fieldwork. Thus, the use of at least three days seems to be more feasible, allowing accuracy of the information [24], precision [15], lower costs due to a higher equipment turnover, and more comfort for participants.

The population of individuals infected with HIV/AIDS, with low income and education, required special attention from the research team. Difficulties included the lack of or improper use of the equipment, failure to return the accelerometer and the difficulty to complete the diary. In order to minimize losses of data and equipment in this study, multiple contacts were made, including home visits.

In conclusion, the choice of two weekdays and Sunday or the average of the weekend, despite differences in the monitoring days, would be more conservative than using Saturday to represent the resting or leisure-time days among HIV infected adults. The different combinations of days categorized as active showed that regardless of the combinations, the final score did not change, which allowed reducing the number of days of accelerometer wearing, without impairing the quality information.

REFERENCES

1. Barros MVG. *Medidas de atividade física: teoria e aplicação em diversos grupos populacionais.* Londrina Midiograf; 2003.
2. Tudor-Locke CE, Myers AM. Challenges and opportunities for measuring physical activity in sedentary adults. *Sports Med.* 2001;31(2):91-100.
3. Macfarlane DJ, Lee CC, Ho EY, Chan KL, Chan D. Convergent validity of six methods to assess physical activity in daily life. *J Appl Physiol.* 2006;101(5):1328-1334.
4. Ham SA, Reis JP, Strath SJ, Dubose KD, Ainsworth BE. Discrepancies between methods of identifying objectively determined physical activity. *Med Sci Sports Exerc.* 2007;39(1):52-58.
5. Craig CL, Marshall AL, Sjostrom M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* 2003;35(8):1381-1395.
6. Hallal PC, Dumith Sde C, Bastos JP, Reichert FF, Siqueira FV, Azevedo MR. [Evolution of the epidemiological research on physical activity in Brazil: a systematic review]. *Rev Saude Publica.* 2007;41(3):453-460.
7. Troiano RP. Large-scale applications of accelerometers: new frontiers and new questions. *Med Sci Sports Exerc.* 2007;39(9):1501.
8. Troiano RP. A timely meeting: objective measurement of physical activity. *Med Sci Sports Exerc.* 2005;37(11 Suppl):S487-489.
9. Trost SG, McIver KL, Pate RR. Conducting accelerometer-based activity assessments in field-based research. *Med Sci Sports Exerc.* 2005;37(11 Suppl):S531-543.
10. Melanson EL, Jr., Freedson PS. Physical activity assessment: a review of methods. *Crit Rev Food Sci Nutr.* 1996;36(5):385-396.
11. Rowlands AV. Accelerometer assessment of physical activity in children: an update. *Pediatr Exerc Sci.* 2007;19(3):252-266.
12. Bouten CV, Koekkoek KT, Verduin M, Kodde R, Janssen JD. A triaxial accelerometer and portable data processing unit for the assessment of daily physical activity. *IEEE Trans Biomed Eng.* 1997;44(3):136-147.
13. Sirard JR, Pate RR. Physical activity assessment in children and adolescents. *Sports Med.* 2001;31(6):439-454.
14. Ward DS, Evenson KR, Vaughn A, Rodgers AB, Troiano RP. Accelerometer use in physical activity: best practices and research recommendations. *Med Sci Sports Exerc.* 2005;37(11 Suppl):S582-588.
15. Baranowski T, Masse LC, Ragan B, Welk G. How many days was that? We're still not sure, but we're asking the question better! *Med Sci Sports Exerc.* 2008;40(7 Suppl):S544-549.
16. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exerc.* 1998;30(5):777-781.
17. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation.* 2007;116(9):1081-1093.
18. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) – Short and Long Forms. 2005; www.ipaq.ki.se.
19. Matthews CE, Ainsworth BE, Thompson RW, Bassett DR, Jr. Sources of variance in daily physical activity levels as measured by an accelerometer. *Med Sci Sports Exerc.* 2002;34(8):1376-1381.
20. Corder K, Brage S, Ekelund U. Accelerometers and pedometers: methodology and clinical application. *Curr Opin Clin Nutr Metab Care.* 2007;10(5):597-603.
21. Corder K, Ekelund U, Steele RM, Wareham NJ, Brage S. Assessment of physical activity in youth. *J Appl Physiol.* 2008;105(3):977-987.

22. Oliveira M. Avaliação da actividade física em contextos epidemiológicos. Uma revisão da validade e fiabilidade do acelerómetro Triatrac-R3D, do pedómetro Yamax Digi-Walker e do questionário de Baecke. *Revista Portuguesa de Ciência do Desporto.* 2001;1(3):73-88.

23. Colley R, Gorber SC, Tremblay MS. Quality control and data reduction procedures for accelerometry-derived measures of physical activity. *Health Rep.* 21(1):63-69.

24. Coleman KJ, Epstein LH. Application of generalizability theory to measurement of activity in males who are not regularly active: a preliminary report. *Res Q Exerc Sport.* 1998;69(1):58-63.

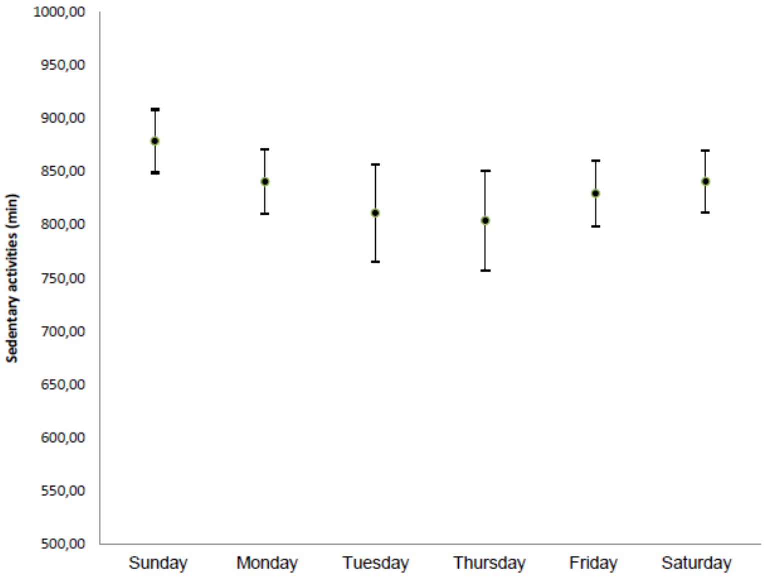

Figure 1. Time spent in sedentary activities during the accelerometer wearing days.

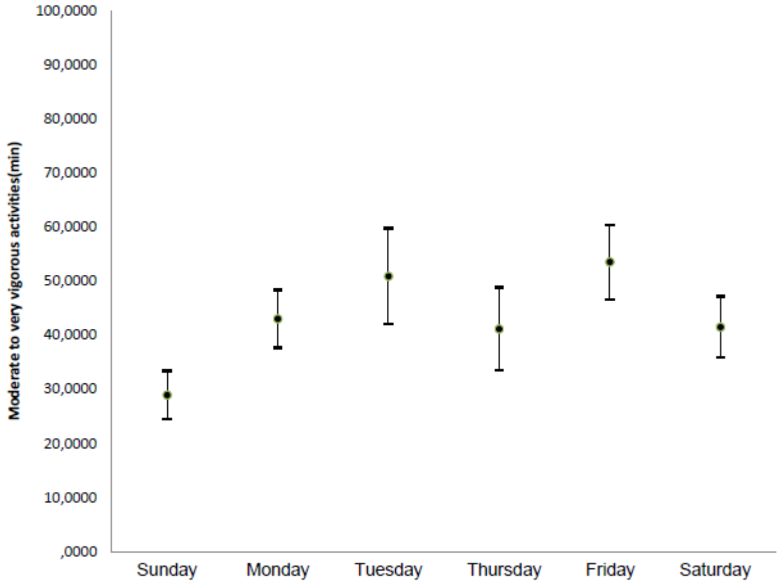

Figure 2. Time spent in moderate to vigorous activities during the accelerometer wearing days.

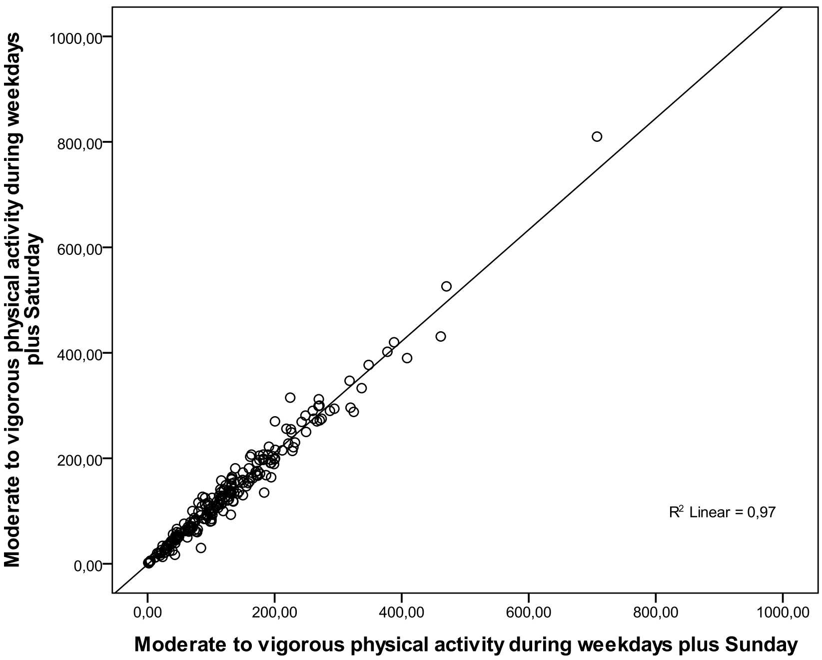

Figure 3. Scaterplot of time spent in physical activity including Saturday or Sunday plus weekdays.

Table 1. Time spent at different physical activity intensities (mean ±SD) according to the day of the week.

	Sedentary	Moderate	Vigorous	Moderate plus vigorous
Sunday	881.1 (221.2)	28.3 (32.8)	0.3 (2.1)	28.6 (33.4)*
Monday	842.7 (212.4)	41.5 (34.3)	1.0 (4.4)	42.6 (35.2)*
Tuesday	813.0 (242.3)	43.8 (47.1)	1.0 (4.1)	44.8 (47.6)*
Thursday	800.9 (201.7)	40.5 (29.9)	1.3 (4.2)	41.8 (32.2)
Friday	828.9 (202.5)	52.4 (44.3)	1.0 (5.6)	53.4 (44.9)* ‡
Saturday	840.8 (216.0)	40.6 (41.8)	0.6 (2.7)	41.3 (42.6)* ‡

* Sunday *vs*. the other days: 0.001<P value<0.06

‡ Friday *vs*. Saturday: P value =0.06

ARTIGO 3

PREVALENCE OF PHYSICAL ACTIVITY AMONG PEOPLE LIVING WITH HIV, ASSESSED BY THE IPAQ AND ACCELEROMETERS.

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ABSTRACT

Objective: To assess the prevalence of physical activity, measured by the International Physical Activity Questionnaire (IPAQ) and accelerometers, among HIV infected individuals and its association between physical activity and demographic or clinical characteristics of those patients.

Methods: A cross-sectional study was conducted from 2006 through 2008 in individuals older than 18 years infected with HIV attending an outpatient care center. Demographic, socioeconomic and lifestyle variables were collected using a questionnaire. Clinical data and laboratory information were obtained from medical records. Physical activity was measured by the IPAQ, short form and by the ActiGraph accelerometer in a subsample. Statistical analysis was performed using the SPSS v 16. Prevalence ratio (95%CI) was calculated for characteristics associated with physical activity, crude and subsequently adjusted for potential confounding variables, using modified Poisson regression models.

Results: A total of 1,240 people living with HIV were studied. Mean age was 39.1 years old (SD±10.1); 50.6% were men; mean years of study was 7.5 (SD±4.1). The prevalence of physical activity measured by the IPAQ and by the accelerometer was 57.7% and 33.3%, respectively.

Conclusions: This study showed higher prevalence rate of physical activity measured by the IPAQ than by the accelerometer, and an independent association with gender, age, education and obesity for physical activity measured by the accelerometer.

Keywords: HIV, Acquired Immunodeficiency Virus, Physical Activity, Inactivity, Prevalence.

INTRODUCTION

Regular physical activity has beneficial effects on health that avert the occurrence of non-communicable diseases.[1] Physical activity is defined as any bodily movement produced by skeletal muscles that results in energy expenditure above resting levels,[2] including leisure-time, occupational, commuting and housework. Population-based studies have shown that individuals engaged in regular physical activity have low morbidity and mortality rates from chronic diseases.[1,3-5]

HIV infected patients are prone to develop chronic, progressive, and fatal diseases, commonly caused by depletion of CD4 lymphocytes. During the course of the illness, many HIV infected individuals experience muscle wasting, weakness, fatigue and depression.[6] Physical activity is a non-pharmacological intervention that might help HIV infected improving aerobic fitness and quality of life, by increasing strength, decreasing fatigue, depression, and anxiety.[7-9]

The current guideline advises moderate-to-vigorous intensity physical activity for 30 minutes at least five days a week. [1, 10] The guideline aims at the general population and there is no specific recommendation for HIV infected individuals or AIDS patients.

Although regular exercise training has been shown to elicit beneficial changes in HIV patients, it is unknown whether there is association between daily physical activity and markers of disease.[11-13]

Physical activity has been investigated through standardized instruments[14, 15] and the International Physical Activity Questionnaire has been recommended in order to allow international comparisons among studies. However, direct measurement methods, such as the accelerometer, are more accurate since they measure frequency, intensity and duration of physical activity.[16, 17]

Considering the lack of consistent data on physical activity in the HIV infected population, the present study was designed to assess the prevalence of physical activity, measured by the IPAQ and accelerometer, among HIV infected individuals.

METHODS

Participants

A cross-sectional study enrolled HIV infected male and female patients, aged 18 years or older, between 2006 and 2008, attending a secondary hospital, which is a reference center for HIV-testing and outpatient treatment for HIV, in Porto Alegre, southern Brazil. Patients under the influence of illicit drugs or alcohol at the time of the interview were excluded, as well as pregnant women, and subjects with participation restriction due to mental disability or restrain of freedom. The Institution Review Board approved the protocol and patients signed an informed consent to participate.

Study Enrollment and Definitions

Patients were interviewed using a standardized questionnaire during the routine visit for HIV treatment. Demographic questions (age, skin color, and gender), socioeconomic questions (education) and lifestyle (physical activity and smoking), among other variables, were collected by certified interviewers. Clinical data (use of highly active antiretroviral therapy and duration of HIV-infection) and laboratory information (CD4 count and HIV viral load) were obtained from medical records, for the three months prior to the interview. Patients were considered on highly active antiretroviral therapy (HAART) use whether taking three antiretroviral drugs; treatment-naïve patients were those who had never used any antiretroviral drug. Viral load below 50 copies/mL HIV RNA was considered undetectable.

Skin color was self-reported and participants were categorized as Whites or non-Whites. Education was measured by years at school, categorized as high school education (yes or no). Smokers were characterized by lifetime consumption of at least 100 cigarettes, and pack-year of smoking was calculated by multiplying the number of packs smoked per day by the number of years smoked. [18] Weight (kg) was measured with patients in light clothing and barefoot to the nearest 100 g with a scale (Filizola Scale, model 31, IN Filizola - SA, São Paulo, Brazil), and height (cm) with an anthropometric ruler, approximated to intervals closer to 0.5 cm. Body mass index (BMI) was calculated by the ratio between weight (kg) and the height square (m^2). The cut-off point of <25 kg/m^2 was used for normal or underweight, 25 to 29.9 kg/m^2 for overweight, and ≥ 30 kg/m^2 for obesity.

Physical activity

Physical activity was evaluated by the short version of the International Physical Activity Questionnaire (IPAQ), and participants were categorized as active if they had performed 150 minutes of moderate to vigorous intensity physical activity, which could be distributed in five days in the week prior to the interview. In a subsample of the participants, living in the city, capable of filling out the diary record and returning the equipment were consecutively selected to measure physical activity using the ActiGraph accelerometer (ActiGraph, Fort Walton Beach, FL). Accelerometer wearing should be continuous, even during sleep time, for four full days (two weekdays and two weekend days), starting on the day following the interview. The accelerometer was attached to the left side of the patient's waist, and patients were recommended to remove the monitor when showering, bathing, or swimming. During these procedures, the time should be recorded, as well as when traveling by bus or car for more than 10 minutes. At the time of the interview, participants received an instruction sheet containing a brief description of the equipment, details about wearing it, and a contact number for calling, if necessary.

Accelerometer

The Actigraph biaxial accelerometer uses arbitrary unit called count, which is a measure unit of the physical activity performed. The counts are summarized and recorded during a specific period of time (epoch) programmed by the researcher. In this study, the data in counts were recorded in 1-minute epochs.[19] Data were read using MAHUffe version 1.7.0.2. (www.mrc-epid.cam.ac.uk), which summarizes the information read from the accelerometer in a Microsoft Office Excel spreadsheet (Microsoft Corporation, Redmond, WA). The placement and return days were excluded from the analysis. The cut-off point for inclusion of valid data was at least a total of 3,000 counts during 3 days. The cut-off point to categorize the intensity level of physical exercise by accelerometer counts was defined according to Freedsom et al:[20] sedentary activities (0-99 counts); mild physical activity (100-1,951 counts); moderate physical activity (1,952-5,724 counts); vigorous physical activity (5,725-9,497 counts); and very vigorous physical activity (> 9,498). The categorization of physically activity was also performed using the sum of the two weekdays and the average of the weekend (D1+D2+(W1+W2)/2); where D1 and D2 = minutes of moderate-to-vigorous physical activity in a two-weekday period; W1 and W2 = minutes of moderate-to-vigorous physical activity during Saturday and Sunday, respectively), resulting in a dichotomous categorization: insufficiently active (<150 minutes) and active (≥ 150 minutes) of moderate-to-vigorous physical per week.[1, 21]

Statistics

Epi Info version 3.5.1 (Centers for Disease Control) was used for double data entry. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows v 16; Chicago, IL, USA).

Data are presented as mean and standard deviation (SD) or frequencies and categorical data were compared by Pearson's chi-square test. Prevalence ratio (95%CI) was calculated for characteristics associated with physical activity, crude and subsequently adjusted for potential confounding variables, using modified Poisson regression models. Confounding factors were selected among variables associated with physical activity, in the bivariate analysis (P value <0.10), or those described as such in the literature.

RESULTS

A total of 1,240 HIV infected patients were enrolled with mean age of 39.9 ±9.6 years, 50.6% were men, and they completed 7.7 ±4.0 at school. The prevalence of physical activity was 57.7% measurement by IPAQ (Table 1).

[Table 1 here]

Women were more active than men (P value = 0.005), even after adjusting for age and education (P value = 0.02). Participants with non-white skin color (P value = 0.02) and with no high school education (P value = 0.04) were detected as more active in the crude analysis, but these associations lost their statistical significance after adjustment for confounding variables, as well as smoking.

In the subsample of 216 participants wearing accelerometer, 57.4% were women, aged 40.4 ± 9.6 years on average, and 53.2% self-reported white skin color. Among participants wearing the accelerometer, 33.3% subjects were active. The prevalence of accelerometer-assessed physical activity and its association with characteristics of participants are presented in Table 2.

[Table 2 here]

The prevalence of physical activity was higher for men and decreased with age. Body mass index (BMI) was inversely associated with physical activity; for obesity, the association remained statistically significant in comparison to BMI below 25 kg/m^2.

Tables 1 and 2 show that clinical characteristics were not associated with being physically active when measured neither by the IPAQ nor the accelerometer. The classification of subjects derived from the IPAQ and the accelerometer measurement had an agreement of 44.4% for HIV infected patients.

DISCUSSION

The prevalence of physically active HIV infected individuals was higher when measured by the IPAQ than assessed by the accelerometer. The difference on prevalence rates might be attributed to the fact that the IPAQ is an indirect method requiring participants to recall the activities performed and their durations, while accelerometers measure them directly. Some studies have reported that physical activity was overestimated by the IPAQ,[22, 23] in comparison to the accelerometer measurement.[24] In a study conducted by Ramirez-Marrero and colleagues, the short version of the IPAQ and accelerometers were used to evaluate physical activity in HIV infected patients, and the prevalence of active individuals was 81% and 54%, respectively.[25]

The prevalence of physical activity reported in this study is in accordance to those assessed in HIV infected individuals, which ranged from 27% to 81%.[25-35] However, the great variability was due to the measurement methods, including different instruments, small sample size, and the characteristics of the studied population.

The hypothesis that HIV infected individuals are less actives than healthy individuals, have shown controversial results. Smit et al[36] found that the energy expenditure of vigorous physical activity was higher among HIV-negative and HIV-positive/HAART-naive individuals than among those on HAART. Jacobson et al.[37] found no statistically significant differences between HIV-infected individuals with or without antiretroviral treatment, but when comparison was made between HIV-infected and those without HIV infection, the latter performed regular physical activity more frequently (46% vs. 60%, respectively). Mohammed et al.[38] found that HIV-positive patients reported more physical activity than individuals without infection (P value = 0.029). However, the group without infection was composed of patients with nonalcoholic fatty liver disease. The study by Fillipas et al.[31] showed that HIV-positive individuals spent more time engaged in vigorous physical activity (P value= 0.03) and in overall physical activity (P value = 0.01) than HIV-negative individuals. Similarly, with regard to energy expenditure at each intensity, they showed that HIV-positive patients had higher expenditure in vigorous-intensity activity (P value = 0.028), moderate-intensity (P value = 0.046) and overall physical activity (P value = 0.019) than HIV-negative individuals. In the study by Mustafa et al.[33] there were no differences between the level of physical activity performed by individuals with or without HIV infection.

In this study, the accelerometer-based measurement classified one third of the patients as physically active, according to the recommendations for non-HIV infected subjects.[6] It should be noted that since HIV infection is now considered a chronic disease, particularly in patients on HAART, physical activity should be emphasized as well as other healthy lifestyle behaviors.[39] Furthermore, in the HIV infected subjects the stage of the disease can affect the engagement in physical activity.

Physical activity, measured by the IPAQ, was more prevalent among women, but most studies have shown that men were more physically active than women.[40-43] Among studies carried out with HIV infected individuals, Shah et al. found that 77.7% of men were physically active vs. 50% of women. However, the sample size was small and 88.2% of participants were males.[34] Among healthy individuals, several studies found high prevalence of physical activity among men, especially with regard to moderate-to-vigorous intensity, such as sports.[40-42] Women are usually engaged in mild-to-moderate physical activity, such as walking, cycling, and domestic activities.[44]

The use of accelerometer is a far more accurate method for physical activity measurement, since it is able to classify individuals, to measure the duration of physical activity, in minutes, and to check its intensity. A possible explanation for our result is that most women who took part in this study were engaged in manual labor, which led to overestimate physical activity measured by the IPAQ.

Studies with non-HIV infected individuals showed a direct association between physical inactivity and body mass index.[45-47] The trend for the inverse association between BMI and physical activity, detected by the accelerometer assessment in this study, was confirmed in studies among HIV infected individuals.[26] Inverse association was found between exercise and body fat,[32] as well as between leisure-time physical activity and subcutaneous body fat and waist/hip ratio.[48]

In conclusion, this study showed higher prevalence rate of physical activity measured by the IPAQ than by the accelerometer, and an independent association with gender, age, and obesity for physical activity measured by the accelerometer.

REFERENCES

1. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation.* 2007;116(9):1081-1093.

2. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* 1985;100(2):126-131.

3. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA.* 1995;273(5):402-407.

4. Berlin JA, Colditz GA. A meta-analysis of physical activity in the prevention of coronary heart disease. *Am J Epidemiol.* 1990;132(4):612-628.

5. Blackburn H, Jacobs DR, Jr. Physical activity and the risk of coronary heart disease. *N Engl J Med.* 1988;319(18):1217-1219.

6. Feinberg MB. Changing the natural history of HIV disease. *Lancet.* 1996;348(9022):239-246.

7. Rigsby LW, Dishman RK, Jackson AW, Maclean GS, Raven PB. Effects of exercise training on men seropositive for the human immunodeficiency virus-1. *Med Sci Sports Exerc.* 1992;24(1):6-12.

8. Stringer WW, Berezovskaya M, O'Brien WA, Beck CK, Casaburi R. The effect of exercise training on aerobic fitness, immune indices, and quality of life in HIV+ patients. *Med Sci Sports Exerc.* 1998;30(1):11-16.

9. Kemppainen JK, Eller LS, Bunch E, et al. Strategies for self-management of HIV-related anxiety. *AIDS Care.* 2006;18(6):597-607.

10. Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee Report, 2008.

11. LaPerriere A, Fletcher MA, Antoni MH, Klimas NG, Ironson G, Schneiderman N. Aerobic exercise training in an AIDS risk group. *Int J Sports Med.* 1991;12 Suppl 1:S53-57.

12. Nixon S, O'Brien K, Glazier RH, Tynan AM. Aerobic exercise interventions for adults living with HIV/AIDS. *Cochrane Database Syst Rev.* 2005(2):CD001796.

13. O'Brien K, Nixon S, Tynan AM, Glazier RH. Effectiveness of aerobic exercise in adults living with HIV/AIDS: systematic review. *Med Sci Sports Exerc.* 2004;36(10):1659-1666.

14. Barros MVG. *Medidas de atividade física: teoria e aplicação em diversos grupos populacionais.* Londrina Midiograf; 2003.

15. Hallal PC, Dumith Sde C, Bastos JP, Reichert FF, Siqueira FV, Azevedo MR. [Evolution of the epidemiological research on physical activity in Brazil: a systematic review]. *Rev Saude Publica.* 2007;41(3):453-460.

16. Hendelman D, Miller K, Baggett C, Debold E, Freedson P. Validity of accelerometry for the assessment of moderate intensity physical activity in the field. *Med Sci Sports Exerc.* 2000;32(9 Suppl):S442-449.

17. Macfarlane DJ, Lee CC, Ho EY, Chan KL, Chan D. Convergent validity of six methods to assess physical activity in daily life. *J Appl Physiol.* 2006;101(5):1328-1334.

18. Cui Q, Carruthers S, McIvor A, Smaill F, Thabane L, Smieja M. Effect of smoking on lung function, respiratory symptoms and respiratory diseases amongst HIV-positive subjects: a cross-sectional study. *AIDS Res Ther.*7:6.

19. Ward DS, Evenson KR, Vaughn A, Rodgers AB, Troiano RP. Accelerometer use in physical activity: best practices and research recommendations. *Med Sci Sports Exerc.* 2005;37(11 Suppl):S582-588.

20. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exerc.* 1998;30(5):777-781.

21. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) – Short and Long Forms. 2005; www.ipaq.ki.se.

22. Sarkin JA, Nichols JF, Sallis JF, Calfas KJ. Self-report measures and scoring protocols affect prevalence estimates of meeting physical activity guidelines. *Med Sci Sports Exerc.* 2000;32(1):149-156.

23. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. *Res Q Exerc Sport.* 2000;71(2 Suppl):S1-14.

24. Fillipas S, Cicuttini F, Holland AE, Cherry CL. The international physical activity questionnaire overestimates moderate and vigorous physical activity in HIV-infected individuals compared with accelerometry. *J Assoc Nurses AIDS Care.*21(2):173-181.

25. Ramirez-Marrero FA, Rivera-Brown AM, Nazario CM, Rodriguez-Orengo JF, Smit E, Smith BA. Self-reported physical activity in Hispanic adults living with HIV: comparison with accelerometer and pedometer. *J Assoc Nurses AIDS Care.* 2008;19(4):283-294.

26. Ramirez-Marrero FA, Smith BA, Melendez-Brau N, Santana-Bagur JL. Physical and leisure activity, body composition, and life satisfaction in HIV-positive Hispanics in Puerto Rico. *J Assoc Nurses AIDS Care.* 2004;15(4):68-77.

27. Arendt BM, Aghdassi E, Mohammed SS, et al. Dietary intake and physical activity in a Canadian population sample of male patients with HIV infection and metabolic abnormalities. *Curr HIV Res.* 2008;6(1):82-90.

28. Clingerman EM. Participation in physical activity by persons living with HIV disease. *J Assoc Nurses AIDS Care.* 2003;14(5):59-70.

29. Domingo P, Sambeat MA, Perez A, Ordonez J, Rodriguez J, Vazquez G. Fat distribution and metabolic abnormalities in HIV-infected patients on first combination antiretroviral therapy including stavudine or zidovudine: role of physical activity as a protective factor. *Antivir Ther.* 2003;8(3):223-231.

30. Eidam CL LA, Guimarães MDC, Oliveira OV. Estilo de vida de pacientes infectados pelo vírus da imunodeficiência humana (HIV) e sua associação com a contagem de linfócitosT CD4+. *Rev Bras Cineantropom Desempenho Hum.* 2006;8(3):51-57.

31. Fillipas S, Bowtell-Harris CA, Oldmeadow LB, Cicuttini F, Holland AE, Cherry CL. Physical activity uptake in patients with HIV: who does how much? *Int J STD AIDS.* 2008;19(8):514-518.

32. Gavrila A, Tsiodras S, Doweiko J, et al. Exercise and vitamin E intake are independently associated with metabolic abnormalities in human immunodeficiency virus-positive subjects: a cross-sectional study. *Clin Infect Dis.* 2003;36(12):1593-1601.

33. Mustafa T, Sy FS, Macera CA, et al. Association between exercise and HIV disease progression in a cohort of homosexual men. *Ann Epidemiol.* 1999;9(2):127-131.

34. Shah M, Tierney K, Adams-Huet B, et al. The role of diet, exercise and smoking in dyslipidaemia in HIV-infected patients with lipodystrophy. *HIV Med.* 2005;6(4):291-298.

35. Salyer J, Lyon DE, Settle J, Elswick RK, Rackley D. Coronary heart disease risks and lifestyle behaviors in persons with HIV infection. *J Assoc Nurses AIDS Care.* 2006;17(3):3-17.

36. Smit E, Crespo CJ, Semba RD, et al. Physical activity in a cohort of HIV-positive and HIV-negative injection drug users. *AIDS Care.* 2006;18(8):1040-1045.

37. Jacobson DL, Tang AM, Spiegelman D, et al. Incidence of metabolic syndrome in a cohort of HIV-infected adults and prevalence relative to the US population (National Health and Nutrition Examination Survey). *J Acquir Immune Defic Syndr.* 2006;43(4):458-466.

38. Mohammed SS, Aghdassi E, Salit IE, et al. HIV-positive patients with nonalcoholic fatty liver disease have a lower body mass index and are more physically active than HIV-negative patients. *J Acquir Immune Defic Syndr.* 2007;45(4):432-438.

39. Sax PE. Strategies for management and treatment of dyslipidemia in HIV/AIDS. *AIDS Care.* 2006;18(2):149-157.

40. Salles-Costa R, Werneck GL, Lopes CS, Faerstein E. [The association between socio-demographic factors and leisure-time physical activity in the Pro-Saude Study]. *Cad Saude Publica.* 2003;19(4):1095-1105.

41. Azevedo MR, Araujo CL, Reichert FF, Siqueira FV, da Silva MC, Hallal PC. Gender differences in leisure-time physical activity. *Int J Public Health.* 2007;52(1):8-15.

42. Monteiro CA, Conde WL, Matsudo SM, Matsudo VR, Bonsenor IM, Lotufo PA. A descriptive epidemiology of leisure-time physical activity in Brazil, 1996-1997. *Rev Panam Salud Publica.* 2003;14(4):246-254.

43. Bauman A, Bull F, Chey T, et al. The International Prevalence Study on Physical Activity: results from 20 countries. *Int J Behav Nutr Phys Act.* 2009;6(1):21.

44. Hallal PC, Victora CG, Wells JC, Lima RC. Physical inactivity: prevalence and associated variables in Brazilian adults. *Med Sci Sports Exerc.* 2003;35(11):1894-1900.

45. Dias-da-Costa JS, Hallal PC, Wells JC, et al. Epidemiology of leisure-time physical activity: a population-based study in southern Brazil. *Cad Saude Publica.* 2005;21(1):275-282.

46. Buchowski MS, Cohen SS, Matthews CE, et al. Physical activity and obesity gap between black and white women in the southeastern U.S. *Am J Prev Med.*39(2):140-147.

47. Santos R, Soares-Miranda L, Vale S, Moreira C, Marques AI, Mota J. Sitting time and body mass index, in a Portuguese sample of men: results from the Azorean Physical Activity and Health Study (APAHS). *Int J Environ Res Public Health.*7(4):1500-1507.

48. Florindo AA, de Oliveira Latorre Mdo R, Jaime PC, Segurado AA. Leisure time physical activity prevents accumulation of central fat in HIV/AIDS subjects on highly active antiretroviral therapy. *Int J STD AIDS.* 2007;18(10):692-696.

Table 1.Characteristics associated with physical activity measured by the IPAQ.

	Total n = 1,240 (%)	Active n (%)	Prevalence Ratio (95%CI)	*Prevalence Ratio (95%CI)
Gender				
Women	612 (49.4)	378 (61.8)	1.0	1.00
Men	628 (50.6)	338 (53.8)	0.87 (0.79-0.96)	0.89 (0.81-0.98)
P value			0.005	0.02
Age (years)				
18-34	471 (38.0)	291 (61.8)	1.0	1.00
35-49	591 (47.7)	323 (54.7)	0.89 (0.80-0.98)	0.90 (0.82-1.00)
50-78	178 (14.3)	102 (57.3)	0.93 (0.80-1.07)	0.94 (0.81-1.09)
P value			0.06	0.17
Education (schooling years)				
≥ 12	143 (11.5)	70 (49.0)	1.0	1.00
< 12	1,097 (88.5)	646 (58.9)	1.20 (1.01-1.43)	1.16 (0.98-1.62)
P value			0.04	0.08
Skin color				
Non-White	548 (44.2)	336 (61.3)	1.0	1.00
White	692 (55.8)	380 (54.9)	0.90 (0.82-0.99)	0.92 (0.83-1.01)
P value			0.02	0.07
Smoking (pack-years)				
Never-smoker	422 (34.0)	238 (56.4)	1.0	1.00
< 20	498 (40.2)	307 (61.6)	1.09 (0.98-1.22)	1.08 (0.97-1.21)
≥ 20	320 (25.8)	171 (53.4)	0.95 (0.83-1.08)	0.98 (0.85-1.12)
P value			0.05	0.2
Body mass index (kg/m^2)				
< 25.0	708 (57.1)	411 (58.1)	1.0	1.00
25.0–29.9	380 (30.6)	217 (57.1)	0.98 (0.88-1.10)	0.98 (0.88-1.09)
≥ 30	152 (12.3)	88 (57.9)	1.00 (0.86-1.16)	0.97 (0.84-1.13)
P value			1.0	0.9
Years since HIV diagnosis				
< 3	485 (39.2)	270 (55.7)	1.0	1.00
3-5.9	350 (28.2)	214 (61.1)	1.10 (0.98-1.23)	1.10 (0.99-1.24)
≥ 6	404 (32.6)	231 (57.2)	1.03 (0.92-1.15)	1.05 (0.94-1.18)
P value			0.3	0.2
Currently on HAART				
No	425 (34.3)	253 (59.5)	1.0	1.00
Yes	815 (65.7)	463 (56.8)	0.95 (0.87-1.05)	0.97 (0.88-1.08)
P value			0.4	0.6
CD4 count (cel/mm^3)				
≥ 350	751 (61.2)	446 (59.4)	1.0	1.00
< 350	476 (38.8)	263 (55.3)	0.93 (0.84-1.03)	0.94 (0.85-1.03)
P value			0.16	0.2
HIV-RNA viral load				
Undetectable	508 (41.6)	294 (57.9)	1.0	1.00
Detectable	713 (58.4)	411 (57.6)	1.00 (0.90-1.10)	0.97 (0.88-1.07)
P value			0.9	0.5

*Prevalence ratio adjusted for gender, age, education.

HIV = Human Immunodeficiency Virus; HAART = highly active antiretroviral treatment; IPAQ = International physical activity questionnaire

Table 2.Characteristics associated with physical activity measured by accelerometer.

	Total n (%)	Active n (%)	Crude Prevalence Ratio (95%CI)	*Prevalence Ratio (95%CI)
Gender				
Women	92	31 (25.0)	1.0	1.00
Men	124	41 (44.6)	1.78 (1.22-2.61)	2.03 (1.41-2.91)
P value			0.003	<0.001
Age (years)				
18-34	68	30 (44.1)	1.0	1.00
35-49	108	34 (31.5)	0.45 (0.23-0.89)	0.64 (0.45-0.92)
50-78	40	8 (20.0)	0.71 (0.49-1.05)	0.40 (0.21-0.77)
P value			0.04	0.005
Education (schooling years)				
≥ 12	30	8 (26.7)	1.0	1.00
< 12	186	64 (34.4)	1.29 (0.69-2.41)	1.30 (0.73-2.33)
P value			0.4	0.4
Skin color				
Non-White	101	37 (36.6)	1.0	1.00
White	115	35 (30.4)	0.83 (0.57-1.21)	0.83 (0.58-1.19)
P value			0.3	0.3
Smoking (pack years)				
Never-smoker	68	25 (36.8)	1.0	1.00
< 20	91	32 (35.2)	0.96 (0.63-1.45)	0.85 (0.57-1.27)
≥ 20	57	15 (26.3)	0.72 (0.42-1.22)	0.72 (0.41-1.27)
P value			0.4	0.5
Body mass index (kg/m^2)				
< 25.0	121	48 (39.7)	1.0	1.00
25.0–29.9	64	22 (34.4)	0.87 (0.51-1.42)	0.92 (0.62-1.36)
≥ 30	31	2 (6.5)	0.16 (0.03-0.52)	0.21 (0.05-0.84)
P value			0.003	0.09
Years since HIV diagnosis				
< 3	86	31 (36.0)	1.0	1.00
3-5.9	58	19 (32.8)	0.91 (0.51-1.59)	1.01 (0.65-1.57)
≥ 6	72	22 (30.6)	0.85 (0.49-1.46)	0.74 (0.48-1.15)
P value			0.8	0.3
Currently on HAART				
No	69	25 (36.2)	1.0	1.00
Yes	147	47 (32.0)	0.88 (0.60-1.31)	1.04 (0.70-1.53)
P value			0.5	0.9
CD4 count (cel/mm^3)				
≥ 350	128	41 (32.0)	1.0	1.00
< 350	85	30 (35.3)	0.91 (0.57-1.47)	0.96 (0.67-1.38)
P value			0.7	0.8
HIV-RNA viral load				
Undetectable	93	31 (33.3)	1.0	1.00
Detectable	120	40 (33.3)	1.0 (0.62-1.59)	1.04 (0.71-1.51)
P value			1.0	0.8

* Prevalence rate adjusted for gender, age, education.
HIV = Human Immunodeficiency Virus; HAART = highly active antiretroviral treatment

ARTIGO 4

ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND LIPODYSTROPHY SYNDROME AMONG HIV-INFECTED PATIENTS IN SOUTHERN BRAZIL.

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Short title: Physical activity and lipodystrophy.

ABSTRACT

Objective: To investigate the association between physical activity and HIV-associated lipodystrophy syndrome, with emphasis on lipohypertrophy and metabolic profile.

Design: A cross-sectional study was conducted from 2006 through 2008 in individuals older than 18 years infected with HIV attending an outpatient care center.

Methods: Eligible participants were invited to participate when they came for regular scheduled medical appointments. A questionnaire including demographic, socioeconomic and lifestyle questions was administered. Clinical data and laboratory information were obtained from medical records or were given request for laboratory examinations. At the end of the interview, objective anthropometric measures were performed. Physical activity was evaluated by the short version of the International Physical Activity Questionnaire (IPAQ). Lipodystrophy was determined by the presence of at least two changes in the body in different areas, using self-perception and/or objective measurements. Statistical analysis was performed using SPSS 16.0. Prevalence ratio (95%CI) was calculated for characteristics associated with physical activity, crude and subsequently adjusted for potential confounding variables, using modified Poisson regression models.

Results: The study consisted of 1,240 participants; 50.6% were men; mean age was 40 ± 9.6 years. The prevalence of lipoatrophy was 53.2% and lipohypertrophy was 46% among HIV-infected individuals. Males, non-Whites, non-smokers, obese, patients on HAART, with CD4 ≥350 cells/mm^3 and undetectable viral load were significantly associated with the presence of lipohypertrophy. Elevated levels of total cholesterol, HDL, LDL, triglycerides and glucose were also associated with lipohypertrophy. Physical inactivity showed to be a risk factor for lipohypertropy only among men, being associated even after adjustment for confounding factors.

Conclusion: The high prevalence of lipohypertrophy, among HIV-infected individuals, was independently associated with inactivity and clinical and behavioral characteristics could increase the risk by 34%. Physically active HAART-naïve subjects had lower levels of total cholesterol, LDL fraction and fasting glucose levels, than those on HAART who only had a significant reduction in triglyceride levels.

Keywords: HIV. AIDS. Lipodystrophy. HIV-associated lipodystrophy syndrome. Physical activity. Exercise. Lifestyle.

INTRODUCTION

Highly active antiretroviral therapy (HAART) has significantly changed the morbidity and quality of life among HIV-infected patients.[1] However, among the adverse effects associated with HAART is the HIV-associated lipodystrophy syndrome, characterized by atrophy in the peripheral regions (fat reduction in the face, arms and legs) and lipohypertrophy in the central region (fat accumulation in the chest, abdomen, neck and dorsocervical region) [2-4], which can be clinically presented isolated or combined and classified as mixed lipodystrophy. [3, 5] The syndrome may also increase the levels of triglycerides, total cholesterol and low density lipoprotein fraction (LDL) and glucose, and reduce the levels of high density lipoprotein (HDL) [6, 7].

Although HIV-associated lipodystrophy syndrome is clearly influenced by the use of HAART, reverse transcriptase inhibitors are strongly associated with lipoatrophy and protease inhibitors to lipohypertrophy and lipid disorders. The pathophysiology of HIV-associated lipodystrophy syndrome is not yet fully elucidated though. There are reports of these changes among HIV-individuals that are not under antiretroviral treatment [6]. Thus, AIDS is now classified as a chronic disease, resulting in increased cardiovascular risk [8].

Behavioral changes and lifestyle, such as diet and physical activity (and/or exercise), could be appropriate non-pharmacological strategies for the prevention or treatment of HIV lipodystrophy syndrome, which is why its effectiveness should be studied. Healthy lifestyle habits are important for the general population and are also relevant for HIV-infected individuals [9]. However, exercise can worsen lipoatrophy[3, 4], even though it has beneficial effects on lipohypertrophy and lipid levels [10-13].

This study aimed to investigate the association between physical activity and HIV-associated lipodystrophy syndrome, with emphasis on lipohypertrophy and metabolic profile.

METHODS

A cross-sectional study enrolled HIV-infected male and female patients, aged 18 years or older, between 2006 and 2008, attending a secondary hospital, which is a reference center for HIV-testing and outpatient treatment for HIV, in Porto Alegre, southern Brazil. Patients under the influence of illicit drugs or alcohol at the time of the interview were excluded, as well as pregnant women and subjects with participation restrictions due to mental disabilities or restraints of freedom. The Institution Review Board approved the protocol and patients signed an informed consent to participate.

Study Enrollment and Definitions

Patients were interviewed using a standardized questionnaire during the routine visit for HIV treatment, including questions pertaining demographic (age, gender), socioeconomic (skin color, education) and lifestyle (physical activity, smoking and alcohol consumption) characteristics by certified interviewers. Clinical data (use of highly active antiretroviral therapy and duration of HIV-infection) and laboratory information (CD4 count and HIV viral load) were obtained from medical records, for the three months prior to the interview. Patients were considered on highly active antiretroviral therapy (HAART) use whether taking three antiretroviral drugs; naïve-treatment patients were those who had never used any antiretroviral drug. Viral load below 50 copies/mL HIV RNA was considered undetectable. Skin color was self-reported and participants were categorized as Whites or non-Whites. Education was measured by years at school, categorized as high school education (yes or no). Smokers were characterized by lifetime consumption of at least 100 cigarettes, and pack-year of smoking was calculated by multiplying the number of packs smoked per day by the number of years smoked[14].

Weight (kg) was measured with patients in light clothing and barefoot to the nearest 100 g with a scale (Filizola Scale, model 31, IN Filizola - SA, São Paulo, Brazil), and height (cm) with an anthropometric ruler, approximated to intervals closer to 0.5 cm. Body mass index (BMI) was calculated by the ratio between weight (kg) and the height square (m^2). Weight, height, waist circumference, hip, arm and neck, and three facial skinfolds - infraorbital, submandibular and buccal) measurements were performed in duplicate and the average was used for analysis. Circumference measurements were performed using inelastic anthropometric tape. The midpoint between the anterior superior iliac spine and iliac crest and the last rib was used for waist circumference. Hip circumference was measured at its largest area. Neck circumference was performed with the patient sitting, with the area uncovered, positioning the tape over the Adam's apple. Circumference of the arm was measured at the midpoint between the acromion and olecranon, with the limb positioned at 90 degrees. Facial skinfolds (infraorbital, buccal and submandibular) were measured with the use of Cescorf brand adipometer.

To identify alcohol consumption abuse, even occasional, binge drinking category was created for individuals with intake of at least five drinks of any beverage on a single occasion.

Inquiries on self-awareness of body changes after HIV infection diagnosis were made. The questions were asked to determine whether the patients had noticed changes in body fat distribution, increase or decrease in general and in specific parts of the body.

Lipodystrophy was determined by the presence of at least two changes in the body in different areas, using self-perception and objective measurements. Self-perception of body changes was based on increase of body fat, or on body parts, including face, dorsocervical fat pads, stomach, chest or breasts; or on the reduction of arms, legs, waist, buttocks, and sunken cheeks in the face. Objective measurements of neck, waist, and hip circumferences, and skin-fold thicknesses in the face. Lipohypertrophy was determined by a combination of at least two measurements at 90^{th} Percentile or positive signs.

Patients for whom information lipid profile - total cholesterol, high density lipoprotein (HDL) fraction and low density lipoprotein (LDL), triglycerides and fasting glucose – could not be obtain from medical records of the examinations performed over the last two months, were given request for laboratory examinations. Blood sample was collected after a 12 hour fasting and all examinations were performed by the same clinical laboratory.

Physical activity

Physical activity was evaluated by the short version of the International Physical Activity Questionnaire (IPAQ), and participants were categorized as active if they had performed ≥ 150 minutes of moderate to vigorous intensity physical activity, distributed during five days in the previous week.

Statistics

Epi Info version 3.5.1 (Centers for Disease Control) was used for double data entry. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows v 16; Chicago, IL, USA). Prevalence ratio (95%CI) was calculated for characteristics associated with physical activity, crude and subsequently adjusted for potential confounding variables, using modified Poisson regression models. Confounding factors were selected among variables associated with physical activity, in the bivariate analysis (P value <0.10), or those described as such in the literature.

RESULTS

A total of 1,240 HIV infected patients were enrolled; mean age was 39.1 ±10.1 years; 50.6% were men, whose average age was 40 ± 9.6 years, and 49.4% were women, whose average age was 38.2 ± 10.4 years.

The characteristics of the participants, classified according to the presence or absence of lipohypertrophy, are shown in Table 1.

[Table 1 here]

Of the total study participants, females, non-Whites, non-smokers, obese, patients on HAART, with CD4 counts greater than 350 cells/mm^3 and undetectable viral load were significantly associated with the presence of lipohypertrophy. Increased levels of total cholesterol, HDL and LDL fractions, triglycerides and glucose were also associated with lipohypertropy.

When gender-related differences were analyzed, physical inactivity, obesity and undetectable viral load in men continued to be associated with lipohypertropy. Among women, those with non-white skin color, obesity, on HAART, CD4 counts greater than 350 cells/mm^3 and undetectable viral load were associated with lipohypertropy.

Table 2 shows the association between physical activity and lipohypertropy in both men and women, adjusted for confounding factors modeled in a progressive way. Physical inactivity showed to be a risk factor for lipohypertropy only among men, being associated even after the full control for confounding factors.

[Table 2 here]

Table 3 shows the association between physical activity measured by the IPAQ and mean fasting glucose and lipid levels. Metabolic parameters seem to be higher among individuals on HAART, in comparison to HAART-naive patients. Among individuals HAART-naive, physically activity had lower mean total cholesterol, LDL and fasting glucose (P value

<0.03) than among inactive individuals, while for those on HAART, only triglycerides levels was higher among the physically inactive (P value = 0.02).

[Here Table 3]

DISCUSSION

This study detected high prevalence of lipohypertrophy (46%) among HIV infected individuals. These results are in accordance with prospective studies, which are confirmed with the use of DEXA, high prevalence of both conditions. Prevalence of lipohypertrophy ranged from 14% to 63%[15]. There was an association between gender and lipoatrophy, higher in men than women, as well as with lipohypertropy, since it was more prevalent in women than in men. The results of this study are consistent with those previously described, since women are at increased risk for central fat accumulation [16].

Lipohypertrophy was also associated with non-white skin color. Non-Whites seem to have higher central fat accumulation[17]. This finding is consistent with that described in the literature[16, 18, 19] and may represent the presence of mixed lipodystrophy.

Lipohypertrophy was also associated with the use of HAART, CD4 count ≥ 350 cells/mm^3 and undetectable viral load. In the gender-related analysis, the association of lipohypertrophy with these clinical variables was observed among women, but remained associated only with undetectable viral load among men. The literature shows some evidence of the association between antiretroviral treatment and the occurrence of lipodystrophy, since the introduction of HAART[20, 21]. The factors most strongly associated with lipohypertrophy are the use of HAART for longer period, use of protease inhibitors and age[17, 22, 23]. In this study, no analysis was performed in the use of HAART by class of antiretroviral drugs, but protease inhibitors are widely used in triple therapy in patients with clinical indication for using pharmacological treatment. Non-smokers had higher prevalence of lipohypertrophy, but this was not observed in the gender-related analysis. A study conducted with 450 male smokers, individuals not infected with HIV, found an association between smoking and increased visceral fat accumulation[24]. However, the effect of nicotine on energy expenditure and appetite suppression may explain less weight gain[25]. Obesity was directly associated with the presence of lipohypertrophy.

Weight, height and BMI are important variables for lipodystrophy assessment. However, these criteria alone are not sufficient to distinguish patients with abnormal fat redistribution (lipoatrophy or lipohypertrophy), since they may be within normal limits in patients with mixed lipodystrophy[3].

This study showed that lipohypertrophy in men was associated with inactivity, independently of age, skin color, education, binge drinking, CD4 and HAART. Such association was not observed among women. Few studies have analyzed the association of physical activity with HIV-lipodystrophy syndrome. A study conducted with 150 HIV-infected individuals taking Stavudine or Zidovudine concluded that physical activity is an independent protective factor for HIV-lipodystrophy syndrome, especially when combined with a proper diet[26]. Physical activity is considered a preventive intervention for lipohypertrophy, which accounts for maintain the body composition[27], and to prevent the accumulation of central body fat[28]. However, despite the beneficial effect of exercise and/or physical activity in preventing lipohypertrophy[29], they may worsen lipoatrophy[4, 13].

With regard to the lipid profile, 35.5% of participants showed increased levels of triglycerides, 30% of total cholesterol, 20.9% of LDL fraction, 3.3% of fasting glucose, and 12.3% had a reduced level of HDL. Lipohypertrophy was associated with elevated total cholesterol, HDL and LDL fractions, triglycerides and fasting glucose. Among women, only elevated levels of HDL and LDL fractions were no associated with lipohypertrophy. The use of hypotriglycemic drugs showed no difference in the prevalence of lipodystrophy (data not shown).

HIV-infected individuals have shown lipid and glucose abnormalities, usually associated with the use of HAART[4, 20, 30, 31]. In a cohort of HIV-infected individuals in Uganda, there was an increase of basal levels of total cholesterol, HDL, LDL and triglycerides 24 months after starting HAART. Triglycerides returned to basal levels at the end of the follow-up period. In this case, the increase in HDL has been described as resulting from the increase in total cholesterol[32], as observed in this study. In addition, individuals who discontinued HAART had a reduction of lipid levels, and in the resumption of treatment, there was an increase in glucose and lipid levels in only eight weeks[33, 34]. Change in triglyceride levels in HIV-infected individuals is a very common finding, regardless of use of HAART[35]. However, many authors consider hypercholesterolemia and hypertriglyceridemia associated with the use of PIs[36, 37].

Elevated serum triglyceride levels are associated with the occurrence of coronary heart disease[38, 39]. Other changes in the lipid profile are also considered risk factors for cardiovascular disease, both in the general population and in HIV-infected individuals[8, 40]. Despite the cardiovascular risk associated with the use and duration of HAART, there is evidence that chronic infection, inflammation and immune function imbalance, caused by HIV infection, contribute to changing the structure and vascular function[41, 42].

Physically active HAART-naive individuals had significantly lower levels of total cholesterol, LDL fraction and glucose. Among HAART-treated subjects, physical activity was associated with lower levels of triglycerides. In adults without HIV infection, several studies have shown that exercise and physical activity have a protective effect on dyslipidemia and is associated with lower levels of total cholesterol, LDL fraction, and in particular, with lower value in serum triglyceride levels[38, 43, 44].

The results of this study showed higher serum cholesterol, HDL, LDL, triglycerides and glucose among inactive individuals. This finding may indicate that the benefits of physical activity are also applicable to HIV-infected individuals, to reduce risk factors for cardiovascular disease. However, there are limitations of the experimental design, since cross-sectional studies cannot establish cause and effect relationship. The lipid profile is influenced by intrinsic factors such as individual metabolism and family history of dyslipidemia and diabetes (genetic)[45] and extrinsic factors such as diet[46, 47] and medication use[48, 49].

In conclusion, the high prevalence of lipohypertrophy, among HIV-infected individuals, was independently associated with inactivity and clinical and behavioral characteristics could increase the risk by 34%. Physically active HAART-naïve subjects had lower levels of total cholesterol, LDL fraction and fasting glucose levels, while those on HAART only had a significant reduction in triglyceride levels. Physical activity is a non-pharmacological strategy appropriate for the prevention or treatment of HIV lipodystrophy syndrome, whereas it has beneficial effects on lipohypertrophy and lipid levels.

REFERENCES

1. Palella FJ, Jr., Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med.* 1998;338(13):853-860.

2. Valente AM, Reis AF, Machado DM, Succi RC, Chacra AR. [Metabolic alterations in HIV-associated lipodystrophy syndrome.]. *Arq Bras Endocrinol Metabol.* 2005;49(6):871-881.

3. Baril JG, Junod P, Leblanc R, et al. HIV-associated lipodystrophy syndrome: A review of clinical aspects. *Can J Infect Dis Med Microbiol.* 2005;16(4):233-243.

4. Carr A. HIV lipodystrophy: risk factors, pathogenesis, diagnosis and management. *AIDS.* 2003;17 Suppl 1:S141-148.

5. Kravcik S. HIV lipodystrophy: a review. *HIV Clin Trials.* 2000;1(3):37-50.

6. Bodasing N, Fox R. HIV-associated lipodystrophy syndrome: assessment and management. *J Infect.* 2003;46(2):87-93.

7. Constans J, Pellegrin JL, Peuchant E, et al. Plasma lipids in HIV-infected patients: a prospective study in 95 patients. *Eur J Clin Invest.* 1994;24(6):416-420.

8. Bergersen BM, Sandvik L, Bruun JN, Tonstad S. Elevated Framingham risk score in HIV-positive patients on highly active antiretroviral therapy: results from a Norwegian study of 721 subjects. *Eur J Clin Microbiol Infect Dis.* 2004;23(8):625-630.

9. Collins RL, Kanouse DE, Gifford AL, et al. Changes in health-promoting behavior following diagnosis with HIV: prevalence and correlates in a national probability sample. *Health Psychol.* 2001;20(5):351-360.

10. Thoni GJ, Fedou C, Brun JF, et al. Reduction of fat accumulation and lipid disorders by individualized light aerobic training in human immunodeficiency virus infected patients with lipodystrophy and/or dyslipidemia. *Diabetes Metab.* 2002;28(5):397-404.

11. Terry L. HIV e exercício. *Revista da Sociedade de Cardiologia do Rio Grande do Sul.* 2008;XV(9):1-7.

12. Terry L, Sprinz E, Stein R, Medeiros NB, Oliveira J, Ribeiro JP. Exercise training in HIV-1-infected individuals with dyslipidemia and lipodystrophy. *Med Sci Sports Exerc.* 2006;38(3):411-417.

13. Roubenoff R, Weiss L, McDermott A, et al. A pilot study of exercise training to reduce trunk fat in adults with HIV-associated fat redistribution. *AIDS.* 1999;13(11):1373-1375.

14. Cui Q, Carruthers S, McIvor A, Smaill F, Thabane L, Smieja M. Effect of smoking on lung function, respiratory symptoms and respiratory diseases amongst HIV-positive subjects: a cross-sectional study. *AIDS Res Ther.*7:6.

15. Peterson S, Martins CR, Cofrancesco J, Jr. Lipodystrophy in the patient with HIV: social, psychological, and treatment considerations. *Aesthet Surg J.* 2008;28(4):443-451.

16. Lichtenstein KA, Delaney KM, Armon C, et al. Incidence of and risk factors for lipoatrophy (abnormal fat loss) in ambulatory HIV-1-infected patients. *J Acquir Immune Defic Syndr.* 2003;32(1):48-56.

17. Bogner JR, Vielhauer V, Beckmann RA, et al. Stavudine versus zidovudine and the development of lipodystrophy. *J Acquir Immune Defic Syndr.* 2001;27(3):237-244.

18. Galli M, Veglia F, Angarano G, et al. Gender differences in antiretroviral drug-related adipose tissue alterations. Women are at higher risk than men and develop particular lipodystrophy patterns. *J Acquir Immune Defic Syndr.* 2003;34(1):58-61.

19. Jacobson DL, Knox T, Spiegelman D, Skinner S, Gorbach S, Wanke C. Prevalence of, evolution of, and risk factors for fat atrophy and fat deposition in a cohort of HIV-infected men and women. *Clin Infect Dis.* 2005;40(12):1837-1845.

20. Carr A, Cooper DA. Adverse effects of antiretroviral therapy. *Lancet.* 2000;356(9239):1423-1430.

21. Carr A. HIV protease inhibitor-related lipodystrophy syndrome. *Clin Infect Dis.* 2000;30 Suppl 2:S135-142.

22. Miller J, Carr A, Emery S, et al. HIV lipodystrophy: prevalence, severity and correlates of risk in Australia. *HIV Med.* 2003;4(3):293-301.

23. Chen D, Misra A, Garg A. Clinical review 153: Lipodystrophy in human immunodeficiency virus-infected patients. *J Clin Endocrinol Metab.* 2002;87(11):4845-4856.

24. Komiya H, Mori Y, Yokose T, Tajima N. Smoking as a risk factor for visceral fat accumulation in Japanese men. *Tohoku J Exp Med.* 2006;208(2):123-132.

25. Chiolero A, Faeh D, Paccaud F, Cornuz J. Consequences of smoking for body weight, body fat distribution, and insulin resistance. *Am J Clin Nutr.* 2008;87(4):801-809.

26. Domingo P, Sambeat MA, Perez A, Ordonez J, Rodriguez J, Vazquez G. Fat distribution and metabolic abnormalities in HIV-infected patients on first combination antiretroviral therapy including stavudine or zidovudine: role of physical activity as a protective factor. *Antivir Ther.* 2003;8(3):223-231.

27. Ramirez-Marrero FA, Smith BA, Melendez-Brau N, Santana-Bagur JL. Physical and leisure activity, body composition, and life satisfaction in HIV-positive Hispanics in Puerto Rico. *J Assoc Nurses AIDS Care.* 2004;15(4):68-77.

28. Florindo AA, de Oliveira Latorre Mdo R, Jaime PC, Segurado AA. Leisure time physical activity prevents accumulation of central fat in HIV/AIDS subjects on highly active antiretroviral therapy. *Int J STD AIDS.* 2007;18(10):692-696.

29. Smith BA, Neidig JL, Nickel JT, Mitchell GL, Para MF, Fass RJ. Aerobic exercise: effects on parameters related to fatigue, dyspnea, weight and body composition in HIV-infected adults. *AIDS.* 2001;15(6):693-701.

30. Carr A, Samaras K, Burton S, et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. *AIDS.* 1998;12(7):F51-58.

31. Guimaraes MM, Greco DB, de OJAR, Penido MG, Machado LJ. [Corporal fat distribution and lipidic and glicemic profiles of HIV-infected patients]. *Arq Bras Endocrinol Metabol.* 2007;51(1):42-51.

32. Buchacz K, Weidle PJ, Moore D, et al. Changes in lipid profile over 24 months among adults on first-line highly active antiretroviral therapy in the home-based AIDS care program in rural Uganda. *J Acquir Immune Defic Syndr.* 2008;47(3):304-311.

33. Seoane E, Resino S, Micheloud D, et al. Lipid and apoprotein profile in HIV-1-infected patients after CD4-guided treatment interruption. *J Acquir Immune Defic Syndr.* 2008;48(4):455-459.

34. Skiest DJ, Krambrink A, Su Z, Robertson KR, Margolis DM. Improved measures of quality of life, lipid profile, and lipoatrophy after treatment interruption in HIV-infected patients with immune preservation: results of ACTG 5170. *J Acquir Immune Defic Syndr.* 2008;49(4):377-383.

35. Grunfeld C, Feingold KR. Metabolic disturbances and wasting in the acquired immunodeficiency syndrome. *N Engl J Med.* 1992;327(5):329-337.

36. Tsiodras S, Mantzoros C, Hammer S, Samore M. Effects of protease inhibitors on hyperglycemia, hyperlipidemia, and lipodystrophy: a 5-year cohort study. *Arch Intern Med.* 2000;160(13):2050-2056.

37. Heath KV, Chan KJ, Singer J, O'Shaughnessy MV, Montaner JS, Hogg RS. Incidence of morphological and lipid abnormalities: gender and treatment differentials after initiation of first antiretroviral therapy. *Int J Epidemiol.* 2002;31(5):1016-1020.

38. Tirosh A, Rudich A, Shochat T, et al. Changes in triglyceride levels and risk for coronary heart disease in young men. *Ann Intern Med.* 2007;147(6):377-385.

39. Sarwar N, Danesh J, Eiriksdottir G, et al. Triglycerides and the risk of coronary heart disease: 10,158 incident cases among 262,525 participants in 29 Western prospective studies. *Circulation.* 2007;115(4):450-458.

40. Baum MK, Rafie C, Lai S, et al. Coronary Heart Disease (CHD) Risk Factors and Metabolic Syndrome in HIV-Positive Drug Users in Miami. *Am J Infect Dis.* 2006;2(3):173-179.

41. Boccara F. Cardiovascular complications and atherosclerotic manifestations in the HIV-infected population: type, incidence and associated risk factors. *AIDS.* 2008;22 Suppl 3:S19-26.

42. Fichtenbaum CJ. Does antiretroviral therapy increase or decrease the risk of cardiovascular disease? *Curr HIV/AIDS Rep.* 7(2):92-98.

43. Guedes DP, Goncalves LA. [Impact of the habitual physical activity on lipid profile in adults]. *Arq Bras Endocrinol Metabol.* 2007;51(1):72-78.

44. Healy GN, Dunstan DW, Salmon J, et al. Breaks in sedentary time: beneficial associations with metabolic risk. *Diabetes Care.* 2008;31(4):661-666.

45. Yamada Y, Matsuo H, Warita S, et al. Prediction of genetic risk for dyslipidemia. *Genomics.* 2007;90(5):551-558.

46. Arendt BM, Aghdassi E, Mohammed SS, et al. Dietary intake and physical activity in a Canadian population sample of male patients with HIV infection and metabolic abnormalities. *Curr HIV Res.* 2008;6(1):82-90.

47. Sheehan LA, Macallan DC. Determinants of energy intake and energy expenditure in HIV and AIDS. *Nutrition.* 2000;16(2):101-106.

48. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation.* 2002;106(25):3143-3421.

49. [I Brazilian guidelines on diagnosis and treatment of metabolic syndrome]. *Arq Bras Cardiol.* 2005;84 Suppl 1:1-28.

Table 1: Socio-demographic and clinical characteristics of patients.

		Prevalence of Lipohypertropy		
	Total (n = 1,240)	Overall n (%)	Men n (%)	Women n (%)
Gender				
Men	612	242 (38.5)	-	-
Women	628	328 (53.6)	-	-
P value		<0.001		
Age (years)				
18-34	471	211 (44.8)	69 (34.3)	142 (52.6)
35-49	591	266 (45.0)	135 (39.8)	131 (52.0)
50-78	178	93 (52.2)	38 (43.2)	55 (61.1)
P value		0.2	0.3	0.3
Skin color				
White	692	298 (43.1)	148 (38.9)	150 (48.1)
Non-white	548	272 (49.6)	94 (37.9)	178 (59.3)
P value		0.02	0.8	0.005
Education (schooling years)				
< 12	1,097	504 (45.9)	199 (37.4)	305 (54.0)
≥ 12	143	66 (46.2)	43 (44.8)	23 (48.9)
P value		1.0	0.17	0.5
Smoking (pack-years)				
Never-smoker	422	221 (54.2)	81 (44.5)	140 (58.3)
< 20	498	211 (42.4)	87 (36.3)	124 (48.1)
≥ 20	320	138 (43.1)	74 (35.9)	64 (56.1)
P value		0.005	0.15	0.06
Physical activity				
Actives	716	324 (45.3)	114 (33.7)	210 (55.6)
Inactives	524	246 (46.9)	128 (44.1)	118 (50.4)
P value		0.6	0.008	0.2
Binge drinking				
Yes	474	212 (44.7)	113 (39.9)	99 (51.8)
No	752	350 (46.5)	129 (37.5)	221 (54.2)
P value		0.6	0.6	0.7
Body mass index (kg/m^2)				
< 25	708	223 (31.5)	94 (24.9)	129 (39.1)
25–29.9	380	220 (57.9)	105 (53.0)	115 (63.2)
≥ 30	152	127 (83.6)	43 (82.7)	84 (84.0)
P value		<0.001	<0.001	<0.001
Years since HIV diagnosis				
< 3	485	206 (42.5)	82 (34.2)	124 (50.6)
3-5,9	350	169 (48.3)	73 (42.4)	96 (53.9)
≥ 6	404	195 (48.3)	87 (40.3)	108 (57.4)
P value		0.14	0.19	0.4
Currently on HAART				
Yes	815	409 (50.2)	167 (39.8)	242 (61.3)
No	425	161 (37.9)	75 (36.1)	86 (39.6)
P value		<0.001	0.4	<0.001
CD4 count (cel/mm^3)				
< 350	476	193 (40.5)	86 (34.1)	107 (47.8)
≥ 350	751	372 (49.5)	153 (41.6)	219 (57.2)
P value		0.002	0.06	0.03
HIV-RNA viral load				
Undetectable	713	280 (55.1)	124 (46.3)	156 (65.0)
Detectable	508	282 (39.6)	113 (32.3)	169 (46.6)

P value		<0.001	<0.001	<0.001
Total cholesterol (mg/dL)				
< 200	854	352 (41.2)	148 (33.5)	204 (49.5)
≥ 200	372	214 (57.5)	90 (51.1)	124 (63.3)
P value		<0.001	<0.001	0.001
HDL (mg/dL)				
< 35	152	50 (32.9)	28 (26.7)	22 (46.8)
≥ 35	1,074	516 (48.0)	210 (40.9)	306 (54.5)
P value		<0.001	0.006	0.3
LDL (mg/dL)				
< 130	966	424 (43.9)	188 (36.7)	236 (52.0)
≥ 130	259	142 (54.8)	50 (47.6)	92 (59.7)
P value		0.002	0.04	0.1
Triglycerides (mg/dL)				
< 150	787	316 (40.2)	107 (29.6)	209 (49.1)
≥150	440	251 (57.0)	132 (51.2)	119 (65.4)
P value		<0.001	<0.001	<0.001
Fasting glucose (mg/dL)				
< 126	1,185	538 (45.4)	223 (37.6)	315 (53.2)
≥126	41	28 (68.3)	15 (60.0)	13 (81.3)
P value		0.004	0.02	0.03

Table 2: Association between physical activity and lipohypertropy adjusted for confounding variables.

	Lipohypertropy	
	Adjusted Prevalence Ratio (CI 95%)	**P value**
IPAQ **Men**		
Actives*	1.0	
Insufficiently actives	1.31 (1.07-1.60)	0.008
Model 1*	1.31 (1.07-1.59)	0.008
Model 2**	1.30 (1.07-1.59)	0.009
Model 3***	1.30 (1.07-1.58)	0.01
Model 4****	1.30 (1.07-1.58)	0.009
Model 5*****	1.34 (1.10-1.63)	0.004
Model 6******	1.34 (1.10-1.63)	0.004
IPAQ **Women**		
Actives*	1.0	
Insufficiently actives	0.91 (0.78-1.06)	0.2
Model 1*	0.91 (0.78-1.06)	0.2
Model 2**	0.92 (0.79-1.08)	0.3
Model 3***	0.93 (0.79-1.08)	0.3
Model 4****	0.92 (0.79-1.08)	0.3
Model 5*****	0.93 (0.80-1.08)	0.3
Model 6******	0.93 (0.80-1.08)	0.3

*adjusted for age
**adjusted for age and skin color
***adjusted for age, skin color and education
****adjusted for age, skin color, education and pack years
*****adjusted for age, skin color, education, binge drinking and CD4.
******adjusted for age, skin color, education, binge drinking, CD4 and HAART.

Table 3. Association between physical activity and metabolic profile among treatment-naive HIV-infected individuals or under antiretroviral therapy.

	HIV patients HAART-naïve (n=425)			
	mean (SD)	**Inactive**	**Active**	**p-value**
Total cholesterol (mg/dL)	173.7 ±37.5	179.6 ±38.0	169.8 ±36.7	0.009
HDL (mg/dL)	49.8 ±13.1	50.3 ±12.2	49.5 ±13.7	0.5
LDL (mg/dL)	99.9 ±32.7	104.6 ±34.0	96.7 ±31.5	0.02
Fasting glucose (mg/dL)	84.3 ±22.3	87.3 ±29.1	82.3 ±16.0	0.03
Triglycerides (mg/dL)	120.6 ±63.3	121.0 ±59.2	120.3 ±66.0	0.9
	HIV patients currently on HAART (n=815)			
Total cholesterol (mg/dL)	187.9 ±45.7	189.5 ±44.9	186.7 ±46.4	0.4
HDL (mg/dL)	51.9 ±14.1	51.1 ±14.6	52.4 ±13.7	0.2
LDL (mg/dL)	103.0 ±38.0	102.8 ±36.5	103.2 ±39.1	0.9
Fasting glucose (mg/dL)	88.2 ±29.9	88.9 ±30.1	87.6 ±29.8	0.5
Triglycerides (mg/dL)	167.9±121.1	179.1 ±122.2	159.4±119.7	0.02

CONSIDERAÇÕES FINAIS

A infecção pelo HIV e o desenvolvimento de AIDS modificaram seus cursos clínicos com o advento de TARV e seus portadores apresentam risco de eventos cardiovasculares fatais e não fatais, tanto pela infecção viral como pelos efeitos adversos da terapia antirretroviral potente.

Como evidenciado nos artigos apresentados, não há um método de referência para aferição de atividade física, o uso de acelerômetro provê informações úteis, mas demanda mais tempo da equipe, maior custo e problemas adicionais com a logística do estudo.

A mensuração objetiva de atividade física realizada por meio do acelerômetro pode ser feita em três dias, sendo utilizado dois dias quaisquer da semana e os dois dias do final de semana ou a média do final de semana.

Foi possível concluir que a prevalência de atividade física não está associada a características clínicas, como foram descritas por alguns autores na literatura científica. Não houve associação entre a atividade física e marcadores laboratoriais e sinais de atividade do HIV em uso de HAART.

Potencial benefício da atividade física sobre a lipo-hipertrofia, observada em homens, deve ser confirmada em outros estudos e, nesse caso, poderia ser recomendada como estratégia preventiva.