



A eficácia de um programa recreativo de futebol em indicadores cardiovasculares e metabólicos. Um estudo em adolescentes brasileiros obesos

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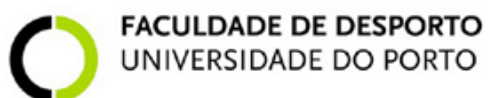
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Resumo

A obesidade na adolescência tem aumentado a um ritmo alarmante, atingindo proporções epidêmicas, tornando-se por isso um grave problema de saúde pública. Este aumento é particularmente preocupante, pois a obesidade segundo a Organização Mundial de Saúde, para além de ser entendida como uma doença, acarreta a ocorrência de diversas comorbidades de que se destacam, entre outras: as complicações metabólicas que contribuem para um risco aumentado de doenças cardiovasculares, alterações significativas nos diferentes componentes da composição corporal e baixos níveis de aptidão física. A obesidade e suas comorbidades são consideradas, nos tempos atuais, um problema de saúde a resolver o mais precocemente possível, a fim de evitar o desenvolvimento de consequências salutaras futuras. Neste sentido, na presente dissertação foi realizada uma revisão de literatura objetivando identificar o efeito da atividade física em marcadores de saúde em adolescentes obesos. Os resultados indicaram que a atividade física está associada a mudanças significativas e benéficas no percentual de gordura, circunferência da cintura, pressão arterial sistólica, insulina, colesterol de lipoproteína de baixa densidade (LDL) e colesterol total. Após esta revisão de literatura, foi realizado um estudo de intervenção, demonstrando que um programa de Futebol recreativo promove, reduções significativas na massa corporal (-3,1%), IMC (-2,7%), circunferência da cintura (-6,6%), percentual de gordura corporal (-5%), pressão arterial sistólica (-2,7%), colesterol total (-8,7%), triglicérides (-14,3%), proteína C-reativa (-28,5%), resistência à insulina (HOMA-IR) (-32,6%) e atividade simpática (-23,9%) quando comparado com os controlos. Concomitantemente, investigou-se a fidedignidade e reprodutibilidade de métodos mais acessíveis, do ponto de vista financeiro e prático, para a prescrição e controlo do treino desta população. Inicialmente foi investigada a concordância de dois equipamentos utilizados para avaliar a variabilidade da frequência cardíaca com o eletrocardiograma (método *gold standard*) e posteriormente a reprodutibilidade dos mesmos. Os resultados mostraram correlações significativas entre os índices de variabilidade da frequência cardíaca obtidos pelo Polar RS800CX e fotoplestimografia quando comparados com o eletrocardiograma, com coeficiente de determinação (R^2) e coeficiente de correlação intraclasse (ICC) que variaram 0,60-0,98 e 0,70-0,99, respectivamente. O reconhecimento destes equipamentos como métodos fiáveis, permitiu o avanço da presente dissertação, no sentido de investigar a fiabilidade do método de detecção do limiar anaeróbio pelo limiar de variabilidade da frequência cardíaca para esta população. Nenhuma diferença significativa foi encontrada para VO_2 , % VO_2 de reserva e frequência cardíaca no limiar anaeróbio determinado pelo limiar de variabilidade e limiar ventilatório. O conjunto de resultados encontrados nos estudos que constituem esta dissertação, permitiu avançar em recomendações para a prescrição e controlo de programas de intervenção mais eficazes no combate e prevenção da obesidade na adolescência.

Palavras-chave: FUTEBOL, ADOLESCENTES, MARCADORES CARDIOVASCULARES, FUNÇÃO AUTONÔMICA CARDÍACA.

Abstract

Adolescent obesity has increased at an alarming rate, reaching epidemic proportions, and becoming so serious public health problem. This increased rate is particularly alarming because obesity, according to the World Health Organization, beyond to being seen as a disease, causes the occurrence of several comorbidities that stand out among others: metabolic complications (presence of metabolic syndrome) that contribute to an increased risk of cardiovascular disease, significant changes in the various components of body composition and low levels of physical fitness. Nowadays, the obesity and its comorbidities are considered a health problem to solve as early as possible in order to avoid the development of future health problems. In this sense, the present thesis carries a literature review in order to identify the effect of physical activity intervention programs in obese adolescents. The results indicated that physical activity is associated with significant and beneficial changes in fat percentage, waist circumference, systolic blood pressure, insulin, low-density lipoprotein cholesterol (LDL), and total cholesterol. After a literature review was conducted, it was performed an intervention study showing that a recreational soccer program promotes, from baseline to post-intervention, soccer participants demonstrated significant reductions in weight (-3.1%), BMI (-2.7%), waist circumference (-6.6%), %body fat (-5%), SBP (-2.7%), total cholesterol (-8.7%), triglycerides (-14.3%), C-reactive protein (-28.5%), insulin resistance (HOMA-IR) (-32.6%) and sympathetic activity (-23.9%) vs. controls ($P < 0.05$). Concomitantly, it was investigated the test-retest reliability of methods more accessible, the financial and practical point of view, to prescribe and control training in this population. Initially, it was investigated the level of agreement of two devices used to assess the heart rate variability and electrocardiogram (gold standard method) and subsequently the reproducibility. The results showed significant correlations between HRV markers obtained by Polar RS800cx and PPG vs. ECG, with coefficient of determination (R^2) and intraclass correlation coefficient (ICC) ranging from 0.60 to 0.98 and 0.70 to 0.99, respectively. The recognition of the devices as reliable methods allowed the advancement of this thesis to investigate the reliability of the detection method of the anaerobic threshold by heart rate variability threshold for this population. No significant difference was found for VO_2 , % $\text{VO}_{2\text{rR}}$, and heart rate at anaerobic threshold determined by heart rate variability threshold and ventilatory threshold. The set of results found in studies that constitute this thesis lead to progress on recommendations for prescription control and intervention programs more effective in fighting and preventing obesity in adolescence.

Keywords: SOCCER, ADOLESCENTS, CARDIOVASCULAR MARKERS, CARDIAC AUTONOMIC FUNCTION.

Lista de abreviaturas

ANS	→ Sistema nervoso autônomo
BMI	→ Índice de massa corporal
BP	→ Pressão arterial
CPET	→ Teste cardiopulmonar
CPR	→ Proteína C-reativa
CVD	→ Doenças cardiovasculares
DBP	→ Pressão arterial diastólica
DCVs	→ Doenças cardiovasculares
DM2	→ Diabetes mellitus tipo 2
DXA	→ Absorciometria de dupla energia de raios-X
ECG	→ Eletrocardiograma
ET-1	→ Endotelina-1
FBF	→ Fluxo sanguíneo do antebraço
FMD	→ Dilatação de fluxo medial
GET	→ Limiar ventilatório
HDL	→ Lipoproteína-colesterol de alta densidade
HF	→ Componente de alta frequência
HGF	→ Fator de crescimento de hepatócitos
HOMA-IR	→ Modelo de avaliação homeostática
HR	→ Frequência cardíaca
HR _{max}	→ Frequência cardíaca máxima
HR _{peak}	→ Pico da frequência cardíaca
HRV	→ Variabilidade da frequência cardíaca
HRVT	→ Limiar de variabilidade da frequência cardíaca
ICC	→ Coeficiente de correlação intraclasse
IL6	→ Interleucina-6
IMC	→ Índice de massa corporal
IMC _{zscore}	→ Curvas em score Z para o índice de massa corporal
LDL	→ Lipoproteína-colesterol de baixa densidade

LF / HF → Balanço simpato-vagal

LF → Componente de baixa frequência

LiVFC → Limiar de variabilidade da frequência cardíaca

LoA → Limite de concordância

LT → Limiar de lactato

MBP → Pressão arterial média

N.U. → Unidades normalizadas

NASH → Núcleo de estudo e saúde do adolescente

NEFA → Ácidos graxos não esterificados

NITRO → Nitroprussiato

PA → Atividade física

PAI-1 → Inibidor do ativador do plasminogênio-1

PEDro → Escala de fisioterapia de evidências de banco de dados

pNN50 → Proporção do número de pares de batimentos cardíacos sucessivos que diferem por mais de 50 ms, dividido pelo número total de ciclos cardíacos

PPG → Fotoplestimografia

RER → Quociente respiratório

RER_{max} → Quociente respiratório máximo

rMSSD → Raiz quadrada da soma das diferenças sucessivas entre os intervalos RR normais adjacentes ao quadrado

R-R intervals → Média de todos os intervalos R-R normais

RSP → Programa de Futebol recreativo

SBP → Pressão arterial sistólica

SD → Desvio padrão

SEE → Erro padrão de estimativa

TEM → Erro técnico de medida

TNF- Δ → Fator de necrose tumoral

VFC → Variabilidade da frequência cardíaca

VO₂ → Consumo de oxigênio

VO₂ de pico → Consumo de oxigênio de pico

VO_{2max} → Capacidade aeróbica máxima
 VO_{2R} → Consumo de oxigênio de reserva
 VO_{2rest} → Consumo de oxigênio no repouso
WC → Circunferência da cintura
WHO → Organização Mundial de Saúde.

Capítulo I

Introdução

1. Introdução geral

A obesidade na adolescência tem aumentado significativamente nas últimas décadas, atingindo na atualidade proporções epidêmicas e tornando-se por isso um grave problema de Saúde Pública. De acordo com o Centro de Controle e Prevenção de Doenças dos Estados Unidos da América, a prevalência de excesso de peso e obesidade na adolescência triplicou nas últimas décadas, tendo passado de 6.5%, em 1981, para 19.6% em 2008 [1]. No Brasil, a prevalência de excesso de peso e obesidade em adolescentes, também registrou um aumento significativo, evoluindo de 4.1% em 1975 para 27.6% em 2009 [2].

O mapeamento do excesso de peso e obesidade é da maior importância, atendendo ao fato de a obesidade em idade pediátrica estar, por um lado, associada a um conjunto variado de comorbidades, e por outro lado, por se tratar de um preditor da obesidade na idade adulta [3, 4] e de se associar a uma mortalidade prematura [5]. Dentre as diversas comorbidades associadas à obesidade na infância e adolescência, destacam-se: a presença de síndrome metabólica [6], o aumento da massa gorda e o decréscimo da massa muscular e óssea [7], além dos baixos níveis de aptidão física [8] e das perturbações psicológicas [9].

A síndrome metabólica é uma das principais consequências do excesso de peso e da obesidade. Esta síndrome é entendida como sendo a associação de um conjunto variado de fatores de risco com responsabilidade no desenvolvimento de doenças cardiovasculares (DCVs) e do diabetes mellitus do tipo 2 (DM2) [10]. Em linhas gerais, consiste na presença de valores elevados de adiposidade abdominal, pressão arterial, triglicerídeos e glicose sanguínea, e em valores reduzidos de lipoproteína-colesterol de alta densidade (HDL) [11], sendo combinado a presença de três ou mais destes indicadores para a sua classificação. No mundo inteiro, a prevalência da síndrome metabólica tem igualmente aumentado significativamente nas últimas décadas. Na atualidade, está presente em aproximadamente 4-7% dos adolescentes com excesso de peso e em mais de 49% dos sujeitos obesos [12]. No Brasil, a prevalência desta síndrome atinge 3 a 6% dos adolescentes com excesso de peso e obesidade [13].

O aumento da massa gorda e a diminuição da massa óssea e muscular [14, 15] são outros aspectos que caracterizam os adolescentes com excesso de peso e obesidade.

Tal fato parece estar associado à baixa participação e envolvimento destes sujeitos em programas regulares de atividade física e desportiva [16]. Adolescentes normoponderais, submetidos a uma prática regular de atividade física, tendem a mostrar um maior conteúdo mineral ósseo ($\approx 13\text{-}20\%$) relativamente aos seus pares menos ativos [17, 18]. Igualmente evidente parecem ser os valores inferiores dos adolescentes com excesso de peso e obesidade na generalidade das componentes da aptidão física [7], de que se destaca a aptidão cardiorrespiratória que se reconhece estar associada ao risco de desenvolvimento de DCVs [19].

A informação acumulada ao longo dos últimos anos sugere que os processos que desencadeiam as DCVs ateroscleróticas tendem a iniciar-se na infância e adolescência e vão sendo influenciados ao longo da vida por diversos fatores, dentre os quais, um processo pró-inflamatório precoce associado à obesidade [20]. Os indivíduos que evidenciam excesso de peso e obesidade tendem a mostrar um estado inflamatório crônico, pois alguns marcadores estão geralmente elevados, como, por exemplo, o fator de necrose tumoral alfa (TNF- Δ), a interleucina-6 e a proteína C reativa [21]. Por esta razão, o tecido adiposo tem sido reconhecido como um órgão multifuncional, que produz e secreta peptídeos e proteínas bioativas, denominadas adipocitocinas [22]. As adipocitocinas influenciam uma variedade de processos fisiológicos, entre eles, o controle da ingestão alimentar, a homeostase energética, a sensibilidade à insulina, a angiogênese, a proteção vascular, a regulação da pressão arterial e a coagulação sanguínea [23].

Ruiz e colaboradores demonstraram que a inflamação de baixo grau apresentou uma correlação negativa com a aptidão cardiovascular e uma positiva com o percentual de gordura corporal em crianças obesas pré-púberes [24]. Além disso, estes autores relataram que a fisiopatologia da obesidade se inicia precocemente em adolescentes e que esse aumento da adiposidade resultaria em níveis reduzidos de adiponectina e elevados de resistina e TNF- Δ [25]. Estas adipocitocinas seriam um mecanismo concomitante à resistência à insulina em adolescentes [26]. Recentemente, os resultados de Steene-Johannessen e colaboradores associaram a inflamação de baixo-grau presente em jovens com a circunferência de cintura elevada, sugerindo que os biomarcadores inflamatórios podem já estar relacionados ao perfil de risco metabólico observado em crianças e adolescentes obesos [27].

Por outro lado, as adipocitocinas também têm demonstrado associação com a disfunção endotelial em adolescentes obesos [24, 28]. A disfunção endotelial, do ponto de vista clínico e sob o enfoque da pesquisa, é definida como uma alteração do relaxamento vascular por redução dos fatores vâsculo-protetores do endotélio como o óxido nítrico, a prostaciclina, entre outros [29]. A ativação endotelial com início da disfunção endotelial propicia um estado pré-constritor, pró-inflamatório e pró-coagulante, alterando a homeostase vascular com consequente formação de um estado pró-aterogênico e pró-trombótico. Esta ativação ocorre precocemente na progressão da doença arterial, propiciando a observação de alterações disfuncionais na reatividade endotelial e microvascular antes de alterações estruturais em adultos, crianças e adolescentes [30].

Não obstante os aspectos referidos, é um fato bem documentado que os sujeitos com excesso de peso e obesidade têm um risco acrescido de mortalidade por complicações de DVCs [31, 32]. Neste sentido, existem evidências que demonstram que o sistema nervoso autônomo cardíaco desempenha um papel importante na fisiopatologia da obesidade [33]. Uma maior estimulação do sistema simpático realizada de maneira crônica e o aumento dos níveis de catecolaminas tem sido atribuídas à obesidade mesmo no período da adolescência [34]. Indivíduos obesos demonstram uma maior atividade simpática quando comparados com seus pares não obesos [35].

Face a este quadro tão alarmante e preocupante, diversas organizações médico-científicas internacionais têm vindo a considerar a obesidade em idade pediátrica um grave problema de Saúde Pública, merecedor de uma prevenção precoce com vista a minimizar as referidas comorbilidades que lhes estão associadas.

A tentativa de melhor compreender e explicar a elevada prevalência de excesso de peso e obesidade que se verifica na infância e na adolescência tem sido o foco de muitas pesquisas [9, 36-38]. Diversos fatores parecem ter alguma responsabilidade nesta patologia, aos quais se destacam fatores genéticos, nutricionais, endócrinos, hipotalâmicos, farmacológicos, ambientais e comportamentais (especialmente o sedentarismo).

A participação regular em atividades físicas é considerada uma importante estratégia de prevenção e tratamento da obesidade [19]. Diversos programas de atividade física

têm sido realizados com o propósito de identificar a sua eficácia em indicadores de saúde no adolescente com excesso de peso e obesidade [19, 39, 40]. Os resultados encontrados têm sido contraditórios em alguns dos indicadores estudados, nomeadamente no índice de massa corporal (IMC) [39, 41], no percentual de gordura corporal [19, 42], na pressão arterial [19, 43] e na tolerância à glicose [7, 8, 19, 39, 44]. Delineamentos de pesquisa e dimensões amostrais muito variadas, bem como a implementação de programas de intervenção diversificados, no tipo de atividade proposta, na sua duração, frequência e intensidade, podem ter contribuído para essa inconsistência [19, 39, 44]. Para além desses aspetos, o desinteresse que as crianças e os adolescentes com excesso de peso e obesidade parecem manifestar relativamente às atividades que lhes são propostas e que, conseqüentemente, as leva a abandoná-las precocemente, pode ter igualmente alguma responsabilidade nessa escassa consistência [39-41, 45].

No entanto, parecem existir evidências de que a participação diária em atividades físicas de intensidade moderada a vigorosa permitem melhorar a composição corporal e a aptidão cardiorrespiratória de adolescentes [43]. Neste sentido, embora não se verifique consensualidade nos resultados encontrados, têm sido avançadas diversas linhas de recomendação com vista à promoção da atividade física e desportiva de crianças e adolescentes [46]. Entre as recomendações apresentadas, destaca-se a necessidade das crianças e adolescentes realizarem, diariamente, pelo menos 60 minutos de atividade com intensidade moderada a vigorosa, além de efetuarem três vezes por semana exercícios de força muscular que tenham impacto no sistema muscular e esquelético. Adicionalmente, salienta-se que as atividades a propor a esta população devem ser apropriadas às suas idades, motivadoras e muito diversificadas [46].

Nesse contexto, pesquisas recentes demonstram que o Futebol parece ser uma atividade capaz de atender a todas as recomendações propostas em adultos [45, 47]. Destaca-se ainda sua popularidade, uma vez que o Futebol é praticado na atualidade por mais de 240 milhões de crianças, adolescentes e adultos no mundo inteiro [48]. No Brasil há aproximadamente 50 milhões de crianças e adolescentes que praticam regularmente o Futebol [48]. Para além desse aspeto salienta-se o fato de se tratar de um desporto motivador, capaz de minimizar o desinteresse e o conseqüente abandono que se tendem a verificar em muitos dos programas de atividades física e

desportiva que têm sido testados [7, 8, 49]. Outro aspeto que ressalta esse esporte como uma ferramenta no combate e prevenção da obesidade em idade pediátrica é o fato de o Futebol não exigir elevados custos para sua prática. Em várias partes do mundo ele é praticado nas ruas, nas praças públicas, escolas, clubes e etc. Além de poder ser praticado com poucos materiais, muitos adolescentes precisam somente da bola, jogando de pés descalços e improvisando as balizas com pedras ou algo parecido. Estas características evidenciam a facilidade de implementação do Futebol pelo mundo.

Um segundo aspeto diz respeito à possibilidade deste desporto poder ser praticado em estruturas e formas de jogo muito variadas (jogos de 3 contra 3; 5 contra 5; 7 contra 7, 11 contra 11), o que torna possível a sua prática em qualquer idade, de forma agradável e apropriada. Um terceiro aspeto prende-se com as exigências que o Futebol coloca aos seus praticantes, nomeadamente uma enorme participação da componente aeróbica e de, em muitos momentos do jogo, o praticante exibir valores de frequência cardíaca superiores a 80-85% da sua frequência cardíaca máxima [50]. Um quarto aspeto remete à diversidade de ações de máxima intensidade que são realizadas durante a sua prática, nos *sprints*, mudanças de direção, saltos e contatos corporais, que exigem dos seus praticantes um elevado gasto calórico, bem como um significativo impacto no sistema muscular e esquelético, contribuindo para a melhoria da massa óssea e muscular [47, 51]. Um quinto aspeto igualmente importante são diversas relações inter e intrapessoais que se estabelecem entre os praticantes [52].

No entanto, apesar de todas essas constatações, são escassos os estudos que centraram o seu foco na tentativa de examinar a eficácia que programas de prática de Futebol poderão ter em diversos indicadores de saúde [7, 8, 45, 47, 49, 53, 54]. A generalidade dos estudos disponíveis foram realizados com adultos de ambos os sexos, tendo os resultados mostrado que o Futebol pode ser uma estratégia eficaz na melhoria de diversos indicadores de saúde (pressão arterial sistólica e diastólica [8], valores de massa gorda [7, 43], relação entre a LDL – lipoproteína de baixa densidade - e o HDL – lipoproteína de alta densidade [51]).

Em crianças e adolescentes, tanto quanto julgamos saber, somente foram realizados dois estudos [7, 8]. Faude e colaboradores investigaram 21 crianças com excesso de peso e obesidade, com idades compreendidas entre os 11 e os 12 anos. Os dois

programas de intervenção realizados, foram o Futebol e um programa padrão de atividade física, sendo realizados três vezes por semana, uma hora por dia, durante seis meses, e avaliando os seguintes aspectos: composição corporal (massa corporal, estatura e o índice de massa corporal - IMC), capacidade aeróbica, aspectos psicológicos, habilidades motoras, impulsão vertical, flexibilidade, equilíbrio, agilidade e resistência. No entanto, após os programas de intervenção, o estudo apresentou uma pequena melhora embora não significativa nas variáveis da composição corporal, e nas outras variáveis houve melhora para ambos os grupos [7].

A segunda pesquisa foi desenvolvida por Weintraub e colaboradores, junto a 22 crianças com excesso de peso e idades entre os 10 e os 11 anos. As crianças foram divididas em dois grupos, um de Futebol e outro praticando um programa diversificado de esportes. As sessões de treino eram oferecidas três vezes por semana, uma hora por sessão, durante seis meses e as variáveis analisadas foram as seguintes: IMC, IMC_{zscore} , nível de atividade física diária, sintomas depressivos, preocupação com o ganho de massa corporal e autoestima. A exemplo do estudo anterior, o treino de Futebol desenvolvido por seis meses mostrou ser tão eficaz na melhoria da aptidão física, de parâmetros relacionados com a saúde e autoestima, quanto um programa de exercício variado [8].

Na literatura consultada, e tanto quanto conseguimos localizar, não existem estudos com adolescentes. Além do fato de que ambas as pesquisas encontradas terem sido realizadas com crianças, limitam-se a analisar variáveis antropométricas, composição corporal, percepção psicológica e aptidão física. Sendo assim, há então, base para considerar existirem lacunas para o investimento de pesquisas sobre programas de treino de Futebol direcionados a adolescentes obesos, especialmente no que diz respeito à influência sobre indicadores de risco para DVCs e metabólicas. É nesse contexto que se insere a presente dissertação de Doutorado.

Capítulo II

Estrutura e objetivos

1. Estrutura da tese

Esta dissertação foi estruturada em cinco capítulos. No primeiro capítulo - **introdução** - é apresentado problema que se pretende estudar. No segundo capítulo - **estrutura e objetivos** – é apresentada a estrutura da dissertação e os objetivos gerais e específicos. No terceiro capítulo – **estudos** - são apresentados os quatro estudos que pretendem concretizar os objetivos desta dissertação. O primeiro estudo tem como objetivo rever o estado da arte do tema em análise, sendo os restantes três de âmbito “experimental” tendo como propósito responder a questões específicas de pesquisa. No quarto capítulo – **discussão global** - são analisados e interpretados os resultados encontrados nos estudos apresentados no capítulo anterior. No quinto capítulo – **conclusões** - são apresentadas as principais conclusões desta dissertação.

2. Objetivos

A presente dissertação teve como objetivo geral investigar o efeito de uma prática regular de Futebol recreativo durante 12 semanas em variáveis metabólicas, hemodinâmicas, função endotelial, modulação autonômica cardíaca, composição corporal, biomarcadores e aptidão cardiorrespiratória em adolescentes obesos. Para dar resposta a este objetivo foram definidos alguns objetivos específicos:

- 1) Rever o estado atual do conhecimento sobre o efeito da atividade física na aptidão cardiorrespiratória, força muscular, composição corporal, variáveis hemodinâmicas, marcadores bioquímicos e função endotelial em adolescentes obesos;
- 2) Examinar os efeitos de um programa de 12 semanas de Futebol recreativo na composição corporal, pressão arterial, biomarcadores inflamatórios, a aptidão cardiorrespiratória e função endotelial em adolescentes obesos;

3) Determinar a concordância e reprodutibilidade da variabilidade da frequência cardíaca em repouso avaliada por meio de fotopletismografia e monitor cardíaco em adolescentes obesos;

4) Investigar a concordância e reprodutibilidade do limiar de variabilidade da frequência cardíaca avaliado pelo monitor cardíaco em adolescentes obesos.

3. Lista de estudo de revisão

- Estudo I

Physical activity in overweight and obese adolescents: Systematic review of the effects on physical fitness components and cardiovascular risk factors.

4. Lista de estudos originais

- Estudo II

Health markers in obese adolescents improved by a 12-week recreational soccer program

- Estudo III

Heart rate variability assessment with fingertip photoplethysmography and polar RS800cx as compared to electrocardiography in obese adolescents.

- Estudo IV

Can heart rate variability be used to estimate ventilatory threshold in obese adolescents?

Capítulo III

Artigo de revisão e originais

Estudo I

Publicado na *Sports Medicine*, doi: 10.1007/s40279-014-0193-7, Vasconcellos, F; Seabra, A; Katzmarzyk, P. T; Kraemer-Aguiar, L. G; Bouskela, E; & Farinatti, P; **Physical Activity in Overweight and Obese Adolescents: Systematic Review of the Effects on Physical Fitness Components and Cardiovascular Risk Factors**, 2014.

Physical activity in overweight and obese adolescents: systematic review of the effects on physical fitness components and cardiovascular risk factors

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Running Title: Physical activity in overweight and obese adolescents.

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Physical activity in overweight and obese adolescents: a systematic review of the effects on physical fitness components and cardiovascular disease risk factors.

ABSTRACT

BACKGROUND: The increasing prevalence of obesity in the pediatric age range has become a major concern. Studies have investigated the role of physical activity (PA) to prevent obesity in this population. However, previous reviews did not focus on the effects of PA in overweight/obese adolescents on physical fitness and risk factors for cardiovascular disease altogether. **OBJECTIVE:** The present systematic review analyzed trials investigating the effect of PA on aerobic capacity, muscle strength, body composition, hemodynamic variables, biochemical markers, and endothelial function in obese/overweight adolescents. **METHODS:** Pubmed, LILACS, Web of Science, Scopus (including EMBASE), and Sports Discus databases were searched for relevant reports without time limits. Inclusion criteria included studies published in English, with overweight and obese adolescents aged 12 to 17 years-old. The review was registered (number CRD42013004632) on PROSPERO, the International Prospective Register of Systematic Reviews. **RESULTS:** The results indicated that PA is associated with significant and beneficial changes in fat percentage, waist circumference, systolic blood pressure, insulin, low-density lipoprotein cholesterol (LDL), and total cholesterol, as well as with small non-significant changes in diastolic blood pressure, glucose, and high-density lipoprotein cholesterol (HDL). **CONCLUSION:** Although limited, results from controlled trials suggest that PA intervention may improve physical fitness and risk factors for cardiovascular disease in adolescents who are overweight or obese.

1 Introduction

Obesity is closely related to the risk of developing cardiovascular diseases (CVD) [55] and is currently considered as a serious public health concern [55, 56]. Epidemiological studies have shown a rapid increase in the prevalence of overweight and obesity not only in adults, but also in children and adolescents, thus increasing the risk of developing early CVD and comorbidities [57, 58]. According to the World Health Organization (WHO), approximately 20% of children and adolescents in western countries are overweight or obese [59]. Evidence also suggests that childhood obesity may persist throughout life, compromising the quality of life and its expectancy [3, 4, 60].

Adipose tissue produces and secretes peptides and proteins called adipocytokines, which are involved in inflammation and immune response [22]. In obesity, the concentrations of various adipocytokines are high and have been associated with hypertension (angiotensinogen), inhibition of fibrinolysis (plasminogen activator inhibitor-1), insulin resistance (tumor necrosis factor- α , interleukin-6 and resistin) [61] and the onset or progression of atherosclerotic lesions (C-reactive protein) [62]. Conversely, adiponectin, which has anti-inflammatory and antiatherogenic properties, is inversely associated with body mass index (BMI) and percentage of body fat [63]. Several mechanisms suggest a causal relationship between obesity and atherosclerosis. These factors are also related to endothelial dysfunction, as evidenced not only in adults but also in children and adolescents [3, 4]. Ruiz et al. [24] demonstrated that low-grade inflammation was negatively associated with cardiovascular fitness and positively related with percentage of body fat in prepubertal obese children. Steene-Johannessen et al. [27] have also analyzed low-grade systemic inflammation present in young people with increased waist circumference, and suggested that inflammatory markers such as C-reactive protein (CRP), hepatocyte growth factor (HGF) and plasminogen activator inhibitor-1 (PAI-1) are related to metabolic risk profile observed in obese children and adolescents.

Given these trends, early intervention to positively impact weight and behaviours that contribute to obesity and comorbidities is important. Multiple strategies to combat childhood obesity appear to be effective in the prevention of obesity in adulthood [64, 65]. Diet and physical activity (PA) – including unsupervised/ spontaneous and

supervised training programs as previously and classically defined [66] – are two of the most common strategies in the treatment and prevention of obesity. Considered as an important strategy to increase energy expenditure [67], regular PA is associated with improvements in body composition [19], cardiorespiratory fitness [42], metabolic syndrome components [68], hemodynamic variables [69] and psychological and socio-affective aspects [70], but the strength of the results varies among studies. Despite several reviews and meta-analyses on the efficacy of PA interventions on obesity and its comorbidities [71, 72], systematic reviews on the effectiveness of PA interventions to induce changes in body composition, physical fitness components, and CVD risk factors among overweight and obese adolescents remain sparse. Although findings from previous reviews [73-75] suggest that PA interventions may be globally effective to improve these factors in children and adolescents, there is still no conclusive evidence.

The present systematic review moves beyond previous studies in two ways. Firstly, given that previous reviews did not analyze physical fitness components and CVD risk factors together, they could not provide a comprehensive understanding of the overall effects of PA. This would be important in order to identify trends related to the possible effects of these types of interventions. Secondly, to our knowledge, only one study has reviewed the efficacy of PA interventions on endothelial function and inflammatory markers in adolescents [62] and no studies have analyzed these factors with other desirable outcomes in adolescents who are obese.

Therefore, it is important to update the emerging evidence in this area, analyzing the results of intervention studies that evaluated the efficacy of PA on a wide range of markers of physical fitness and CVD risk factors in overweight and obese adolescents. Thus, the objective of this study was to systematically review the effect of PA interventions on body composition, physical fitness components, hemodynamic variables, biochemical markers, endothelial function and low-grade inflammation in overweight and obese adolescents (aged 12-17 years).

2 Methods

A literature review was conducted in parallel by F.V. and I.D. in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA)

guidelines [76] and registered on PROSPERO, the International Prospective Register of Systematic Reviews, as number CRD42013004632. An extensive search of online electronic databases was conducted in the Pubmed, LILACS, Web of Science, Scopus (including EMBASE), and Sports Discus without time limits. Text words, key words and subject headings used in the searches included: *(adolescent) AND (prevent OR intervention) AND (physical activity) AND (obesity OR overweight OR (weight gain)) OR ((increase OR gain OR change) AND (BMI OR body mass index OR fat mass))*. The inclusion criteria included studies published in English, with overweight and obese adolescents (12 to 17 years of age), as defined from BMI percentiles for age and sex. Studies were also eligible for inclusion in the present review if applied any type of PA intervention, alone or combined with other kind of intervention, regardless of their duration. Repeated publications for the same studies were excluded. In the presence of any doubt about study inclusion, a final consensus decision was taken after the full text was jointly reviewed.

Study quality was assessed using the Physiotherapy Evidence Database (PEDro) scale (www.pedro.fhs.usyd.edu.au), which has been shown to have good reliability and validity [30]. The PEDro scale has 11 possible points that examine external validity (criterion 1) and internal validity (criteria 2-9) of controlled trials, and whether there is sufficient statistical information for interpreting results (criteria 10-11). The items of the scale are: i) eligibility criteria were specified; ii) subjects were randomly allocated to groups; iii) allocation was concealed; iv) groups were similar at baseline; v) subjects were blinded; vi) therapists who administered the treatment were blinded; vii) assessors were blinded; viii) measures of key outcomes were obtained from more than 85% of subjects; ix) data were analysed by intention to treat; x) statistical comparisons between groups were conducted; xi) point measures and measures of variability were provided. The first criterion is not included in the final score. Moreover, due to the nature of PA interventions, patient and therapy blinding and allocation is unlikely, therefore the total score a trial could receive was 8 points. A cut point of 6 on the PEDro scale was used to indicate high-quality studies as this has been reported to be sufficient to determine high quality versus low quality in previous studies [77, 78]. The studies were evaluated by two experienced investigators and in the event of disagreement a third reviewer was invited.

3 Results

The electronic search identified 1248 potentially relevant studies and the manual search of reference lists identified another 16. A total of 24 studies met all the inclusion criteria for this review. A total of 1635 participants underwent PA programs and completed their respective studies. In all studies, a significance level of 0.05 was set for the type I error. Figure 1 summarizes the selection process of the included studies

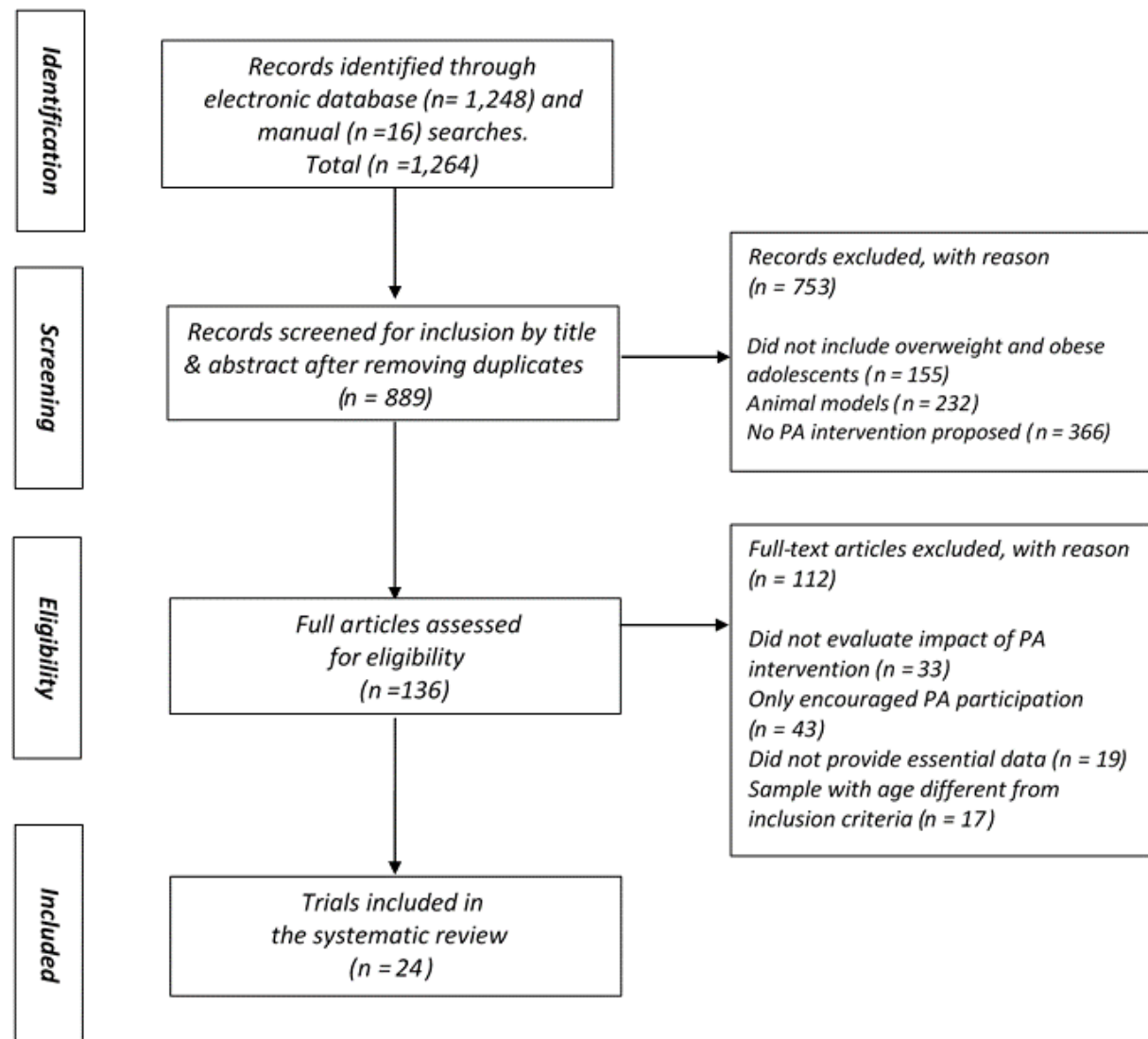


Figure 1. Flow diagram, illustrating the details of the search strategy, screening of potentially qualifying reports (n), selection of the included trials and reasons for study exclusion. Note. PA = Physical Activity.

Table 1 presents the characteristics of the 24 studies included in the systemic review. Seventeen studies were classificated as ‘high quality’ studies (range: 6 to 8 of PEDro scale score), and seven as ‘low quality’ studies (range: 4 to 5 in PEDro scale score).

In most low quality studies, the following methodological limitations were found: i) subjects were not randomly allocated to groups; ii) the allocation was not concealed; iii) subjects, therapists, or evaluators were not blinded. Fifteen of the 24 studies were PA-only intervention [43, 79-92] and 9 studies were PA plus another kind of intervention (lifestyle or dietary) [21, 93-100]. Fifteen studies included both girls and boys [21, 43, 81, 82, 84, 87, 89, 90, 92, 94-99], five included only girls [85, 89, 94, 95, 98], and four included only boys [81, 95, 99]. No difference whatsoever could be identified between sexes in the reviewed studies, girls and boys seeming to respond similarly to PA, at least for the variables presently analyzed.

Seventeen studies had a follow-up not exceeding three months [21, 43, 79, 81, 83, 85-89, 91, 93-96, 98, 100], while only seven studies provided longer follow-ups [80, 82, 84, 90, 92, 97, 99]. This fact may be due to the difficulty in maintaining the participants for a longer period of time, as a result of the difficulty in keeping the team, the lack of interest of researchers for a long-term monitoring, or the choice of unattractive activities leading to high drop-out during the study. Furthermore, the short duration of follow-ups might also reflect the reality of schools or holiday calendars in many countries.

TABLE 1 Characteristics of the studies that examined the effect of physical activity on overweight and obesity in adolescence

Study	PEDro Scale	Obesity status [BMI - kg/m ² , percentile or fat percentage]	Year	Sample size	Country	Sex	Age, y (mean $\pm$ SD or range)	Physical activity	Duration (weeks)
Flores ^[32]	5	≥ 25	1995	110	USA	F	12 - 13	Dance $\rightarrow$ 3x / W - 1h	12
Neumark-Sztainer et al. ^[33]	6	≥ 85 th	2003	201	USA	F	15.4 $\pm$ 1.1	Varied activities $\rightarrow$ 4x / W - 1h	32
Bayne-Smith et al. ^[47]	6	$\geq 20\%$	2004	442	USA	F	16.2 $\pm$ 1.2	Circuit training $\rightarrow$ 5x / S - 20min and others	12
Watts et al. ^[34]	5	≥ 85 th	2004	19	Australia	M / F	14.3 $\pm$ 1.5	Circuit training $\rightarrow$ 3x / W 1h	8
Carrel et al. ^[35]	6	≥ 95 th	2005	50	USA	M / F	12 - 14	Strength $\rightarrow$ 3x / W - 45min	36
Balagopal et al. ^[48]	7	≥ 30	2005	21	USA	M / F	16 $\pm$ 0.4	Aerobic activities $\rightarrow$ 3x / W - 45min and others	12
Nassis et al. ^[36]	4	≥ 85 th	2005	19	Greece	F	13.1 $\pm$ 1.8	Circuit training + sports $\rightarrow$ 3x / W - 40min	12
Meyer et al. ^[37]	5	≥ 97 th	2006	67	Germany	M / F	14.7 $\pm$ 2.2	Sports and walking $\rightarrow$ 3x / W - 1h	24
Melnyk et al. ^[49]	6	≥ 25	2007	23	USA	M / F	15.4 $\pm$ 0.5	Sports $\rightarrow$ 2x / W - 1h and others	8

Kim et al. ^[38]	6	≥ 25	2007	40	Korea	M	16.9 $\pm$ 0.1	Jump roping $\rightarrow$ 5x / W – 40min	6
McMurray et al. ^[43]	5	≥ 85 th	2007	58	USA	M / F	15.2 $\pm$ 0.5	Exercise bike $\rightarrow$ 3x / W – 1h	12
Johnston et al. ^[50]	6	≥ 85 th	2007	60	USA	M / F	12.3 $\pm$ 0.7	Circuit training and sports $\rightarrow$ 4x / W – 40min and others	12
Wong at al. ^[39]	7	≥ 25	2008	24	Singapore	M	13.8 $\pm$ 1.1	Circuit training and sports $\rightarrow$ 2x / W – 55min	12
Foschini et al. ^[51]	6	≥ 95 th	2009	32	Brazil	M / F	16.5 $\pm$ 1.7	Aerobic activity and strength $\rightarrow$ 3x / W – 30min and others	12
Tjonna et al. ^[52]	8	≥ 30	2009	62	Norway	M / F	14 $\pm$ 0.6	Interval running $\rightarrow$ 2x / W – 4x 4min	12 and 48
								Multidisciplinary treatment in hospital and others	12 and 48
Lee et al. ^[55]	6	≥ 25	2010	18	Korea	F	16.7 $\pm$ 0.7	Running $\rightarrow$ 4x / W – 50min and others	12
Van der Heijden et al. ^[40]	5	≥ 95 th	2010	12	USA	M / F	15.5 $\pm$ 0.5	Strength $\rightarrow$ 2x / W – 1h and others	12
Ounis et al. ^[53]	6	≥ 97 th	2010	28	Tunisia	M / F	13.2 $\pm$ 0.7	Running, jump and sports with ball $\rightarrow$ 4x / W – 90min and others	8
Johnston et al. ^[54]	7	≥ 85 th	2010	60	USA	M / F	12.3 $\pm$ 0.7	Circuit training and sports $\rightarrow$ 4x / W – 40min and others	24
Shih et al. ^[41]	5	≥ 23	2010	106	China	M	15.8 $\pm$ 0.1	Running $\rightarrow$ 5x / W – 40min	12
Buchan et al. ^[42]	7	≥ 20	2011	57	England	M / F	16.4 $\pm$ 0.7	Running $\rightarrow$ 3x / W – 20min	7
Davis et al. ^[44]	6	≥ 85 th	2011	38	USA	M / F	15.8 $\pm$ 1.1	Circuit training $\rightarrow$ 2x / W – 1h	16
Lee et al. ^[45]	7	≥ 95 th	2012	45	USA	M	14.9 $\pm$ 1.7	Strength $\rightarrow$ 3x / W – 1h Aerobic $\rightarrow$ 3x / W – 1h	12
Farah et al. ^[46]	7	≥ 95 th	2013	43	Brazil	M/F	15.2 $\pm$ 0.4	High intensity training $\rightarrow$ 3x / W Low intensity training $\rightarrow$ 3x / W	24

USA, United States of America; F, Female; M, Male; M / F Male and Female; x, Times; W, weeks; H, hour; min, minutes; Others, Other methods of intervention beyond the physical activity; BMI, body mass index.

With regard to the experimental designs, ten studies could be classified as controlled trials [21, 80, 84, 85, 91, 93, 95, 98-100] and four adopted a within-group pre vs. post intervention design [79, 81, 83, 86-88]. The other studies compared two groups performing different activities or interventions [43, 89, 90, 92, 96, 97]. Among the controlled trials, in four studies subjects were not randomly assigned into intervention and control groups [83, 87-89]. Studies that combined PA with other kind of interventions did not report additional effects due to those treatments upon the observed outcomes [21, 93-100].

3.1 Effect of physical activity on BMI and physical fitness variables

Table 2 summarizes the effects of interventions tested in the reviewed studies on BMI and other physical fitness variables. Twenty-two studies quantified the impact of PA on BMI [21, 43, 79-88, 91-100]. Fifteen of these studies were effective in reducing the BMI [21, 43, 79, 84-86, 88, 91, 92, 94-96, 98-100], six studies did not report any significant change [80-83, 93, 97], and only one study showed a BMI increase after the intervention [87]. Of the 19 studies that measured the percentage of body fat [21, 81-88, 91-93, 95-100], 12 found a decrease [21, 43, 82, 85, 88, 91-93, 96-99] and seven reported no change [81, 83, 84, 86, 87, 95, 100]. Nine out of 10 studies that measured waist circumference showed significant improvements after the intervention programs [43, 83-85, 88, 91, 92, 97, 100]. Fifteen studies presented results for both BMI and fat percentage [34-39, 41, 44, 46, 47, 49-52, 54]. From these, six trials reported a decrease in body fat after PA [37, 41, 44, 47, 51, 52], whereas nine did not find significant differences [34-36, 38, 39, 46, 49, 50, 54]. One study investigated the impact of PA on tricipital skinfold thickness [99], which decreased after the intervention.

Nine studies adopted the BMI as criterion for obesity classification [21, 43, 79, 85, 86, 88, 94, 97, 100]. Five out of these applied a cut-off point of BMI > 25 [31, 48, 37, 38, 44], two used BMI > 30 [51, 47], one used BMI > 23 [40], and one BMI > 20 [41]. Nonetheless, no differences related to these cut-off points were noticed with regard to the impact of PA on BMI: eight studies found a decrease after intervention [21, 43, 79, 85, 86, 88, 94, 100], while only one did not observe alteration [97]. The same trend repeated for other variables; for instance, fat percentage decreased [44, 47, 40, 41], cardiorespiratory fitness improved [41, 44], and insulin did not change [37, 40] in studies that used different BMI cut-off points.

Fourteen studies considered weight percentiles estimated for age and sex [80-84, 87, 89-92, 95, 96, 98, 99], and one adopted the fat percentage as reference [93]. Overall, the results of these studies were similar and not affected by the criteria used to define obesity or overweight. For instance, 12 out of 14 studies that used weight percentiles as criterion to define obesity observed the impact of PA on BMI – seven reported a decrease [84, 91, 92, 95, 96, 98, 99], in four no change was detected [80-83], and one found an increase [87]. Five studies observed the impact of PA on the waist

circumference – four detected a decrease [83, 84, 91, 92] and in only one no change was found [81].

High quality studies reported better results on BMI and physical fitness variables than lower quality studies. Twelve and eleven high quality studies reported decreases in BMI and fat percentage respectively, while in only four studies no significant change was found. Results from low quality studies were inconsistent, reporting either increase, decrease or stability of BMI and fat percentage after PA intervention.

Only ten studies assessed changes in cardiorespiratory fitness [43, 79, 80, 82, 91-93, 96, 97, 100]. Seven of these studies showed an improvement in cardiorespiratory fitness [43, 82, 91, 92, 96, 97, 100] while three did not report any significant difference pre and post intervention [79, 80, 93]. With regard to muscle strength effect, all six studies showed an improvement after PA intervention [43, 81, 87, 96, 97, 100]. No difference between low and high-quality studies could be detected for the results regarding physical fitness variables.

3.2 Effect of physical activity on hemodynamic variables

Table 2 exhibits the effects of PA interventions on blood pressure (BP) and heart rate (HR). Data on resting BP were available from ten studies [43, 84-86, 92, 93, 95-97, 99]. Seven of the nine studies showed significant decreases in systolic BP (SBP) after the intervention [43, 84, 86, 92, 93, 96, 97], while three studies did not report significant changes [85, 95, 99]. Ten studies examined the diastolic BP (DBP) [43, 84-86, 92, 93, 95-97, 99]. Three of them observed a reduction in their values [93, 96, 97], but the other seven did not report significant changes [43, 84-86, 92, 95, 99]. Only seven studies measured the HR at rest or during submaximal exercise [79, 81, 83, 85, 86, 92, 99]. Four of them showed a reduction due to the intervention [79, 83, 86, 92], while the other three did not find significant differences [81, 85, 99]. No clear tendency was detected with regard to different outcomes when comparing high quality and low quality studies, as classified by the PEDro scale.

TABLE 2 – Effect of physical activity interventions on physical fitness and hemodynamic variables.

Study	PEDro scale	Body composition			Cardiorespiratory fitness	Muscle strength	SBP	DBP	HR
		BMI	Fat %	Waist circumference					
Flores [32]	5	↓	NE	NE	↔	NE	NE	NE	↓
Neumark-Sztainer et al. [33]	6	↔	NE	NE	↔	NE	NE	NE	NE
Bayne-Smith et al. [47]	6	↔	↓	NE	↔	NE	↓	↓	NE
Watts et al. [34]	5	↔	↔ (↓Tr. ↓Ab.)	↔	NE	↑	NE	NE	↔
Carrel et al. [35]	6	↔	↓	NE	↑	NE	NE	NE	NE
Balagopal et al. [48]	7	↓	↓	NE	NE	NE	NE	NE	NE
Nassis et al. [36]	4	↔	↔	↓	NE	NE	NE	NE	↓
Meyer et al. [37]	5	↓	↔	↓	NE	NE	↓	↔	NE
Melnyk et al. [49]	6	↓	NE	NE	NE	NE	NE	NE	NE
Kim et al. [38]	6	↓	↓	↓	NE	NE	↔	↔	↔
Johnston et al. [50]	6	↓	↔	NE	NE	NE	↔	↔	NE
Wong et al. [39]	7	↓	↔	NE	NE	NE	↓	↔	↓
Foschini et al. [51]	6	↓	↓	NE	↑	↑	↓	↓	NE
Tjonna et al. [52]	8	↔	↓	↓	↑	↑	↓	↓	NE
Lee et al. [53]	6	↓	↔	↓	↑	NE	NE	NE	NE
Van der Heijden et al. [40]	5	↑	↔	NE	NE	↑	NE	NE	NE
Ounis et al. [53]	6	↓	↓	NE	NE	NE	NE	NE	NE
Johnston et al. [54]	7	↓	↓	NE	NE	NE	↔	↔	↔
Shih et al. [41]	5	↓	↓	↓	NE	NE	NE	NE	NE
Buchan et al. [42]	7	↓	↓	↓	↑	↑	↓	↔	NE
Lee et al. [45]	7	↓(st) ↔(at)	↓(st) ↓(at)	↓(st) ↓(at)	↑(st) ↑(at)	↑(st) ↔(at)	NE	NE	NE
Farah et al. [46]	7	↓	↓	↓	↑	NE	↓	↔	↔

PEDro scale, Physiotherapy evidence database scale ; BMI, Body mass index; ↓, Significant decrease in the mean value; ↔, No significant change in the mean value; ↑, Significant increase of the mean value; Tr., Percentage of fat in the trunk; Ab., Percentage of fat in the abdomen; NE, Not evaluated st, strength training; at, aerobic training. SBP, Systolic blood pressure; DBP, Diastolic blood pressure; HR, heart rate.

3.3 Effect of physical activity on biochemical markers

Studies investigating the effects of PA on biochemical markers are shown in Table 3. Of the twelve studies that measured insulin level [81-85, 87, 91, 92, 95-97, 100], six reported a decrease [82-84, 96, 97, 100] and five did not detect significant changes [81, 85, 87, 91, 95]. Plasma glucose levels were measured in ten studies [82, 83, 85-87, 91, 95-97, 100], most of them reporting significant improvements. Nine studies

examined the response of high-density lipoprotein cholesterol (HDL) to PA interventions and no significant change was reported [84-87, 95-97, 99]. However, of the seven studies that measured low-density lipoprotein cholesterol (LDL) levels [84-87, 95, 96, 99], four showed a significant decrease [84, 95, 96, 99], while three did not report significant changes [85-87]. Five studies showed a decrease in the total cholesterol level [84, 95, 96, 99, 100], but other five did not observe significant changes [81, 85-87, 93]. Most studies that observed biochemical markers were classified as having high quality by the PEDro scale, therefore it was not possible to ascertain differences between high and low quality studies.

3.4 Effect of physical activity on endothelial function and inflammatory markers

As shown in Table 3, few studies have investigated the effects of PA on inflammatory markers in overweight and obese adolescents. Of the seven studies that evaluated C-reactive protein (CRP) levels [21, 83-86, 88, 98], three showed a reduction [21, 88, 98], three did not report significant changes [83, 85, 86] and only one study reported an increase after the intervention [83-85]. Five studies have examined the response of interleukin-6 (IL-6) to PA [21, 83, 85, 88, 98], three of them showing a significant decrease in their levels [21, 88, 98] and two reporting no significant change [83, 85]. Three studies evaluated the adiponectin levels [83, 85, 97], two of them detecting an increase in the basal levels [85, 97]. Among the two studies that measured the fibrinogen levels [21, 84], one reported a reduction [21], but one showed an increase after the intervention [84]. Only three studies assessed the endothelial function in obese adolescents after PA interventions [81, 84, 97]. In all cases the endothelial function measured by flow mediated dilation of the brachial artery (FMD) showed an improvement after PA intervention. Positive effects of PA on endothelial function and inflammatory markers have been reported by studies of different quality levels.

TABLE 3 – Effects of physical activity intervention on biochemical, endothelial function and inflammatory variables

Study	PEDro scale	Insulin	Glucose	HDL	LDL	Total cholesterol	CRP	IL-6	Adiponectin	Fibrinogen	Endothelial function
Bayne-Smith et al. [47]	6	NE	NE	NE	NE	↔	NE	NE	NE	NE	NE
Watts et al. [34]	5	↔	NE	NE	NE	↔	NE	NE	NE	NE	↑FMD
Balagopal et al. [48]	7	NE	NE	NE	NE	NE	↓	↓	NE	↓	NE
Carrel et al. [35]	6	↓	↔	NE	NE	NE	NE	NE	NE	NE	NE
Nassis et al. [36]	4	↓	↔	NE	NE	NE	↔	↔	↔	NE	NE
Meyer et al. [37]	5	↓	NE	↔	↓	↓	↑	NE	NE	↑	↑FMD
Kim et al. [38]	6	↔	↓	↔	↔	↔	↔	↔	↑	NE	NE
Johnston et al. [50]	6	↔	↔	↔	↓	↓	NE	NE	NE	NE	NE
Wong at al. [39]	7	NE	↔	↔	↔	↔	↔	NE	NE	NE	NE
Foschini et al. [51]	6	↓	↔	↔	↓	↓	NE	NE	NE	NE	NE
Tjonna et al. [52]	8	↓	↓	↔	NE	NE	NE	NE	↑	NE	↑FMD
Ounis et al. [53]	6	NE	NE	NE	NE	NE	↓	↓	NE	NE	NE
Lee et al. [55]	6	↓	↑	↔	NE	↓	NE	NE	NE	NE	NE
Van der Heijden et al. [40]	5	↔	↔	↔	↔	↔	NE	NE	NE	NE	NE
Johnston et al. [54]	7	NE	NE	↔	↓	↓	NE	NE	NE	NE	NE
Shih et al. [41]	5	NE	NE	NE	NE	NE	↓	↓	NE	NE	NE
Lee et al. [45]	7	↔(st)	↔(st)	NE	NE	NE	NE	NE	NE	NE	NE
Farah et al. [46]	7	↔	NE	NE	NE	NE	NE	NE	NE	NE	NE

PEDro scale, Physiotherapy evidence database scale; HDL, High density lipoprotein; LDL, Low density lipoprotein; ↓, Significant decrease in the mean value; ↔, No significant change in the mean value; ↑, Significant increase of the mean value; NE, Not evaluated; st, strength training; CRP, C-reactive protein; IL-6, interleukin-6; FMD, Flow-mediated dilation.

3.5 Effects of intensity, frequency, duration, and type of activity

As exhibited in Table 1, only five studies applied interventions with less than two training sessions per week [39, 40, 44, 49, 52]. In most studies the weekly frequency was of three times [32, 34, 36, 36, 42, 43, 44, 48, 51, 54]. In 13 studies the duration of training sessions was shorter than one hour [35, 36, 38, 39, 41, 42, 47, 48, 50-52, 54,

55], while in nine studies sessions were from 1 to 1.5 hours [32-34, 37, 40, 43, 49, 53, 55]. With reference to PA intensity, only four studies applied high intensity programs [40, 42, 52, 47], while in six studies the intensity was reported as low to moderate [37, 41, 45, 46, 48, 55]. However, the isolate and combined effects of frequency, duration, and intensity of PA programs in obese and overweight adolescents seem not to have been addressed, therefore information about optimal dose-response relationships regarding fitness, hemodynamic, and inflammatory markers are not available.

The predominant type of PA within the different interventions was running, either performed continuously with low intensity [37, 41, 45, 46, 48, 55] or intermittently with high intensity [40, 42, 52, 53]. Nine other studies applied cycle ergometer exercise [34, 36, 38, 39, 43, 44, 49-51], four observed the effects of school activities [47, 33, 54, 35], and only one with dance [32]. Of the four studies performed in schools, three did not report significant changes [33, 35, 47] and one showed a decrease in BMI [54]. Three studies found reduction in fat percentage [35, 47, 54] and one reported an increase in cardio-respiratory fitness [35]. Only two studies measured the blood pressure, one of them showing a decrease [47] and the other one no changes [54]. Heart rate [54], glucose [35], cholesterol [47], and insulin [35] were assessed by only one study, and only insulin levels were reported to decrease after PA.

On the other hand, 18 out of the 20 studies investigating the effects of PA intervention out of school sets reported data about the BMI. Of these, 14 [32, 37-39, 41, 42, 44-46, 48-51, 53] reported a decrease, three did not find differences [34, 36, 52], and one reported an increase in BMI due to PA [39]. A reduction in fat percentage and waist circumference vs. no change was found in nine out of 16 [38, 41, 42, 45, 46, 48, 51-53 vs. 34, 36, 37, 38, 40, 44, 50] and nine out of 10 [36-38, 44, 41, 42, 45, 46, 51 vs. 34] studies, respectively. Beneficial effects were reported with regard to blood pressure by six out of eight studies [37, 39, 42, 46, 51, 52 vs. 38, 50]. Seven studies assessed cardio-respiratory fitness and six of them [42, 44-46, 51, 52] reported an increase, whereas in just one no alteration could be detected [32]. Muscle strength increased in all studies that observed these variables [34, 40, 42, 45, 51, 52]. With regard to biochemical markers, eleven studies analysed the insulin level – in six it remained stable [34, 38, 40, 45, 46, 50], while a decrease was reported by the other five [36, 37, 44, 51, 52].

The glucose decreased in two studies [38, 52], increased in one [44], and remained unaltered in six [36, 39, 40, 45, 50, 51] community-based trials. The PA was shown to be ineffective to change HDL by the eight trials [37-40, 44, 50-52]. Three [37, 50, 51] out of six studies showed a decrease in LDL and four [37, 44, 50, 51] out of eight studies a reduction in total cholesterol vs. no change in respectively three [37, 50, 51] and four [34, 38, 39, 40] studies. The CRP was assessed in seven studies, three observing a reduction after PA [41, 48, 53], three not finding changes [36, 38, 39], and one reporting an increase [37]. Five studies observed the IL-6, three of them reported a decrease [41, 48, 53] and two did not observed significant changes [36, 38]. The adiponectin was evaluated by there studies and in two an increase due to PA was reported [38, 52], while in one no alteration was found [36]. Only two studies measured the fibrinogen, and results are mixed – one study found an increase [37] and the other a decrease [48] in its levels. Finally, all three studies that observed the endothelial function reported an improvement due to PA intervention [34, 37, 52].

4 Discussion

This systematic review appraised the peer-reviewed literature published without date restriction that reported the effects of PA interventions on body composition, physical fitness components, hemodynamic variables, biochemical markers, endothelial function, and low-grade inflammation in overweight and obese adolescents. There is accumulated evidence suggesting that PA is an effective strategy to prevent and treat obesity and its comorbidities. Such evidence is fairly consistent, as demonstrated by a relatively large number of studies [64, 101-103]. While the 24 studies included in this review varied widely in their objectives, designs, mode, and setting of intervention delivery, PA appears to promote beneficial effects in obese adolescents [64, 68, 104]. It is worthy to point out that very often the studies reported results that not always reflected their main purpose. This is important since studies designed to test one outcome generally do better on that specific variable than on other outcomes, which may introduce a measurement bias. For instance, Nassis et. al. [83] did not observe a significant decrease in BMI, body fat and inflammatory markers, but the main objective of the study was to investigate the effect of exercise on insulin sensitivity. Other studies [81, 85] aimed to observe responses related to vascular dysfunction and insulin sensitivity, but reported secondary outcomes on BP and HR.

The present review aimed to scrutinize studies with adolescents aged 12-17 years because this is a critical age in terms of adherence to PA [65], which contributes with the onset of overweight and obesity [70]. On the other hand, as mentioned in Section 1 much of the available data with this population are controversial and have not been yet summarized by previous reviews. Notwithstanding, it is important to notice that most studies did not provide information about the biological age of adolescents enrolled in the PA programs [43, 79, 80, 82, 84-86, 90, 93-95, 97, 99, 100]. It is therefore difficult to analyze the effects of maturation on their results, albeit it's well accepted that adolescents who are obese are frequently more advanced in biological maturation than non-obese adolescents of similar chronological age [105].

Moreover, it's also likely that many subjects within 15-17 years-old range are already biologically adult, and youth in the midst of pubertal maturation and growth spurt might respond differently to PA intervention than late adolescents who are approaching or who are biologically mature [106]. Unfortunately, just a few studies have controlled the pubertal status or any other indicator of biological maturation and all of them just reported that subjects were at post puberty stage [48, 53, 46, 51, 40, 36, 41, 45, 34, 43]. Therefore, it must be acknowledged that to compare studies including adolescents with different maturation stages can be problematic. However to use chronological age cut-off points was the only alternative, due to the lack of data about biological age in the reviewed studies.

4.1 Body composition, cardiorespiratory fitness and muscle strength

Body composition measurements were analyzed in 22 studies included in this systematic review. All of them except one reported a favorable change in at least one body composition variable. Nonetheless, a meta-analysis by Harris et. al. [40] could not confirm the effectiveness of school-based PA programs on body composition, cardiorespiratory fitness and muscle strength. Hills et. al. [107] suggested that different anthropometric assessment methods and cut-off points for determining overweight and obesity in adolescents may contribute to such inconsistent results. A recent review ratified this opinion, proposing that the ineffectiveness of some PA interventions in children and adolescents could be due to a lack of strict control on the criteria and methods for assessing body composition [108].

For instance, the effects of PA upon other body composition markers as body fat have been investigated by a significant number of studies, but their results are still inconclusive. This could be partially explained by the relatively short intervention periods [109], but also by the great variability of techniques applied to determine body fat [37]. However, in agreement with this systematic review, previous studies using randomized controlled designs and sophisticated assessment, such as dual-energy X-ray absorptiometry (DXA), have reported a significant decrease in body composition after PA interventions [110, 111]. Another potential source of bias, particularly with regard to BMI, is the fact that depending on the maturation stage it can be potentially influenced by differential growth in height and weight [59]. However, since in most studies included in the present review the duration of PA intervention was no longer than 12 weeks, it is unlikely that differences in the rate of height and weight increasing would have significantly changed their results.

Albeit physical activity programs may likely induce favorable changes in body composition, it is important to mention that not all studies ratified such premise. In this sense, the relationship between sample size within each study and the observed outcomes shall be taken into account. For instance, the majority of studies (15 studies) have shown a significant reduction in BMI after the intervention program, while seven others did not observe the same effect. However, these seven studies represented over 55% of the total sample of all studies included in the present review. Additionally, the sample sizes in studies assessing the effect of combined diet and physical activity (9 studies) and only physical activity (15 studies) were 47% and 53%, respectively. Therefore, we have to be cautious about the independent effect of physical activity on body composition.

In most of the reviewed studies aerobic exercise was considered an effective strategy to increase cardiorespiratory fitness in obese adolescents [81, 83]. However, cardiorespiratory fitness assessment in this population is usually performed through submaximal tests, which may explain the difficulty of comparing the available data. Only two studies included in this systematic review reported an increase of cardiorespiratory fitness in children and adolescents by assessing their maximal oxygen uptake ($\text{VO}_{2\text{max}}$) [82]. However, regardless the assessment methods current evidence suggests that PA intervention programs may improve the cardiorespiratory

fitness in children who are overweight and obese [45]. Only a few studies have investigated the effect of PA programs on the muscle strength of obese adolescents, and their results are generally favorable, either after programs including resistance training [101] or team sports [7, 8]. A previous systematic review [112] concurs with these results, suggesting that it is quite plausible that adolescents who are obese increase their muscle strength in response to PA programs.

4.2 Hemodynamic variables

The effects of PA programs on hemodynamic variables in overweight and obese adolescents has not been extensively evaluated. It is well accepted that in adults the possible effects of PA on BP change rely to a large extent on pretreatment baseline levels [75]. Our results suggest that this is also the case in obese and overweight adolescents. One study [93] found a significant decrease of DBP and SBP in adolescents with relatively high baseline BP at rest. However the same was not detected by studies with normotensive obese adolescents [85, 95]. Weight control programs that did not include PA appear to be less likely to influence hemodynamic variables. Watts [101], for example, demonstrated that dietary and PA interventions were more efficacious than dietary intervention alone in achieving declines in BP and HR.

4.3 Biochemical markers

Current evidence suggests a significant correlation between the degree of adiposity and biochemical markers [113]. Children and adolescents who are obese tend to exhibit higher levels of total cholesterol compared to normal weight ones [114]. The present systematic review indicated that PA may induce beneficial effects on biochemical variables, as LDL cholesterol, insulin, and glucose levels [84], while, in some studies these variables remained unchanged [86]. These disparities may be related to the type, intensity and volume of PA programs [115]. Dietary characteristics can also contribute to such inconclusive results, since the dieting pattern may have an independent action from PA and weight reduction over several biochemical markers [116].

4.4 Endothelial function and inflammatory markers

As mentioned in Section 1, a proinflammatory state associated with disturbances in endothelial function can accelerate the atherosclerotic process [117]. An association between endothelial dysfunction, low-grade inflammation and weight excess has been observed in children and adolescents [24, 27, 28, 52, 118], as well as an increased risk of morbidity and atherosclerotic coronary disease in adulthood [118, 119]. Such evidence reinforces the need for early detection and treatment of these risk factors. Studies examining the effect of PA on low-grade inflammation related to obesity in adolescents are scarce and do not provide consistent results. Some studies have shown that PA could reduce inflammatory markers [21, 88, 98], whereas others did not report significant differences [83-86]. A possible explanation for this discrepancy could be the relatively wide variation in the components of PA programs, as the type of exercise, weekly frequency, intensity, and duration, among other factors.

With respect to endothelial function, we could find only three studies that evaluated it through flow-mediated dilation [81, 84, 97]. All of them reported improvement after intervention with PA. For this reason, it has been suggested that PA may exert a direct and beneficial effect on vascular function, likely due to increased bioavailability of nitric oxide resulting from the shear stress during activity [120].

4.5 Effects of intensity, frequency, duration, and type of activity

Available recommendations [46] state that children and adolescents should engage in moderate to vigorous PA during one hour at least five days per week, which should be complemented by strength activities performed three times per week. However, some studies have suggested that high intensity exercises performed thrice a week during 20 min, would be enough to improve physical fitness components in adolescents [41], while others indicated that PA duration would be a major factor to the improvement of health-related markers in obese and overweight adolescents [50, 54].

The approach of the studies presently reviewed reflects such inconsistency. Unfortunately, research on the dose-response relationships between frequency, duration, and intensity of PA intervention and improvement of fitness, hemodynamic, and inflammatory markers in this population appears to be lacking, and should be addressed in the future. Further research is also warranted about the effects of ludic

activities (as team sports) upon components of physical fitness and cardiovascular disease risk factors. These activities (basketball, soccer etc.) have been classified as of high intensity [46] and acknowledged as an alternative to increase adherence of adolescents to regular PA [121]. However, we could not find studies investigating the role of different combinations of training intensity and volume variables within this kind of PA intervention on fitness and risk markers.

With regard to the type of PA, as mentioned in section 3.5 continuous or intermittent running and cycle ergometer exercise were predominant, followed by few studies with PA at schools and dance. This can be due to the fact that training variables are easier to control in this kind of activity, and therefore to estimate outcomes in terms of energy expenditure or weight reduction. However, not a single study reported whether the adolescents enjoyed the PA intervention or if they had some sort of participation in defining its characteristics. In which concerns the set of PA intervention, although the number of school-based trials is small (only four out of 24), their samples are large and correspond to an important percentage of the overall subjects when considered all included studies. Differences between school and community-based studies are sometimes based in a comparison of one vs. 20 studies, but considering the samples altogether, the total *N* can be quite similar. Therefore, comparisons regarding the effectiveness of PA programs developed in school and community sets are still inconclusive.

In brief, it is very difficult to synthesize information about the optimal dose-response relationship regarding intensity and volume training variables, to produce favorable effects on fitness and health-related markers in adolescents who are obese or overweight. First of all, there is a lack of research addressing this specific issue. Secondly, the methodological variation within studies is too low for some variables (for instance, weekly frequency), whereas with regard to others the variation is too high (for instance, intensity). In both cases, direct comparisons searching to establish the better combination are unlikely to be made, and this issue unquestionably warrants additional future research.

4.6 Limitations

Some limitations of the results from this systematic review should be mentioned. Firstly, despite of the strict inclusion criteria, it must be acknowledged that the reviewed studies were very heterogeneous. Study populations differed in several aspects (sample size, age and sex, country of recruitment and specific BMI criteria to define overweight and obesity), as well as PA programs varied widely both in their components (intensity, duration and frequency) and in type of the intervention. Moreover, not a single study presently reviewed reported data about the persistence of the beneficial effects once the intervention was finished, or provided a more qualitative analysis of the characteristics of PA programs. The focus was exclusively on statistical significance of differences within/between groups, which might be affected by sample size and variability. On the other hand, this kind of follow-up would be crucial to define how much PA would be needed to maintain the favorable gains, as well to compare the magnitude of long-term responses due to different kinds of intervention.

Secondly, most of the studies did not provide information about the drop-out rates across the intervention programs. As stated in section 1, one of the main purposes of any PA intervention with adolescents who are overweight or obese should be to promote the interest and enjoyment of participation [65]. Traditionally, the literature in the area of obesity prevention has focused upon PA interventions that are very monotonous, boring, and similar to those commonly used with adults [39, 40]. In fact, typical PA interventions for overweight and obese adolescents have generally incorporated a variety of aerobic and resistance activities aimed at accommodating individual differences in body mass and PA interests (e.g., rowers, cycle ergometer, circuit activities), and rarely attempted to link interests of children in team-games and sport activities [122]. Involving youth in the design of interventions could be an alternative to PA programs aiming at health improvement of adolescents who are overweight or obese. Moreover, future research should acknowledge that focusing on dose-response relationships within aerobic exercise training (e.g., the exercise physiology model) might not be the appropriate model to increase enrollment of this population.

Recently published studies have suggested that team-games and sport activities in addition to meeting children's interest to participate in PA can be a highly effective alternative for the prevention/reduction of childhood obesity and comorbidities [121, 123-125]. These studies have shown that the impact of such activities on physical fitness components and body composition is similar to the impact of typical PA intervention programs. Furthermore, team-games and sport activities seem to be more beneficial in improving psychological and socio-affective dimensions [7, 8, 121, 124].

However, team sports are frequently not friendly for obese adolescents and should be adapted to increase their attraction to this population. Further research is certainly warranted to investigate options that could increase the enrollment of adolescents who are obese in this kind of sports. On the other hand, this raises the issue of resistance training effectiveness to improve weight and health outcomes in obese adolescents [8]. Most studies about resistance training and obese adolescents date across the past 30-40 years. Given limited success of the obese in team sports, resistance programs may attract them and should be further investigated with regard to different outcomes related with cardiovascular risk.

5 Conclusion

In conclusion, despite the diversity of methods and intervention designs employed by the included studies, this systematic review detected important trends regarding the effects of PA programs for the treatment and prevention of overweight and obesity at an early ages. Interventions including PA programs are very likely to induce favorable adaptations on body composition and physical fitness of overweight and obese adolescents. Even though the evidence in this sense remains inconclusive, our findings suggest that PA programs may also improve biochemical variables, inflammatory markers, and endothelial function in this population.

Future studies should focus on large-scale studies and especially in large randomized controlled trials using different types of activities and components of training (intensity, duration and frequency) to confirm these findings. Another major challenge for the future is to design studies to investigate the response of specific risk factors to PA programs, rather than to assess these factors marginally as part of protocols designed with other purposes. In other words, if children exhibit normal cholesterol, blood

pressure or any other risk factor at baseline, there is no reason to expect much change. Inclusion criteria of research aiming at disclosing the specific effects of PA over any risk factor should not consider only the body weight or body composition in the selection of subjects, but also the profile related to that given risk factor.

Another challenging aspect is the need to identify the reasons for poor compliance of children and adolescents to PA intervention programs. Most of the studies reviewed have applied typical PA programs in which control of intensity and volume could be more easily performed. Unfortunately, none of the reviewed studies assessed the level of satisfaction and compliance of adolescents to the intervention program. In addition to the potential clinical benefits, it is important to better understand what types of activities can motivate adolescents to adopt an active lifestyle, without which any initiative becomes innocuous.

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Estudo II

Em revisão no Journal of Sports Science, Fabrício Vasconcellos; André Seabra; Felipe A. Cunha; Rafael A. Montenegro; Eliete Bouskela; Paulo Solberg; José Firmino; Paulo Farinatti; **Health markers in obese adolescents improved by a 12-week recreational soccer program**, 2014.

Health markers in obese adolescents improved by a 12-week recreational soccer program

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Running Title: Recreational soccer and obese adolescents

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Abstract

Objective: The effects of a recreational soccer program (RSP) upon body composition, heart rate variability (HRV), biochemical markers, cardio-respiratory fitness, and endothelial function in obese adolescents were investigated.

Design and Methods: Twenty adolescents aged 12-17 yrs and body mass index [BMI] $\geq$ 95th age- and gender-specific percentile were randomly assigned to RSP (n=10, 2 girls) and non-exercise (n=10, 4 girls) groups. The 12-week RSP included 60-min sessions performed 3 times/week. BMI, waist circumference, blood pressure, blood glucose, lipid profile, insulin, C-reactive protein, HRV, and maximal oxygen consumption (VO_{2peak}) were evaluated following standardized procedures. Body composition was determined by dual-energy X-ray absorptiometry and endothelial function by venous occlusion plethysmography.

Results: After intervention, RSP exhibited significant reductions in BMI (-2.7%), waist circumference (-6.6%), %body fat (-5%), systolic blood pressure (-2.7%), total cholesterol (-8.7%), triglycerides (-14.3%), C-reactive protein (-28.5%), insulin resistance (-32.6%), and sympathetic activity (-23.9%) vs. controls ($P<0.05$). Significant increase was observed in parasympathetic activity (pNN50: +44.3%; total power: +58.7%; HF: +33.5%), VO_{2peak} (+23.7%), and HDL-c (+18.0%) ($P<0.05$). Vascular conductance (+36.47%, $P=0.005$) increased and vascular resistance (-25.27%, $P=0.041$) decreased in RSP, but not in controls.

Conclusions: A 12-week recreational soccer intervention was effective to improve biochemical, cardiovascular, and fitness health markers in obese adolescents.

Keywords: body composition; cardiorespiratory fitness; inflammatory markers; sports; exercise; health

INTRODUCTION

The prevalence of obesity in adolescence has increased worldwide [59] and this has become a major public health concern [126]. Obesity during childhood may influence the genesis and progression of atherosclerosis in adult life, being related to cardiometabolic comorbidities such as hyperinsulinemia, glucose intolerance, hypertension, and dyslipidemia [126].

Team sports has been considered a strategy to prevent overweight and obesity, as well as to improve cardiovascular risk in adults [60]. However, less evidence is available with regard to this kind of intervention in obese adolescents [107]. It must be acknowledged that traditional physical activity (PA) programs, such as cycling and running, are more easily performed when individualized routines are prescribed. However, obese adolescents are not always motivated by these types of exercise [45], and low adherence evidently makes any PA intervention innocuous. In this context, team sports seems to be a good alternative to increase PA participation among adolescents [45], since they appear to be more interested in sports activities that are social, outdoors and competitive [121]. However, data about the beneficial effects of recreational team sports participation upon health markers in obese adolescents are scarce [38].

Soccer is one of the most popular team sports, and previous studies have shown that its practice can improve health markers in adults [45, 53]. Nevertheless, few studies have investigated the effects of recreational soccer on cardiovascular risk markers in adolescents. Furthermore, most of the available research applied programs not exclusively based on soccer practice [127-129], or evaluated very restricted markers of cardiovascular risk [130].

In brief, research is lacking about the effectiveness of soccer programs adapted to obese adolescents upon health markers. Hence, the purpose of this randomized controlled trial was to investigate the impact of a 12-week recreational soccer program (RSP) upon the body composition, biochemical risk markers for cardiovascular disease, cardio-respiratory fitness, cardiac autonomic activity, and endothelial function in obese adolescents.

METHODS AND PROCEDURES

Participants

Participants were randomly selected among adolescents attended by the Nucleus for Studies on Adolescent Health of the University of Rio de Janeiro State (NSAH), Brazil, where they were provided systematically medical, psychological, and nutritional assistance. To be eligible for participation in the study, subjects should be within 12 to 17 years-old, to exhibit body mass index (BMI) $\geq$ 95th age- and gender-specific percentile [131] and to be in the later stages of pubertal maturation (pubic hair stage 4 and 5). Exclusion criteria included medical conditions contraindicating the participation in physical activities, the use of medication influencing the observed outcomes, and participation in structured exercise, nutrition or weight loss programs within 6 months prior to the initial screening.

A sample of 32 obese adolescents qualified for the study (10 girls) (mean $\pm$ SD; age=14.5 $\pm$ 1.6 yrs), being randomly assigned to experimental and non-exercise control groups. For ethical reasons, those assigned as controls were invited at the end of the experiment to enroll in the RSP program. Six adolescents in each group dropped off the study for reasons not related to the soccer program. Therefore, 10 adolescents (2 girls, age=14.1 $\pm$ 1.1 yrs, BMI=30.3 $\pm$ 4.6 kg/m²) completed the soccer intervention, and other 10 (4 girls, age=14.8 $\pm$ 1.4 yrs, BMI=32.2 $\pm$ 4.9 kg/m²) composed the obese control group. A third group of 10 non-obese adolescents (3 girls, age=14.6 $\pm$ 1.6 yrs, BMI=19.4 $\pm$ 10.6 kg/m²) was also randomly selected from NSAH and evaluated only at baseline, exclusively in order to provide reference values to evaluate possible cardiac autonomic and endothelial dysfunction, as well as the effects of RSP upon these markers in the obese group.

All subjects were instructed not to change their regular physical activity habits. The study protocol was approved by institutional ethics committee (CEFADE 12/2013). All parents or legal guardians signed informed consent forms providing authorization for the children to participate in the study.

Soccer intervention

The RSP was performed three times a week during 12 weeks at the University of Rio de Janeiro State facilities. Adolescents always trained in the same period of the day. Each session consisted of 10-min warm-up followed by 40 min of games performed in small pitch areas (such as 2 vs. 2, 3 vs. 3 and 4 vs. 4), and 10-min cool-down. Training intensity was recorded by portable heart rate monitors (Polar RS800cx, Polar™, Kempele, Finland). Two licensed exercise instructors supervised the training sessions.

Anthropometry, biological maturity status and blood pressure assessment

Body mass, height, hip circumference, waist circumference (WC), and blood pressure were measured according to standard procedures [132]. Body mass was assessed with a digital scale (Filizola™, Sao Paulo, SP, Brazil), height with a fixed stadiometer (Sanny™, São Paulo, SP, Brazil), and waist and hip circumferences with a metal anthropometric tape. The BMI was calculated and adolescents were classified as obese according to age-specific BMI cut-offs for boys and girls [131]. The maturation stage of pubic hair was evaluated as part of a comprehensive clinical examination by a pediatrician with previous experience in the assessment of secondary sex characteristics, according to criteria proposed by Tanner (1962) [133]. Blood pressure was assessed by an automated Omron 705IT device (Omron™ Healthcare Co., Kyoto, Japan) in a controlled and quiet environment, after 10-min resting at the supine position.

Body composition

Fat percentage and fat free mass were assessed by dual-energy X-ray absorptiometry (Hologic QDR 4500, Hologic™, Bedford, MA, USA – DXA). The equipment was calibrated according to manufacturer instructions. Subjects were scanned in the supine position using standard protocols. Scans were performed in high resolution and analysed by the same trained technician. Principles underlying body composition analyses with DXA were described elsewhere [134].

Cardio-respiratory fitness

The cardiopulmonary exercise test was performed in cycle ergometer CG-04 (Inbramed™, Porto Alegre, RS, Brazil) using a ramp-incremental protocol with initial load fixed at 25W and increasing 10W every minute. The VO_2 was continuously measured until exhaustion using an automated open-circuit breath-by-breath metabolic system (Ultima Cardio2, Medical Graphics™, St Louis, MI, USA). The metabolic system was calibrated before each test according to manufacturer instructions.

The test was considered as maximal if at least three of the following four criteria were satisfied [135]: a) maximum voluntary exhaustion defined by attaining score 10 on Borg CR-10 scale; b) 90% of predicted HR_{max} [$220 - \text{age}$] or presence of heart rate plateau (ΔHR between two consecutive work rates ≤ 4 bpm); c) presence of VO_2 plateau (ΔVO_2 between two consecutive work rates of less than $2.1 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$); d) maximal respiratory exchange ratio (RER_{max}) > 1.10 . The oxygen uptake at rest ($\text{VO}_{2\text{rest}}$) was measured as described elsewhere [136].

Heart rate variability (HRV)

The HRV was recorded during 25 min at rest using a cardi tachometer (Polar RS800cx, Polar™, Kempele, Finland) and 5 min windows were extracted and downloaded for analysis by specific software (Polar Precision Performance, Polar™, Kempele, Finland). The HRV indices were analyzed using the Kubios™ HRV software (Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Kuopio, Finland), considering the last 5 min of recording. The sampling frequency was 1000 Hz, and signal artefacts were filtered by excluding R-R intervals with differences of more than 20% vs. the preceding R-R interval [137].

Biochemical markers

Assessments were performed before the beginning of RSP and within 48 hours after the last training session. Serum was collected from centrifuged samples after which LDL, HDL, total cholesterol and triglyceride levels were determined fluorometrically using an automatic analyzer (Cobas Fara™, Roche, Neuilly-sur Seine, France) and

enzymatic kits (Roche Diagnostics™, Mannheim, Germany). The blood collected from a non-heparinized syringe was centrifuged for 2 min, after which it was pipetted and frozen at -20 °C until analyzed for insulin levels using an enzyme immunoassay ELISA kit (Dako Cytomation™, Cambridgeshire, UK). The C-reactive protein was assessed by Latex high sensitivity with automatic analyzer (Biosystems A25 Chemistry Analyzer™, BioSystems, Massachusetts, USA). Oral glucose tolerance test (OGT) was performed using the first blood sample after 12-hour fasting, followed by ingestion of 75g dextrose with water, and a second blood drawn after 2 hours. The homeostasis model assessment for insulin resistance (HOMA-IR) was calculated as the product between fasting insulin (mU/ml) and fasting glucose (mmol/L)/22.5.

Endothelial function assessment

The endothelial function was evaluated by measuring the forearm blood flow (FBF) using venous occlusion plethysmography (VOP) (Hokanson EC6; D.E. Hokanson™ Inc, Bellevue, WA) with a mercury-in-Silastic strain gauge [30]. The venous occlusion plethysmography was performed in three stages: 1) Basal blood flow and basal vascular conductance; 2) Blood flow after ischemia and vascular conductance after ischemia; 3) Blood flow after 0.4 mg oral spray nitroprusside (NITRO - Nitrolingual BurnsAdler™ Pharmaceuticals Inc, Charlotte, NC, USA) and vascular conductance after NITRO.

Measurements were performed in the morning (7:00 to 10:00 a.m.) after 8-10 hours overnight fasting, at the supine position, in a quiet temperature-controlled room (20-22°C), and after emptying the bladder. The forearm length (medial epicondyle of humerus to ulnar styloid) and maximal circumference were measured using a flexible tape measure. To avoid underestimation of FBF, the forearm circumference was required to be < 28 cm in all subjects [138]. For the analysis of forearm vascular conductance, FBF was normalized for the flow per BP unit, as follows: $FVC = (FBF / \text{mean BP}) \times 1000$ [139].

Inflammatory biomarkers

Adiponectin, interleukin-6 (IL-6), leptin, tumour necrosis factor- α (TNF- α), resistin, and endothelin-1 (ET-1) were measured by ELISA (Enzyme Linked Immunosorbent Assay,

R & D Systems™, Minneapolis, MN, USA), while non-esterified fatty acids (NEFA) were assessed by enzymatic colorimetric method assay (Wako Chemicals™, Richmond, VI, USA). Intra- and inter-assay coefficients and sensitivity for adiponectin, IL-6, leptin, TNF- α , resistin, ET-1, and NEFA were respectively: 5.8%, 2.5%, and 0.246 $\mu\text{g/ml}$; 2.4%, 3.1%, and 0.039 pg/ml ; 2.3%, 3.1%, and 7.8 ng/ml ; 6.2%, 7.8%, and 0.106 pg/ml , 5.35%, 0.18%, and 0.026 ng/ml ; 5.44%, 3.07%, and 0.087 pg/ml ; 4.7%, 3.7%, and 0.0014 mmol/l .

STATISTICAL ANALYSIS

Data normality of all variables was confirmed by Kolmogorov-Smirnov test and therefore results were expressed as mean (SD). Baseline differences between groups were tested by Student t-test. Analysis of covariance (ANCOVA) for repeated measures adjusted for gender was used for within and between-group comparisons. Significance level was set at 0.05 and calculations were performed using the software SPSS 21.0 (SPSS™ Inc., Chicago, IL, USA).

RESULTS

The mean values for training duration and %HRmax were 52.1 ± 5.6 min/session and $84.5 \pm 4.1\%$, respectively. Table 1 presents the sample characteristics at baseline. No significant differences between intervention and control groups were observed for anthropometric, body composition, blood pressure, cardio-respiratory fitness, biochemical markers, endothelium function and inflammatory biomarkers. Adolescents of RSP and obese control groups were classified according to the HOMA-IR as insulin resistant, above 5.22 and 3.82 for pubertal boys and girls, respectively [140].

Table 1 - Mean (SD) values for baseline anthropometric characteristics, blood pressure, cardio-respiratory fitness, heart rate variability, biochemical markers, and endothelial function in intervention and obese control groups.

Variables	Intervention Group (n=10)	Obese Control Group (n=10)	P value
Anthropometric			
Age (years)	14.1 (1.3)	14.8 (1.4)	0.147
Height (cm)	163.1 (8.3)	161.2 (8.2)	0.915
Weight (Kg)	82.2 (13.7)	86.3 (17.4)	0.483
Body mass index (kg/m ²)	31.1 (5.2)	32.2 (4.9)	0.388
Tanner stage (range)	4 – 5	4 – 5	0.476
Fat percentage (%)	41.1 (6.1)	42.0 (5.4)	0.747
Fat free mass (Kg)	43.2 (8.2)	48.3 (7.5)	0.136
Waist circumference (cm)	98.7 (10.0)	103.5 (14.5)	0.333
Blood pressure			
Systolic blood pressure (mmHg)	128 (10)	128 (9)	0.820
Diastolic blood pressure, (mmHg)	81 (5)	79(5)	0.292
Mean blood pressure (mmHg)	70 (5)	70 (7)	0.321
Cardiorespiratory fitness			
VO ₂ at rest (ml.kg ⁻¹ .min ⁻¹)	3.0 (0.6)	3.6 (0.7)	0.842
VO ₂ peak (ml.kg ⁻¹ .min ⁻¹)	25.2 (3.2)	22.9 (3.1)	0.234
Heart rate peak (bpm)	191 (17)	187 (14.5)	0.321
Biochemical markers			
Total cholesterol (mg.dL ⁻¹)	166.4 (21.6)	168.7 (32.7)	0.749
HDL (mg.dL ⁻¹)	33.6 (6.9)	32.7 (18.7)	0.497
LDL (mg.dL ⁻¹)	101.1 (13.6)	99.6 (36.2)	0.758
Triglycerides (mg.dL ⁻¹)	118.4 (38.8)	120.3 (72.6)	0.941
C-reactive protein (mg.dL ⁻¹)	0.43 (0.32)	0.39 (0.13)	0.102
Fasting glucose (mg.dL ⁻¹)	92.9 (6.4)	87.6 (8.9)	0.196
Glucose tolerance (60 min) (mg.dL ⁻¹)	121.5 (31.8)	131.4 (42.5)	0.584
Glucose tolerance (120 min) (mg.dL ⁻¹)	96.0 (13.7)	99.3 (15.3)	0.633
Insulin (uUI/mL)	37.6 (12.4)	38.9 (11.7)	0.354
HOMA-IR	8.2 (1.1)	8 (0.8)	0.783
Inflammatory biomarkers			
Leptin (pg/ml)	27.5 (13.2)	35.2 (17.8)	0.375
IL-6 (pg/ml)	2.2 (1.7)	1.7 (0.7)	0.534
Resistin (ng/ml)	8.3 (4.5)	7.7 (2.7)	0.741
TNF- α (pg/ml)	3.1 (2.1)	2.7 (1.1)	0.169
Adiponectin (ng/ml)	5587.4 (1879.3)	5784 (2083.9)	0.877
ET-1 (pg/ml)	2.1 (0.5)	1.7 (0.5)	0.225
NEFA (mmol/L)	0.6 (0.1)	0.4 (0.2)	0.112

IL-6 - Interleukin-6; TNF- α - Tumoral necrosis factor- α ; ET-1 - Endothelin-1; NEFA - Non-esterified fatty acids; NE – Not evaluated. *P* values refer to differences between groups.

Table 2 shows data obtained for body composition, blood pressure, and cardio-respiratory fitness after intervention. Between and within-group differences due to RSP were detected for weight, BMI, and WC ($P < 0.01$). Additionally, the intervention group showed a significant decrease in percentage body fat ($P < 0.001$), while no change was observed in the control group. After RSP, the systolic blood pressure (SBP) was significantly lower in the intervention vs. control group, but no changes were found for diastolic blood pressure (DBP) or mean blood pressure (MBP). The VO_{2peak} increased ($P < 0.001$) significantly only in the intervention group. No significant change was observed for peak HR and VO_{2rest} in both groups

Table 2 - Changes in body composition, blood pressure and cardio-respiratory fitness due to recreational soccer practice in obese control and intervention groups.

	Intervention Group			Obese Control Group			<i>P value between groups after 12 weeks</i>
	12 weeks	Change from baseline (%)	<i>P value within group</i>	12 weeks	Change from baseline (%)	<i>P value within group</i>	
Body composition							
Age (years)	14.3 (1.3)	1.4	NS	15 (1.8)	1.4	NS	NS
Height (cm)	162.4 (7.9)	-0.4	NS	164.5 (7.5)	0.9	0.020	NS
Weight (kg)	77.8 (7.9)	-5.4	0.014	91.5 (19.5)	5.8	<0.001	<0.001
Body mass index (kg/m ²)	30.4 (4.2)	-2.3	0.024	33.5 (5.8)	3.7	0.001	<0.001
Tanner stage (range)	4 – 5	0	NS	4 – 5	0	NS	NS
Fat percentage (%)	38.9 (6.1)	- 4.9	<0.001	41.7 (5.1)	- 0.8	NS	0.024
Fat free mass (Kg)	45.0 (8.0)	5.9	NS	49.9 (8.9)	3.1	NS	NS
Waist circumference (cm)	90.5 (8.9)	- 6.5	0.004	101.9 (17.0)	- 1.6	NS	NS
Blood pressure							
Systolic blood pressure (mmHg)	123(13)	-3.9	0.006	129.2 (5.9)	0.7	NS	0.025
Diastolic blood pressure (mmHg)	79 (14)	-2.5	NS	79.4 (4.4)	1.0	NS	NS
Mean blood pressure (mmHg)	68 (13)	-2.9	NS	91.3 (4.1)	2.1	NS	NS
Cardiorespiratory fitness							
VO ₂ at rest (ml.kg ⁻¹ .min ⁻¹)	3.2 (1.7)	6.7	NS	3.3 (0.8)	-8.3	NS	NS
VO ₂ peak (ml.kg ⁻¹ .min ⁻¹)	33.1 (9.2)	31.3	<0.001	24.0 (3.9)	5.3	NS	0.013
Heart rate peak (bpm)	182 (14)	-4.7	NS	193.4 (13.7)	3.6	NS	NS

NS - no significant difference.

Figure 1 depicts data from the HRV analysis at pre and post intervention. No significant differences were found between the obese control and RSP groups at baseline ($P > 0.05$), but both were different to non-obese group ($P < 0.05$). After 12 weeks of soccer practice, the RSP group showed a significant increase in parasympathetic activity [i.e. high frequency component (HF)] ($P=0.047$), while HR at rest ($P = 0.040$) and sympathetic activity [i.e. low frequency component (LF)] ($P = 0.047$) decreased. These markers remained unaltered in the obese control group ($P > 0.282$). Moreover, differences between RSP vs. non-obese controls were no longer detected after the intervention ($P > 0.196$).

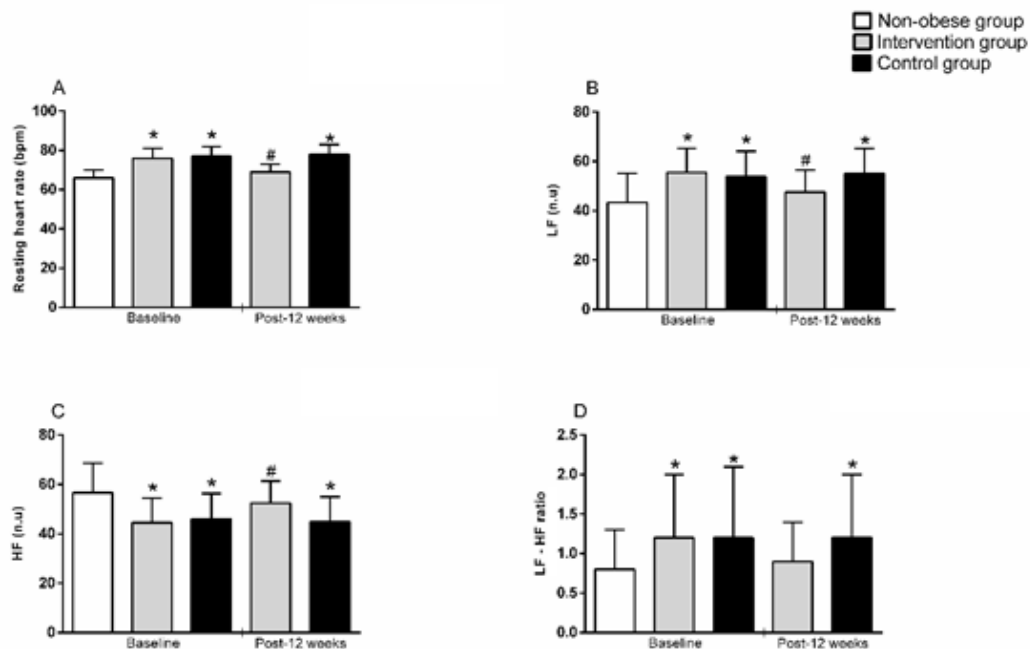


Figure 1. Mean (SD) values for heart rate variability indices in non-obese, obese control, and intervention groups at baseline and after 12 weeks of recreational soccer practice. LF: Low-frequency component; HF: High-frequency component; nu: Normalized units; #: Significant difference within group ($P < 0.03$). *: Significant difference vs. non-obese group ($P < 0.05$).

Table 3 presents the changes in biochemical and inflammatory markers due to RSP. Significant increase pre vs. post were found for HDL, and decrease in total cholesterol, triglycerides, C-reactive protein, fasting glucose, and HOMA-IR in the intervention group compared to controls. The LDL increased significantly in the obese control, but not in the RSP group. Glucose tolerance and insulin levels remained unaltered in both groups. While endothelin-1 (ET-1) and tumoral necrosis factor- α (TNF- α) significantly decreased in the RSP group after intervention, no significant variation was detected for the other inflammatory markers.

Table 3. Changes in biochemical and inflammatory biomarkers due to recreational soccer practice in obese control and intervention groups.

	Intervention Group			Obese Control Group			<i>P value between groups after 12 weeks</i>
	12 weeks	Change from baseline (%)	<i>P value within group</i>	12 weeks	Change from baseline (%)	<i>P value within group</i>	
Biochemical markers							
Total cholesterol (mg.dL ⁻¹)	150.2 (25.2)	-9.7	0.008	181.4 (30.2)	7.5	0.021	0.001
HDL (mg.dL ⁻¹)	44.6 (5.0)	32.7	0.004	38.7 (17.0)	18.3	NS	0.038
LDL (mg.dL ⁻¹)	100.9 (12.9)	-0.2	NS	117.0 (31.7)	17.5	0.016	NS
Triglycerides (mg.dL ⁻¹)	97.9 (19.6)	-17.3	0.018	145.4 (91.4)	20.9	0.008	0.001
C-reactive protein (mg.dL ⁻¹)	0.37 (0.18)	-14.0	<0.001	0.41 (0.23)	5.1	NS	0.004
Fasting glucose (mg.dL ⁻¹)	91.9 (6.4)	-1.1	NS	94.3 (8.3)	7.6	0.007	0.029
Glucose tolerance (60min) (mg.dL ⁻¹)	118.4 (28.3)	-2.6	NS	110.6 (24.6)	-15.8	NS	NS
Glucose tolerance (120min) (mg.dL ⁻¹)	94.4 (21.8)	-1.7	NS	106.1 (24.0)	6.8	NS	NS
Insulin (uUI/mL)	31.5 (9.2)	-16.2	NS	37.1 (18.6)	-4.6	NS	NS
HOMA-IR	6.8 (0.9)	-17.1	0.003	8.4 (1.0)	5.0	NS	0.003
Inflammatory biomarkers							
Leptin (pg/ml)	29.9 (18.9)	8.7	NS	30.9 (15.3)	-12.2	NS	NS
IL-6 (pg/ml)	2.1 (1.9)	-4.5	NS	2.3 (0.8)	35.3	NS	NS
Resistin (ng/ml)	8.4 (3.7)	1.2	NS	8.3 (2.9)	7.8	NS	NS
TNF- α (pg/ml)	2.1 (0.8)	-32.3	0.039	2.5 (1.7)	-7.4	NS	NS
Adiponectin (ng/ml)	5788.7 (2725)	3.6	NS	5784.7 (2527.4)	0.0	NS	NS
ET-1 (pg/ml)	1.7 (0.5)	-19.0	0.042	1.7 (0.2)	0.0	NS	NS
NEFA (mmol/L)	0.5 (0.2)	-16.7	NS	0.4 (0.1)	0.0	NS	NS

IL-6 - Interleukin-6; TNF- α - Tumoral necrosis factor- α ; ET-1 - Endothelin-1; NEFA - Non-esterified fatty acids; NS - no significant difference.

Figure 2 presents data for endothelial function at baseline and post-intervention. At baseline, blood flow and vascular conductance after ischemia were higher in non-obese controls vs. RSP ($P = 0.049$) and obese controls ($P = 0.047$). After the 12-week intervention, most variables remained unaltered and no difference between and within-groups were detected for basal blood flow ($P = 0.347$), basal vascular conductance ($P = 0.237$), blood flow after nitroprusside ($P = 0.487$), and vascular conductance after nitroprusside ($P = 0.621$). On the other hand, the vascular conductance and blood flow after ischemia increased in RSP ($P < 0.047$), but not in the obese control group ($P = 0.472$). Additionally, values in RSP became similar to those exhibited by the non-obese control group ($P = 0.191$).

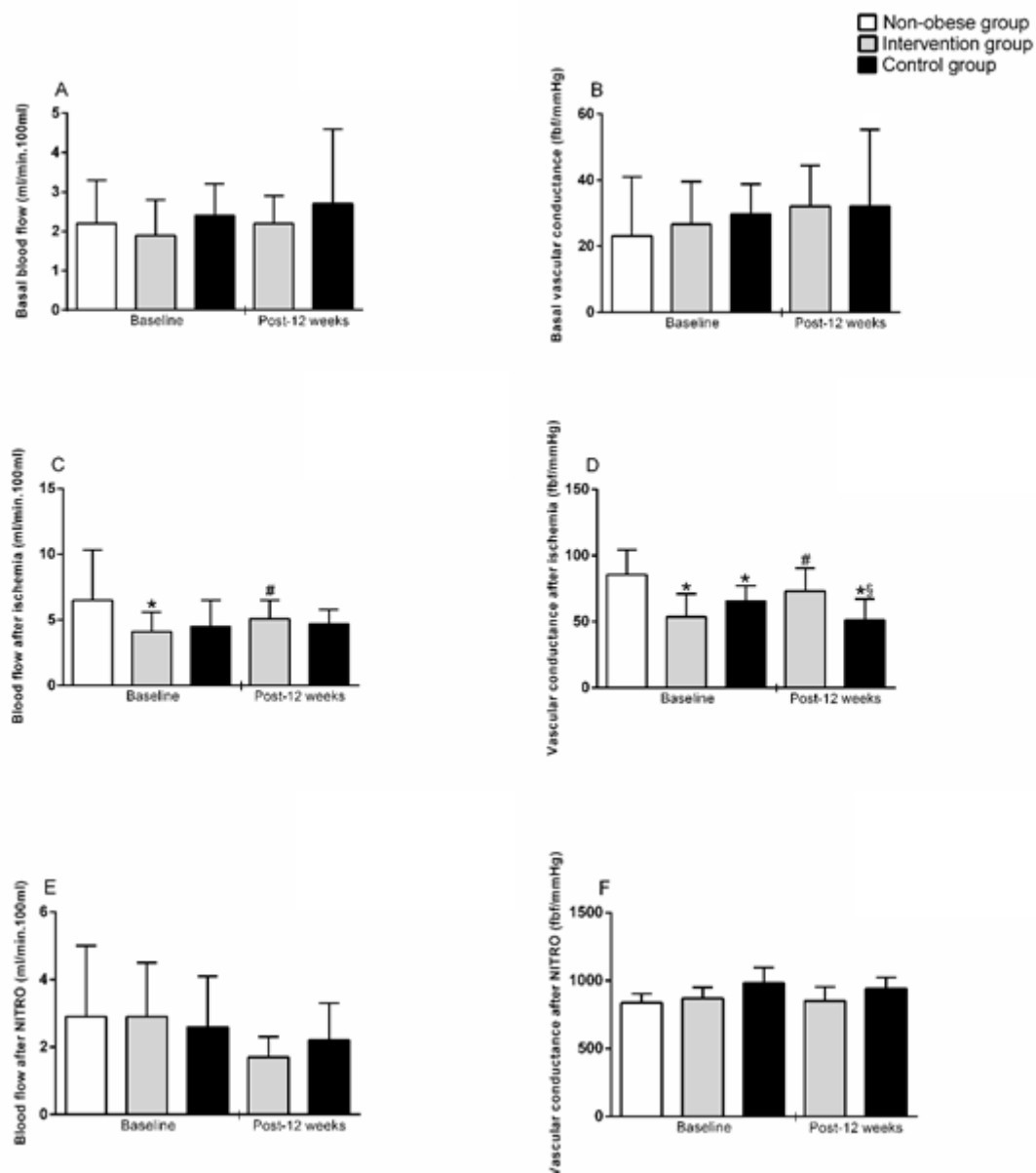


Figure 2. Mean (SD) values for endothelial function in non-obese, control and intervention groups at baseline and after 12-weeks of recreational soccer practice. NITRO: Nitroprusside; #: Significant difference within group ($P < 0.01$); *: Significant difference vs. non-obese group ($P < 0.05$); §: Significant difference between groups after 12 weeks of recreational soccer intervention ($P < 0.04$).

DISCUSSION

The purpose of this study was to investigate the impact of a RSP upon the body composition, blood pressure, cardio-respiratory fitness, cardiac autonomic activity, biochemical risk markers, and endothelial function in obese adolescents. Our findings demonstrated that recreational soccer performed three times a week during 12 weeks resulted in beneficial changes in body mass and composition, VO_{2peak} , resting blood pressure, autonomic cardiac activity, plasma lipid and glucose profile, C-reactive protein, and endothelial-dependent vasodilation.

In the present study, DXA was used to assess changes in body composition, ratifying the results of previous studies that soccer practice might help decreasing percentage body fat [38]. On the other hand, the beneficial impact of PA programs on the blood pressure of adolescents who are overweight or obese has not been extensively evaluated [85, 93]. In the present study, only SBP at rest decreased by approximately 8 mmHg after RSP, which concurs with some previous trials [84, 93, 96] reporting a decrease of 5 to 6 mmHg in SBP in similar populations after traditional aerobic training programs. The lowered SBP was concomitant to higher parasympathetic outflow and lower sympathetic outflow after RSP. Altogether, these findings reflect an improvement of hemodynamic and cardiac autonomic function, which can be considered as a cardio-protective effect of RSP [141]. This premise is reinforced by the fact that HRV indices in the RSP group approached the values exhibited by the non-obese control group— actually, all differences between RSP and non-obese groups at baseline were no longer detected after the intervention. These results indicate that the cardiac autonomic function may be improved by a relatively short program of recreational soccer.

It has been suggested that recreational soccer would be able to promote similar gains in VO_2 peak vs. continuous training, provided the amount of training hours was equivalent [53]. However, some studies failed to ratify this premise: Faude et al. [7], for instance, applied a soccer program three times a week during six months to obese and overweight children, and did not find an increase in VO_2 peak. However, in that study, the program consisted in warm-up (10% of total time), different small-sided games (50% of total time), technique drills (20% of total time), and fitness courses with the ball (20% of total time). In the present

study the routines were entirely based in small-sided games (70% of total time), which is in fact the essence of recreational soccer and probably increased the time of exposure to intensities compatible with $\text{VO}_{2\text{peak}}$ improvement [142].

Obese and overweight adolescents normally exhibit higher levels of total cholesterol and LDL-cholesterol compared to normal weight adolescents [143]. In the present study, the RSP was capable to increase HDL-cholesterol and to decrease total cholesterol, triglycerides, and fasting glucose in obese adolescents. The LDL-cholesterol remained stable in the intervention group, but exhibited a significant increase in controls, which may also be considered as a positive training effect [109]. Data from a recent systematic review concur with these findings, indicating that those markers generally improve in obese adolescents after PA intervention [38]. We were not able to find other studies specifically investigating the effects of soccer practice upon the lipid profile in adolescents, but the impact of traditional aerobic training of different intensities on lipid profile was lower compared to the present RSP intervention [38]. Again, a possible explanation for this difference could be the larger amount of moderate to high intensity work performed during the small-sided games [50].

Previous studies reporting beneficial effects of exercise upon C-reactive protein applied traditional aerobic training with moderate to high intensity [88]. As aforesaid, this was probably the case of the present intervention, based on small-sided games trying to reproduce the actual soccer practice, characterized by high intensity intermittent running bouts within an overall aerobic work [50]. On the other hand, intervention programs proposing activities with lower intensity did not have the same effect [84, 85]. This is an important issue, since the exercise intensity seems to be determinant of C-reactive protein response. Improvement in HOMA-IR is often associated with decreases in BMI, particularly as an effect of regular PA [87]. It is well accepted that aerobic training induces favorable adaptations in HOMA-IR [96], but the present study provides original information showing that insulin resistance in obese adolescent can be improved exclusively through a recreational soccer intervention. In fact, of the 10 adolescents initially classified as insulin resistant in the RSP group, half no longer exhibited this condition at the end of the intervention. These findings warrant further research

to ratify the potential effects of recreational soccer upon these important risk markers for cardiovascular and metabolic disease.

Endothelial dysfunction is one of the first markers of atherosclerosis and is often present in overweight patients. Our findings demonstrated that after ischemia the vascular conductance increased and vascular resistance decreased in the RSP group, while in the obese control group there was a non-statistically significant trend towards the opposite. Additionally, endothelial function markers in the RSP group approached at the end of the intervention the pattern observed for the non-obese controls.

No significant change in endothelial function could be detected in the oral nitroprusside spray condition. The fact that the endothelial function after oral nitroprusside spray remained unaltered before vs. after RSP, indicates that probably the smooth muscle function was still preserved in our cohort of overweight and obese adolescents [138]. In other words, only the endothelial dependent vasodilation responded to RSP. This finding suggests that the endothelium of our sample of overweight adolescents was already unhealthy, but also that this fact was at least in part counteracted by the RSP. This is the first study investigating the effects of a soccer program on the endothelial function in adolescents, which makes difficult comparisons with previous research. Recent studies showed that maximal aerobic exercise could improve the endothelial function in overweight or obese children and adolescents [81]. However, these studies applied individualized exercise routines, as running, cycling, or circuit training, which might be less motivating to adolescents in comparison with team sports. Another important difference of previous trials with regard to the present study is the absence of an overweight/obese untrained control group. Previous studies used only normal weight adolescents as controls.

The RSP promoted significant improvements in endothelin-1 (ET-1) and tumoral necrosis factor alpha (TNF- α) levels. The ET-1 is an endothelium-derived vasoconstrictor associated with endothelial dysfunction. The hyperinsulinemia stimulates the production of ET-1 by endothelial cells, which may compromise the vasodilator effects of nitric oxide and increase the production of superoxide [144]. On the other hand, the improvement of TNF- α represented a decrease of

insulin resistance and lipid metabolism [145]. However, 12 weeks of RSP seemed not to be enough to promote changes in other inflammatory markers [83].

In conclusion, our findings support the hypothesis that a 12-week recreational soccer intervention can improve health markers of adolescents who are overweight or obese. Beneficial effects were observed in body mass, body composition, blood pressure, cardiac autonomic activity, physical fitness, biochemical markers, and endothelial function. These results are original and reinforce the importance of sports practice by overweight and obese adolescents.

Conflict of interest statement: The authors do not have any conflict of interest to declare concerning the present manuscript.

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Estudo III

Em revisão na Blood Pressure Monitoring; Vasconcellos F; Seabra A; Cunha F; Montenegro R; Bouskela E; Farinatti P; **Heart rate variability assessment with fingertip photoplethysmography and polar RS800cx as compared to electrocardiography in obese adolescents**, 2014.

TITLE PAGE

Heart rate variability assessment with fingertip photoplethysmography and polar RS800cx as compared to electrocardiography in obese adolescents

Short title: Accuracy and reliability of HRV assessment from PPG and Polar RS800cx system

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Abstract

Obesity in adolescents may be related to autonomic dysfunction due to insulin resistance and/or increased central fat. This fact may affect the accuracy and reliability of the evaluation of autonomic activity at rest. The study investigated the accuracy and reliability of short-term resting heart rate variability (HRV) assessed by means of fingertip photoplethysmography (PPG) and cardiofrequencimeter (Polar RS800cx) in obese adolescents. Fourteen adolescents (15 ± 2 years old) classified as obese and exhibiting insulin resistance performed the following procedures: a) anthropometric measurements; and b) two 25-min HRV recordings in a supine position using simultaneously electrocardiography (ECG), PPG, and Polar RS800cx. The results showed significant correlations between HRV markers obtained by Polar RS800cx and PPG vs. ECG, with coefficients of determination (R^2) and intraclass correlation coefficients (ICC) ranging from 0.60 to 0.98 (P value ranging from 0.03 to 0.05) and 0.70 to 0.99 (P value ranging from 0.01 to 0.05), respectively. The technical error of measurement and ICC for test-retest reliability ranged from 8.9% to 45.8% and 0.38 to 0.68 for ECG, 8.0% to 30.5% and 0.29 to 0.61 for Polar RS800cx, and 7.2% to 54.6% and 0.45 to 0.64 for PPG. In conclusion, HRV indices calculated from Polar RS800cx and PPG appear to be as accurate and reproducible as data from ECG when evaluating the autonomic control of heart rate at rest in obese adolescents.

Keywords: cardiac autonomic function, obesity, heart rate monitor, spectral analysis, test-retest reliability.

1. Introduction

Heart rate variability (HRV) is a non-invasive method to assess the modulation of cardiac autonomic nervous system (ANS) activity and has been widely used in clinical and research sets [147-149]. The HRV reflects beat-to-beat changes in heart rate (HR), expressing the sympatho-vagal interaction obtained by the variation of both instantaneous HR and R-R intervals within the cardiac cycle [150]. Lower variance in HRV might be explained by either lower parasympathetic or higher sympathetic activity, and has been associated with the development of pathological conditions such as metabolic syndrome [151], stroke [152], chronic fatigue [153, 154], obesity [155, 156], and especially hypertension [157, 158].

The prevalence of obesity among children and adolescents increases worldwide [159]. Previous studies have reported that obese adolescents often exhibit low parasympathetic or high sympathetic activity at rest [148, 149]. As a consequence, obese adolescents may exhibit increased heart rate and cardiac output at rest, as well as decreased baroreflex sensitivity and higher blood pressure [160-162]. The assessment of autonomic activity in obese adolescents is therefore clinically relevant, and HRV indices are frequently used as markers of sympathetic and parasympathetic modulation [148, 152]. Evidently, it is important that results obtained from HRV are accurate and reliable, really reflecting the modulation of ANS activity to the heart.

Several techniques have been applied to assess HRV, as electrocardiography (ECG), cardiometers (e.g. Polar S810 or RS800cx), and photoplethysmography (PPG). It is expected that independent measurements obtained from different techniques are accurate and reliable [150]. Previous studies have shown fair associations between HRV indices measured by ECG and cardiofrequencimeters [163, 164], or between ECG and PPG [165-168]. However, the agreement of HRV measures performed by these methods appears to rely on population characteristics [169]. Despite of this, most studies investigating the agreement and reliability of techniques to assess HRV investigated only healthy adults [163-167, 170-172]. Since a certain degree of autonomic unbalance is expected in obese adolescents and given the potential influence of this condition upon HRV assessment [173], it would be important to

investigate the level of agreement of HRV indices obtained by different techniques.

Thus, the main purpose of the present study was to investigate the level of agreement between HRV indices in time and frequency domains derived from the Polar RS800cx monitor and a PPG device vs. ECG in obese adolescents. Additionally, the test-retest reliability of short-term HRV assessments obtained using the Polar RS800cx and PPG was determined.

2. Materials and Methods

2.1 Participants

Fourteen obese adolescents (3 girls; 15 ± 2 years old) enrolled in the study, being recruited from schools in the city of Rio de Janeiro, RJ, Brazil. In order to participate in the study subjects had to be classified as obese, according to the body mass index (BMI) 95th percentile for gender and age (e.g. 15 years – 25.2 kg/m² for boys and 26.4 kg/m² for girls) [174], and exhibit insulin resistance, according to the level of homeostasis model assessment for insulin resistance (HOMA-IR), above 5.22 and 3.82 for pubertal boys and girls respectively [140]. Exclusion criteria were: a) Use of medication having impact on metabolic, endocrine, cardiovascular or weight management; b) Participation in weight management program, including exercise or nutritional intervention, within six months prior to the study; and c) Sexual maturation above 3 for breast development, pubic hair, or genital size according to Tanner classification charts, or menarche (Tanner & Whitehouse, 1976). The study had institutional ethical board approval and all parents or legal guardians signed informed consent forms providing authorization for the children to participate in the study.

2.2 Procedures

Each subject visited the laboratory three times on three separate days. On the first day, anthropometric measurements were taken (height, body mass, and waist/ hip circumferences), and body composition was assessed by dual-energy X-ray absorptiometry (DXA) (Hologic QDR 4500 – HologicTM, Bedford, MA, USA). On the second and third visits, a short-term HRV assessment was performed

using simultaneously three different devices (i.e. ECG, PPG, and Polar RS800cx). In the laboratory, subjects laid in a quiet and thermoneutral environment (22 to 24°C) with minimum disturbance and light. Measures were performed after 8-h fasting and individuals refrained from caffeine beverages and exercise during 24 hours prior to the experiment. In all cases, 25-min HRV recordings were made with subjects in the supine position. In order to optimize the stability of HRV signs, all indices were calculated based on the last 5-min of each recording. The adolescents were advised not to talk or move excessively, and to keep spontaneous non-regulated breathing rhythms during the 25-min recording.

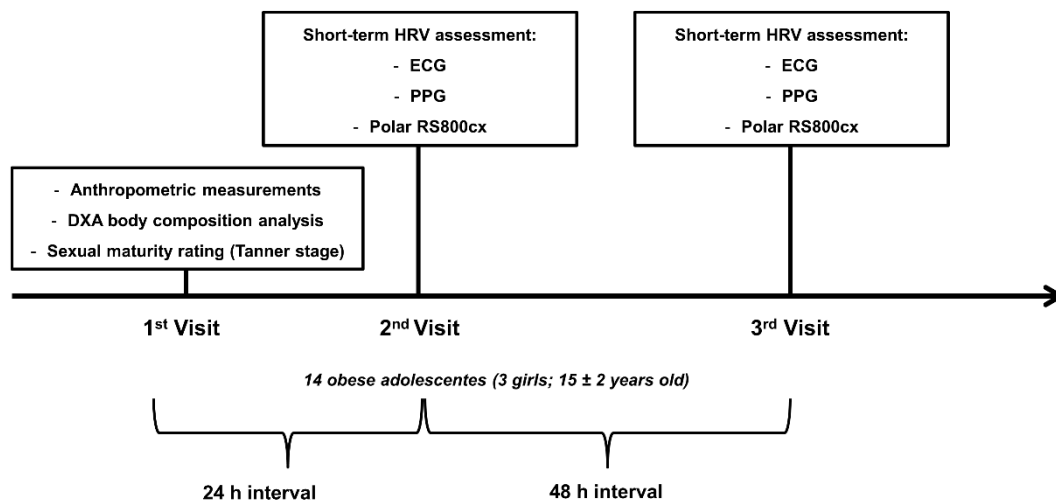


Figure 1. Study design overview. DXA = dual-energy X-ray absorptiometry; ECG = electrocardiograph; PPG = photoplethysmograph

Measurements were preceded by 20 min at rest with all HRV devices already placed, in order to reduce bias due to stress and to allow stabilization of signals from each device. Thereafter the ECG, PPG and Polar RS800cx assessments were synchronized manually and data were recorded during 5 min. The tests were repeated within 48 h to determine test-retest reliability of the measurements, respecting all experimental conditions of the first test and at the same time of the day, between 8:30-11:30 a.m.

2.3 Instrumentation and data acquisition

The ECG (Micromed™, Brasilia, DF, Brazil) was monitored continuously via three cutaneous electrodes placed to record the CM5 lead, according to the manufacturer's instructions. Data were analyzed off-line by two experienced evaluators that identified the R-peak at each QRS complex, by means of specific software with a sampling frequency of 600Hz per channel and using a 12-bit digital resolution (Elite Ergo PC 3.2.1.5, Micromed™, Brasilia, DF, Brazil). The PPG finger cuff (FMS, Finapress Medical Systems™, Amsterdam, the Netherlands) was placed on the left middle finger and beat-by-beat blood pressure was assessed with height correction on the left arm. The PPG infrared detector is able to detect small variations caused by changes in microcirculation, which reflect changes in blood volume and blood vessel wall movement. The BeatScope 1.1a software (FMS, Finapress Medical Systems™, Amsterdam, the Netherlands) was used to scan automatically for the presence of waveforms that looked like arterial pressure pulsations or beats with a digital resolution of 2.5 mV and 16-bit. After the electrode and finger cuff placements, the elastic electrode belt of the Polar (RS800cx, Polar™, Kempele, Finland) was placed just below the chest, with conductive gel being applied according to the manufacturer's instructions. In order to evaluate the HRV, 5-min windows were extracted and downloaded for analysis by specific software (Polar Precision Performance, Polar™, Kempele, Finland). The record sampling frequency was set at 1,000 Hz, providing a temporal resolution of 1 ms for each RR period [175]. The R-R interval data were downloaded by Polar Precision Performance Software (Polar™, Kempele, Finland).

2.4 Calculation of heart rate variability indices

A Fast Fourier Transform (Welch's method) with a Hanning window and 50% overlap was used to estimate the power density spectrum of R-R interval variability using the Kubios™ HRV software (Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Kuopio, Finland), based on R-R intervals averaged for 5-min windows. The sampling frequency was 1000 Hz, and signal artifacts were filtered by excluding R-R interval values with differences of more than 20% of the preceding R-R interval [137]. Time-domain

analysis consisted in measures of HR, R-R intervals (average of all normal R-R intervals), pNN50 (percentage of normal R-R intervals differing more than 50 milliseconds of its adjacent), and rMSSD (square root of the sum of successive differences between adjacent normal R-R intervals squared). In the frequency-domain, the power spectrum density function was integrated in the two classical frequency bands, as follows: 1) Low frequency band (LF: 0.04 to 0.15 Hz), and 2) High frequency band (HF: 0.15 to 0.40 Hz) [150]. The HF was used as an index of vagal modulation, whereas LF was considered primarily as a marker of sympathetic nervous system activity [176, 177]. The spectral values were expressed as normalized units (n.u.). The LF / HF ratio was adopted as an index of sympatho-vagal balance.

2.5 Statistical analysis

All data is presented as mean $\pm$ SD, unless stated otherwise. As aforementioned, seven indices were selected for statistical evaluation according to their clinical relevance [178]: HR, R-R intervals, pNN50, and rMSSD in the time-domain, and HF, LF and LF/HF ratio in the frequency-domain. The level of agreement between ECG vs. Polar and ECG vs. PPG for each variable was assessed using paired Student t tests, intraclass correlation coefficient (ICC) with 95% limits of agreement (95% LoA), and ordinary least squares regression analysis. An ICC > 0.80 was considered as good to excellent agreement and ICCs between 0.60 and 0.80 were considered as substantial agreement [179]. However, the methods were considered interchangeable only if the lower 95% LoA value exceeded 0.75 [171]. The distribution of these differences was graphically displayed using Bland-Altman plots, which include the associated 95% limits of agreement (the mean difference $\pm$ 1.96 times the standard deviation of the differences) [180].

Test-retest reliability of HRV indices was evaluated by calculating the within-subject standard deviation (SD), technical error of measurement (TEM), and intraclass correlation coefficient (ICC). The TEM was calculated by the formula:

$$TEM = \sqrt{\frac{\sum d_i^2}{2n}} \quad [181],$$
 where D is the difference between two measurements recorded by a given observer, $\sum d^2$ is the summation of deviations raised to the second power, i is the number of deviations, and N is the number of volunteers

measured. The ICC was calculated using a one-way random effects model [182]. Statistical significance for all inferential statistical tests was set at $P \leq 0.05$. All statistical analyzes were performed using IBM SPSS Statistics 21 (SPSS™ Inc., Chicago, IL, USA).

3. Results

Table 1 shows data for anthropometric characteristics, HOMA-IR, and range of Tanner maturation stage of the sample. Subjects exhibited high levels of HOMA-IR, therefore being classified as insulin resistant. The sexual maturation was homogenous within the sample, all subjects ranging from 4 to 5 in the Tanner classification.

Table 1. Means (SD) of the anthropometrics characteristics of the sample (n = 14), except to Tanner stage.

Age (years)	Tanner stage (range)	Weight (Kg)	Height (cm)	Body fat (%)	WC (cm)	HC (cm)	HOMA-IR	
							boys	girls
15 (1.6)	4 – 5	91.2 (21.6)	166.7 (9)	42 (6.5)	101.8 (13.4)	111.1 (13.6)	5.31 (1.1)	4.01 (0.9)

WC: waist circumference; HC: hip circumference; BMI: body mass index; HOMA-IR: homeostasis model assessment for insulin resistance

Table 2 depicts the number of counts, heart rate, R-R interval, pNN50, rMSSD, LF, HF and LF/HF obtained using the three different devices. In general, agreements between HRV indices obtained by Polar RS800cx and PPG vs. ECG were moderate to strong (with R^2 and ICC ranging from 0.60 to 0.98 and 0.70 to 0.99, respectively). However, there was no substantial agreement between ECG vs. PPG and ECG vs. Polar for pNN50 (time-domain), LF, and HF (frequency-domain), when taking into account the interchangeable agreement criteria – in this sense, despite of the moderate to excellent agreement level (based on ICC ranging from 0.70 to 0.87), the 95% LoA value was lower than 0.75 (with 95% LoA ranging from 0.31 to 0.66%) in all cases.

Table 2. Sample mean (SD) counts, heart rate, R-R interval, pNN50, rMSSD, LF, HF and LF/HF for the three different technologies to assess the HRV. The mean difference (Mean diff), the standard deviation of the differences (S_d), the interclass correlation coefficient (ICC) with 95% limits of agreement (95% LoA), and the interchangeable agreement (I.A.) for the ECG vs. Polar and ECG vs. PPG differences for each HRV index also shown. Any discrepancies between the individual means and the mean differences are due to rounding error. The regression results for the relationship between the ECG vs. Polar and ECG vs. PPG for each HRV index. The β_0 is the y-intercept, R^2 is the coefficient of determination, and SEE is the standard error of the estimate.

Variables	ECG	Polar	PPG	Relationships	HRV differences			Regression analysis results					
	Mean (SD)	Mean (SD)	Mean (SD)		Mean diff	S _d	ICC (95% LoA)	I.A.	B ₀	B ₁	R ²	P values	SEE
Counts	345 (42)	345 (45)	335 (44)	ECG vs. Polar	-0.14	7.3	0.99 (0.96 to 0.99)	Yes	28.4	0.99	0.98	< 0.001	6.6
				ECG vs. PPG	10.6	14.7	0.91 (0.76 to 0.98)	Yes	47.2	0.94	0.88	< 0.001	14.4
Time-domain													
Heart rate (beats.min ⁻¹)	70 (8)	69 (9)	69 (9)	ECG vs. Polar	0.57	1.3	0.98 (0.96 to 0.99)	Yes	7.0	0.99	0.98	< 0.001	1.0
				ECG vs. PPG	0.20	2.1	0.96 (0.90 to 0.99)	Yes	5.4	0.97	0.94	<.0001	2.0
R-R interval (ms)	875 (109)	885 (122)	879 (116)	ECG vs. Polar	-10.1	20.9	0.98 (0.94 to 0.99)	Yes	93.4	0.99	0.98	< 0.001	15.9
				ECG vs. PPG	-3.9	29.7	0.96 (0.90 to 0.99)	Yes	75.9	0.97	0.93	< 0.001	28.9
pNN50 (ms)	44 (20)	38 (14)	44 (18)	ECG vs. Polar	5.6	10.3	0.77 (0.47 to 0.92)	No	-2.0	0.86	0.75	< 0.001	10.3
				ECG vs. PPG	-0.6	9.6	0.88 (0.67 to 0.96)	No	0.74	0.87	0.77	< 0.001	10.0
rMSSD (ms)	88 (55)	68 (24)	87 (51)	ECG vs. Polar	13.8	15.9	0.90 (0.75 to 0.80)	Yes	-11.6	0.98	0.97	< 0.001	8.4
				ECG vs. PPG	1.8	18.7	0.94 (0.83 to 0.98)	Yes	1.45	0.93	0.88	< 0.001	19.5
Frequency-domain													
LF (n.u.)	48 (21)	56 (17)	45 (21)	ECG vs. Polar	-7.5	13.6	0.70 (0.31 to 0.89)	No	-6.40	0.77	0.60	= 0.001	14.1
				ECG vs. PPG	3.2	10.7	0.87 (0.66 to 0.96)	No	8.30	0.87	0.76	< 0.001	10.8
HF (n.u.)	52 (21)	44 (17)	55 (21)	ECG vs. Polar	7.6	13.5	0.70 (0.32 to 0.89)	No	8.57	0.77	0.60	= 0.001	14.1
				ECG vs. PPG	-3.3	10.7	0.87 (0.66 to 0.96)	No	2.86	0.87	0.76	< 0.001	10.9
LF/HF ratio	1.3 (1.2)	1.6 (1.2)	1.3 (0.9)	ECG vs. Polar	-0.3	0.4	0.92 (0.77 to 0.97)	Yes	-0.27	0.95	0.86	< 0.001	0.4
				ECG vs. PPG	0.08	0.4	0.93 (0.80 to 0.97)	Yes	0.10	0.92	0.89	< 0.001	0.4

ECG: electrocardiography; Polar: cardiofrequencymeter system; PPG: photoplethysmography; R-R intervals: average of all normal R-R intervals; pNN50: percentage of normal R-R intervals differing more than 50 milliseconds of its adjacent; rMSSD: square root of the sum of successive differences between adjacent normal R-R intervals squared; HF: high frequency band (0.15 to 0.40 Hz); LF: low frequency band (0.04 to 0.15 Hz); LF/HF ratio: sympatho-vagal balance.

Figure 2 shows the distribution of differences between HRV indices (R-R intervals, rMSSD and LF/HF ratio) derived from ECG vs. Polar RS800cx and ECG vs. PPG for each of the 14 subjects. Except for the LF/HF ratio comparison between ECG vs. Polar RS800cx, no significant difference was detected between all other HRV indices when comparing ECG vs. Polar RS800cx and ECG vs. PPG (R-R intervals: mean difference = -10.0 and 3.9 ms, $t = -1.8$ and -0.5 , $P = 0.09$ and 0.63 ; rMSSD: mean difference = 20.9 and 1.8 ms, $t = 1.9$ and 0.4 , $P = 0.07$ and 0.72 ; LF/HF ratio: mean difference = -0.3 and -0.2, $t = -2.9$ and 0.8 , $P = 0.01$ and 0.44), respectively.

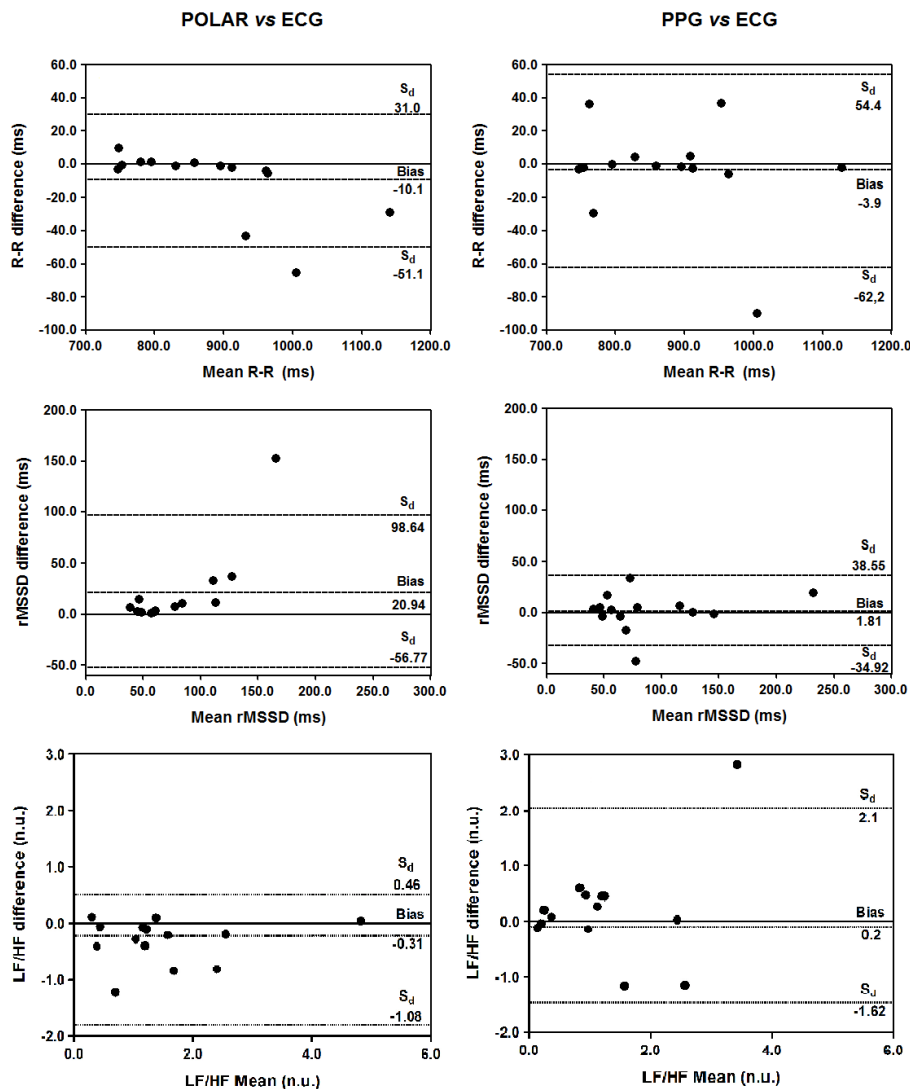


Figure 2. Bland-Altman plot showing individual differences between HRV indices derived from ECG vs. Polar RS800cx and ECG vs. PPG. The first and third horizontal dashed lines in each graph represent the 95% limits of agreement. S_d = standard deviation of the differences. ECG: electrocardiography; Polar: cardiofrequencymeter system; PPG: photoplethysmography; R-R intervals: average of all normal R-R intervals; rMSSD: square root of the sum of successive differences between adjacent normal R-R intervals squared; LF/HF ratio: sympatho-vagal balance.

Figure 3 shows the HRV indices derived from ECG, Polar RS800cx and PPG and test-retest reliability statistics for both 5-min assessment trials. No significant difference was observed between trials for Polar RS800cx and PPG. TEM and ICC for the HRV indices (test-retest) ranged from 8.9% to 45.8% and 0.38 to 0.68 for ECG; 8.0% to 30.5% and 0.29 to 0.61 for Polar RS800cx; and 7.2% to 54.6% and 0.45 to 0.64 for PPG, respectively.

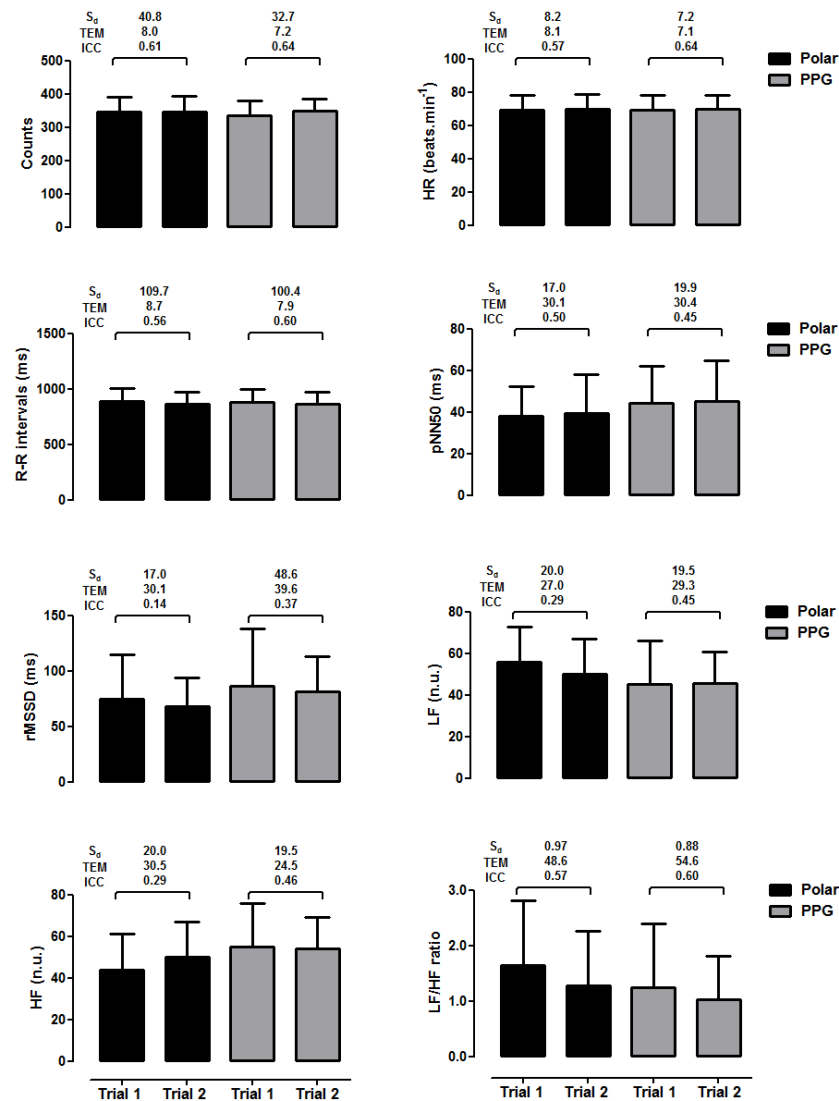


Figure 3. Mean ± SD HRV indices derived from Polar RS800cx and PPG during the 5-min data collection period for the two trials (n = 14). The values under each error bar are the test-retest reliability statistics for each device: S_d = within-subject standard deviation; TEM = technical error of measurement; ICC = intraclass correlation coefficient; Polar: cardiofrequencymeter system; PPG: photoplethysmography; R-R intervals: average of all normal R-R intervals; pNN50: percentage of normal R-R intervals differing more than 50 milliseconds of its adjacent; rMSSD: square root of the sum of successive differences between adjacent normal R-R intervals squared; HF: high frequency band (0.15 to 0.40 Hz); LF: low frequency band (0.04 to 0.15 Hz); LF/HF ratio: sympatho-vagal balance.

4. Discussion

The present study investigated the level of agreement between HRV indices measured by means of Polar RS800cx and PPG vs. ECG recording (gold standard technique), and determined the test-retest reliability of short-term HRV assessment using Polar and PPG devices in obese adolescents. The major finding was that HRV indices derived from Polar RS800cx and PPG had moderate to excellent agreement levels with ECG (except for pNN50, LF and HF). The reliability found for time and frequency-domain HRV indices were very similar to the ECG values in both Polar RS800cx and PPG devices. In practical terms, the test-retest reliability of both Polar and PPG after 25 min (stabilization period of 20-min and additional 5-min assessment) at rest was equivalent reliability found for ECG, indicating that these techniques would be adequate to assess HRV in obese adolescents.

The HRV indices observed in the present study are consistent with reference values reported by previous studies with obese adolescents, regardless of the assessment method. For instance, Kaufman *et al.* [184] reported values similar to ours in 16 obese adolescents (11.5 ± 0.8 years old), with mean ($\pm$ SD) obtained from ECG for HF (n.u.), LF (n.u.), LF/HF ratio, and R-R intervals (ms) of 58.2 (11.8), 41.8 (11.8), 1.6 (0.84), and 828 (144), respectively. Based on these values, the adolescents in that study were considered as exhibiting dysfunction of cardiac autonomic modulation [184].

The agreement levels presently observed between the Polar RS800cx and PPG vs. ECG ($ICC \geq 0.8$) in obese adolescents were similar to previous research investigating the validity and reliability of short-term HRV derived from ECG compared to Polar [163, 164, 169, 171, 183, 185] and PPG [165-167] in healthy adults. The exceptions were LF, HF and pNN50 assessed by Polar RS800cx (0.70; 0.70; and 0.77, respectively – see Table 2). Nunan *et al.* [163] analyzed the validity of the Polar S810 vs. ECG and found small and marginal mean differences between the two devices for R-R intervals (-2.4 ms) in youth healthy adults. Our findings with obese adolescents were quite similar, since the mean differences between the methods were higher than the values obtained by Nunan *et al.* (R-R intervals: -10.1 ms; LF: -7.5 n.u.; HF: 7.6 n.u.). Additionally, those

authors reported correlation coefficients of 0.99, 0.86, and 0.85 for R-R intervals, LF, and HF, respectively, indicating a good to excellent agreement with ECG [163]. The same study found ICC near to perfect for R-R intervals (0.98), and satisfactory correlation for LF and HF (0.70) [163]. In the present study, the best correlations were found for time domain variables (i.e. heart rate: 0.98; R-R intervals: 0.98; pNN50: 0.77; and rMSSD: 0.90). Differences between data from Nunan *et al.* [163] and the present study with regard to the agreement with ECG of indices of spectral analysis can be due to the fact that Nunan *et al.* have not compared the counts measured by each unit. This is an important issue, since after assessment the R-R intervals pass through filters of artifacts that often reduce the number of counts, which might influence the HRV spectral analysis. Another aspect that may also explain differences of agreement between ECG and Polar presently found versus previous studies [163, 186] was that in our study the time adopted for acclimatization was longer, which could have minimized the influence of stress upon HRV. In other words, extending the stabilization time of the RR signal might decrease the amount of artifacts and reduce bias, particularly in subjects with compromised autonomic activity.

In which concerns the agreement between ECG and PPG, Selvaraj *et al.* [167] found high correlation (0.87 ± 0.19) and no significant difference between methods for all HRV indices in adults aged 21 to 28 years. In the present study the ICC between ECG vs. PPG was also high for most of HRV indices (ICC > 0.80), suggesting that the PPG would be a valid assessment method. However, it is worthy noticing that such agreement could only be found after manually removing artifacts, which can be a limitation of the method.

We could not find previous studies investigating the reliability of HRV indices produced by the observed devices in obese adolescents. However, our findings are in agreement with reliability values previously reported for healthy adults [163, 186-188]. Nunan *et al.* [163] reported ICCs ranging from 0.19 to 0.94 and TEM between 10.4 and 66.0 for the test-rest reliability of the Polar device, while Lu *et al.* [187] found ICCs ranging from 0.45 to 0.98 for PPG. The reproducibility of HRV indices from ECG, by previous research and the present study seemed to be compatible with those calculated using the Polar and PPG. For instance,

Marks et al. [188] reported ICCs from 0.45 to 0.81, while Pitzalis et al. [186] found ICCs between 0.20 and 0.79 and TEMs between 0.37 and 56.6, for HRV indices obtained from repeated ECG in healthy adults. These results are in agreement with ours (TEM from 8.9% to 45.8% and ICC from 0.38 to 0.68 for ECG), and are not distant of the reproducibility levels identified for Polar and PPG. In brief, the reproducibility of HRV indices obtained from ECG in the present study was similar to data reported by previous research, and compatible to reproducibility of HRV indices provided by Polar and PPG. In brief, HRV indices obtained using Polar and PPG in obese adolescents were as reliable as in ECG. Since the ECG has been considered as gold standard for HRV analysis, our results reinforce the premise that these techniques may be used to HRV analysis in this population.

The main limitation of the present study was that only two consecutive HRV assessments were performed so that it was not possible to check whether the reliability would be improved by further assessments. Additionally, additional research should be performed to investigate the effects of potentially confounding factors as mental stress, mood, alertness, or hydration on test-retest reliability of short-term HRV assessment in obese adolescents.

5. Conclusion

In conclusion, HRV indices obtained from short-term assessment using Polar RS800cx and PPG showed significant agreement levels and equivalent reproducibility versus ECG. These findings suggest that Polar RS800cx and PPG might be considered as accurate and reliable devices for evaluating the autonomic modulation to the heart, at rest in obese adolescents.

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The authors have no conflict of interest to declare

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Estudo IV

Em revisão no International Journal of Sports Medicine; Fabrício V. A. Vasconcellos; André Seabra; Rafael A. Montenegro; Felipe A. Cunha; and Paulo Farinatti; **Can heart rate variability be used to estimate gas exchange threshold in obese adolescents?**; 2014.

Can heart rate variability be used to estimate gas exchange threshold in obese adolescents?

Running title: Heart rate variability in obese adolescents

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Can heart rate variability be used to estimate gas exchange threshold in obese adolescents?

Running title: GET vs. HRVT methods in obese adolescents

ABSTRACT

This study investigated the agreement and reliability of oxygen uptake ($\dot{V}O_2$), $\dot{V}O_{2R}$ reserve ($\dot{V}O_{2R}$), heart rate (HR) and power output at intensities corresponding to the gas exchange threshold (GET) and heart rate variability threshold (HRVT) during maximal cardiopulmonary exercise testing (CPET) in obese and eutrophic adolescents. A further aim was to establish whether the HRVT was able to detect changes in cardio-respiratory fitness in obese adolescents after 3-month of recreational soccer practice. First, 25 obese and 10 eutrophic adolescents (aged 12 to 17 yr) visited the laboratory twice to perform cycling CPET to test the reliability of CPET outcomes at GET and HRVT. Furthermore, the level of agreement between GET and HRVT was determined for a subgroup of 10 obese adolescents after performing a 3-month recreational soccer program. No significant difference was found for $\dot{V}O_2$, $\% \dot{V}O_{2R}$, HR, and power output at the GET and HRVT ($P > 0.05$), which were equally able to detect improvements in aerobic fitness after the soccer intervention. Correlations between GET and HRVT for $\dot{V}O_2$ and $\% \dot{V}O_{2R}$ ranged from 0.89 to 0.95 ($P < 0.001$) and test-retest reliability ranged from 0.59 to 0.82 ($P < 0.006$). Overall, HRVT seems to be a reliable alternative for prescribing aerobic exercise intensity in obese adolescents.

Key-Words: Exercise Prescription; Autonomic Nervous System; Anaerobic Threshold; Aerobic Capacity; Fitness.

Introduction

Premature obesity has been appointed as a major public health problem [38]. It has been shown that children and adolescents who are overweight and obese are more likely to have limited aerobic capacity [maximal oxygen uptake ($\dot{V}O_{2\max}$)] due to peripheral fatigue related to the need to move a larger body during exercise [189, 190]. On the other hand, higher aerobic capacity seems to have an independent effect on the risk for developing cardiovascular disease, regardless of the body mass or composition. In other words, obese subjects that are fit have lower risk of developing cardiovascular disease compared to those with lower aerobic capacity, which has been referred as the “fat but fit” paradigm [191].

Hence strategies to optimize exercise prescription for this specific population are important [38]. The determination of the metabolic transition (or anaerobic) thresholds has often been used to prescribe aerobic exercise intensity for subjects with exercise intolerance, such as children and adolescents who are overweight or obese [189]. However, anaerobic thresholds are usually determined through ventilatory or lactate assessment within maximal cardiopulmonary exercise testing (CPET), which demands expensive apparatus, specialized human resources, and sophisticated facilities for safety support.

For that reason, alternative methods have been created to estimate the gas exchange threshold (GET), with lower cost than standard methods such as the lactate threshold (LT). Recent studies have used time and frequency domains of heart rate variability (HRV) as a measure of autonomic cardiac nervous system (i.e. parasympathetic and sympathetic modulation) at rest or during exercise [192]. They have proposed that the LT and GET would correlate with a specific marker of vagal withdrawal, denominated HRV threshold (HRVT) [175, 193, 194]. Indeed, accumulated evidence has suggested that HRVT might be a reliable and simple tool to estimate GET [175, 194-198]. It is worth mentioning that a recent study suggested that the HRVT method was capable of identifying the second, but not the first GET in elite ski-mountaineers [192]. However, these data do not concur with the accumulated evidence, which has consistently showed that the HRV method would be limited to identify a variation of root mean square of

standard deviations (rMSSD) at high intensity exercise (i.e. at the respiratory compensation point or near to maximal physical effort) due to the appearance of very low frequency artifacts from exercise-induced hyperventilation [199, 200].

The HRVT method has been applied to determine GET in adolescents who are obese or overweight [201-203]. However, we could not find previous research investigating the agreement between GET and HRVT in this population. This would be important nonetheless, since early autonomic cardiac dysfunction has been reported in obese or overweight children [148, 162, 204]. It is well accepted that obese subjects may exhibit excess sympathetic activity [205], which could evidently compromise the reliability and validity of HRVT for determining GET.

Thus, the present study aimed to verify the agreement and reliability of CPET outcomes at GET and HRVT in obese and normal weight adolescents. Furthermore, the ability of HRVT to reflect changes in cardio-respiratory fitness in obese adolescents after three months of recreational soccer practice was investigated. It was hypothesized that: a) obese adolescents would demonstrate higher oxygen uptake ($\dot{V}O_2$), oxygen uptake reserve ($\dot{V}O_{2R}$), heart rate (HR), and power output at GET and HRVT methods, when compared to eutrophic adolescents; and b) GET and HRVT methods would equally reflect improvements in cardio-respiratory fitness in obese adolescents after a recreational soccer training intervention.

Materials & Methods:

Subjects

Thirty-five adolescents (26 boys) aged 12 to 17 yr, who enrolled in a “Soccer for Health” program at the University facilities, volunteered to participate in the study. The characteristics of the subjects are shown in Table 1. The sample was assigned to two groups: 25 obese and 10 eutrophic adolescents. Adolescents were classified as obese when the body mass index (BMI) was above the 95th percentile for their age and gender [131]. Exclusion criteria included the participation in structured exercise, nutrition or weight loss programs within 6 months prior to the initial screening. The study was performed in accordance with

the ethical standards required by the journal [206] and all participants signed informed consent.

Procedures

The study design is shown in Figure 1. In the first part of study, each subject visited the laboratory three times on separate days interspersed with 24 to 48 h intervals. On the first visit, anthropometric measurements were taken, pubic hair development (Tanner stage) was determined, and subjects were familiarized with equipment and test protocols. On the second and third visits, maximal incremental CPET on a cycle ergometer were performed on two different occasions, each separated by two or three days, to investigate the level of agreement between GET and HRVT and test-retest reliability of CPET outcomes at GET and HRVT. Cycling exercise was adopted to decrease potential risks related to balance and bias due to mechanical efficiency in a sample of obese adolescents [207]. In the second part of the study, a subgroup of 10 obese adolescents was invited to participate in a 3-month recreational soccer program. At the end of the soccer intervention, the obese adolescents performed maximal CPET to investigate the ability of the HRVT method to reflect changes in cardio-respiratory fitness.

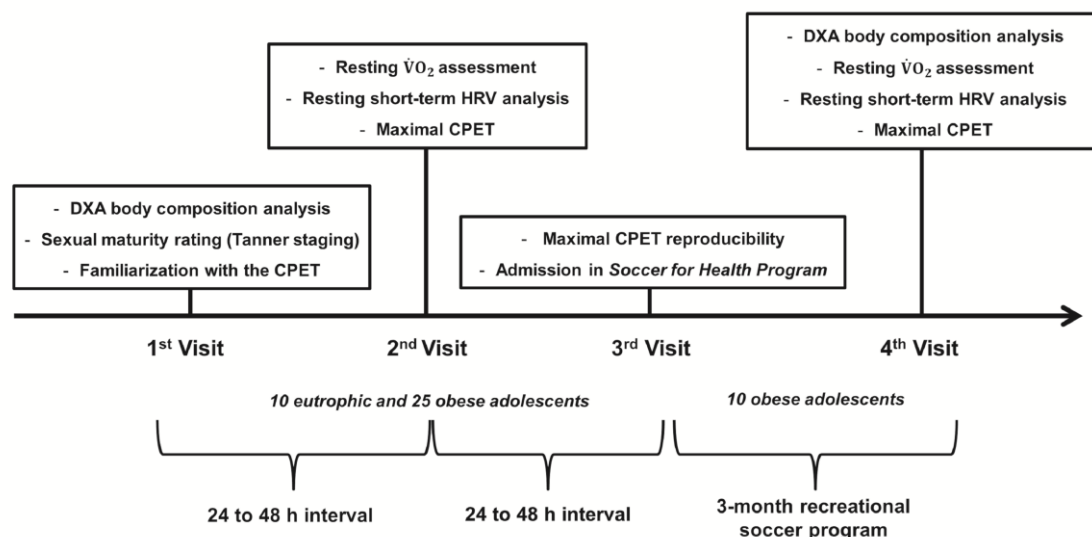


Figure 1. Study design overview. DXA = dual-energy X-ray absorptiometry; CPET = cardiopulmonary exercise testing; $\dot{V}O_2$ = oxygen uptake; HRV = heart rate variability.

Resting $\dot{V}O_2$ assessment

The resting $\dot{V}O_2$ was determined prior to calculation of % $\dot{V}O_2R$ in accordance with the following available strict recommendations [208]: abstention of physical exercise, alcohol, soft drinks and caffeine in the 24 h preceding the assessment, fasting for 8 h prior to the assessment, and minimum effort when travelling to the laboratory. In the laboratory, subjects laid in a calm environment for 10 min, after which the $\dot{V}O_2$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) was measured for 40 min as described elsewhere [136]. The resting $\dot{V}O_2$ was taken as the average of the last 5 min of steady-state data.

Biological maturity status and body composition assessment

Body mass and height were assessed respectively by digital balance scales (Welmy™, São Paulo, SP, Brazil) and a stadiometer graded in millimeters (American Medical do Brazil™, São Paulo, SP, Brazil). Body fractioning was assessed by Dual-Energy X-ray Absorptiometry (Hologic QDR 4500, Hologic™, Bedford, MA, USA) to determine fat mass percentage, muscular mass, bone mineral density, and fat mass distribution. The maturation state of pubic hair was evaluated as part of a comprehensive clinical examination, by a pediatrician with previous experience in the assessment of secondary sex characteristics, according to criteria proposed by Tanner [133].

Maximal Cardiopulmonary Exercise Testing (CPET)

Maximal CPET was performed on cycle ergometer (Cateye EC-1600, Cateye™, Tokio, Japan) using an individualized ramp protocol, with similar ergonomic adjustments and cadence kept at ~55 rpm. The initial load in the CPET was set at 25W with increments of 10W/min until voluntary exhaustion or incapacity to sustain the cadence for more than 5 seconds. All tests were preceded by a 3-min warm-up that involved a self-selected cadence at a work rate of 0W.

Tests were considered maximal if the participants satisfied at least three of the four following criteria [135]: a) maximum voluntary exhaustion as reflected by a score of 10 on the Borg CR-10 scale; b) 90% of the predicted maximal heart rate

[$HR_{\max} = 220 - \text{age}$], or presence of a heart rate plateau (ΔHR between two consecutive work rates ≤ 4 bpm); c) presence of a $\dot{V}O_2$ plateau ($\Delta \dot{V}O_2$ between two consecutive work rates $< 2.1 \text{ mL.kg}^{-1}.\text{min}^{-1}$); and d) a maximal respiratory exchange ratio ($RER_{\max}$) > 1.10 . Participants were verbally encouraged to perform a maximal effort.

Breath-by-breath pulmonary gas exchanges and minute ventilation were recorded throughout CPET and were determined using an Ultima Cardio₂ metabolic cart (Medical GraphicsTM, Saint Louis, MO, USA). Prior to testing, the gas analyzers were calibrated according to the manufacturer's instructions. The $\dot{V}O_2$ peak was determined as the highest $\dot{V}O_2$ value obtained during CPET.

Determination of the heart rate variability threshold (HRVT)

The HR and R-R intervals were registered continuously by a telemetric HR monitor (PolarTM, model RS800cx, Polar Electro Oy, Kempele, Finland) at rest and during the CPET. Before the HRVT determination, artifacts were removed by filtration, or manually by visual inspection when necessary. Even though there are many mathematical strategies to determine the HRVT, the time domain HRV indexes as the rMSSD seems to be strongly correlated with parasympathetic nervous activity. Therefore, the HRVT was determined by analyzing rMSSD, using R-R intervals within each 60 s stage throughout CPET, as described elsewhere [194, 203]. The HRVT was defined as a HRV deflection point represented by no further decreases in rMSSD values, which reflects parasympathetic withdrawal. The HRV analysis was performed using the Kubios HRV analyzer software (MatlabTM version 2.0 beta, Kuopio, Finland).

Determination of gas exchange threshold (GET)

The GET was determined using the combined procedure described by Gaskill et al. [209]. This procedure includes the following methods: a) Ventilatory equivalent method, with the GET defined as the $\dot{V}O_2$ corresponding to the first sustained rise in the ventilatory equivalent of O_2 without a concurrent rise in the ventilatory equivalent of CO_2 ; b) Excess carbon dioxide method, with the GET being defined as the $\dot{V}O_2$ corresponding to the first sustained rise in excess CO_2 ; and c)

Modified V-slope method, with the GET defined as the $\dot{V}O_2$ value corresponding to the first point of increase in $\dot{V}O_2$ - $\dot{V}CO_2$ slope. Visual inspection to determine GET was independently performed by two experienced investigators. If the difference between evaluators with regard to $\dot{V}O_2$ at GET was within 3%, the mean value was adopted as the final result. When the difference exceeded 3%, a third investigator was asked to determine GET. The combination of these three methods has been shown to improve the accuracy and reliability of GET determination [209].

Soccer intervention

The recreational soccer program was performed three times a week, during 12 weeks from 9 to 10 a.m. Each session consisted of a 10-min warm-up followed by adapted soccer drills and games (40 min of games performed in small pitch areas, such as 2 vs. 2, 3 vs. 3 and 4 vs. 4), and a 10-min cool-down. Training intensity corresponded to approximately 80% of maximal heart rate (HR_{max}) during the adapted small-sided drills and games. The intensity was monitored by means of a portable heart rate monitor (PolarTM RS800cx, Polar Electro Oy, Kempele, Finland). Exercises and games were progressively intensified as individually tolerated. Two licensed exercise instructors supervised the training sessions.

Statistical Analysis

Data normality was ratified by the Kolmogorov-Smirnov test. Data are therefore presented using means and standard deviations. Baseline differences between groups were tested by Student t-test and Qui-square (Tanner stage). Analysis of variance (ANOVA) for repeated measures was used to compare each variable over time (baseline and 3-months follow-up) in the obese group. In order to determine the level of agreement and correlations between GET and HRVT methods for $\dot{V}O_2$ and $\dot{V}O_2R$, Bland-Altman plots, intra-class correlations (ICC), and standard errors of estimate (SEE) were calculated within groups. Test-retest agreement and reproducibility between GET and HRVT methods for $\dot{V}O_2$ and $\dot{V}O_2R$ were assessed using ICC, mean differences of systematic bias, and 95% limits of agreement [151]. All statistical analyses were performed using IBM SPSS

Statistics 21 (SPSS™ Inc., Chicago, IL, USA). In all cases, statistical significance was fixed at $P \leq 0.05$.

RESULTS

Table 1 summarizes data describing the physical characteristics and resting autonomic cardiac responses of the eutrophic and obese groups at admission. Both groups were matched with regard to age, sexual maturation status, and height. As expected, body weight, fat mass percentage, and body mass index (Z-score) were higher in obese vs. eutrophic adolescents ($P < 0.05$). In addition, total power of HRV analysis was significantly lower in obese vs. eutrophic ($P < 0.001$).

Table 1. Mean (SD) physical characteristics and cardiac autonomic responses at admission in eutrophic and obese adolescents.

Variables	At admission		
	Eutrophic (n = 10)	Obese (n = 25)	P value
Age (years)	14.5 (1.58)	14.5 (1.5)	0.467
Tanner Stage	4.3 (0.32)	4.4 (0.21)	0.423
Weight (kg)	56.8 (5.56)	91.1 (17.97)	< 0.001
Height (cm)	167.2 (10.57)	165.5 (8.61)	0.591
BMI (Z-score)	0.4 (0.90)	2.9 (0.78)	0.044
Relative Fat Mass (%)	22.8 (14.17)	43 (5.88)	< 0.001
R-R interval (ms)	932.7 (138.7)	880.5 (118.4)	0.270
rMSSD (ms)	68.9 (24.9)	63.9 (24.1)	0.583
pNN50 (%)	43.8 (16.2)	36.1 (17.7)	0.243
LF (n.u.)	49.2 (17)	58.2 (14.5)	0.121
HF (n.u.)	50.8 (17)	41.5 (14.6)	0.114
LF:HF ratio	1.4 (1.5)	1.6 (0.9)	0.488
Total power (ms ²)	12450.9 (5967.9)	5054.2 (3050.1)	< 0.001

rMSSD = root mean square of standard deviations; pNN50 = the proportion of consecutive inter-beats intervals that differed by more than 50 milliseconds; LF = low frequency band; HF = high frequency band; LF:HF ratio = LF:HF ratio = sympathovagal balance.

Table 2 depicts the results obtained for HR and metabolic responses at rest and maximal effort in obese and eutrophic. Similar values were found for resting $\dot{V}O_2$ and HR between groups. Similar HR_{peak} and power outputs were also detected across groups. However, at admission the $\dot{V}O_{2peak}$ was significantly lower in obese vs. eutrophic groups ($P<0.001$). Although obese adolescents exhibited a 29% increase in $\dot{V}O_{2peak}$ after 3 months of soccer intervention ($P=0.002$), no changes were found in this group for either peak power output ($P=0.88$), or time to exhaustion ($P=0.98$).

Table 3 shows $\dot{V}O_2$ and $\% \dot{V}O_2R$ at the GET and HRVT in obese and eutrophic groups. No differences across groups was found for $\dot{V}O_2$ [$F(1,2) = 44.632$; $P=0.453$] or power output [$F(1,2) = 35.893$; $P=0.632$] at the GET and HRVT. On the other hand, $\% \dot{V}O_2R$ and HR at the GET and HRVT, were higher in obese vs. eutrophic adolescents. Moreover, a three months soccer intervention induced physiological adaptations in obese adolescents, represented by a decrease in $\% \dot{V}O_2R$ and higher power output at the GET and HRVT.

Table 2. Mean (SD) values for weight and cardiorespiratory variables during maximal CPET in obese and non-obese adolescents at admission and after 3 months of recreational soccer program.

Variables	At admission			After 3 months		$\Delta\%$
	Eutrophic (n = 10)	Obese (n =25)	<i>P</i> value	Obese (n = 10)	<i>P</i> value	
Weight (kg)	56.8 (5.56)	91.1 (17.97)	< 0.001	77.8 (7.9)	0.043	-14.5
Resting HR (bpm)	70.6 (9)	68.5 (9)	0.564	70.3 (8.1)	0.353	2.6
HR _{peak} (bpm)	191.5 (11)	184.5 (16)	0.136	190.3 (12.3)	0.512	3.2
Resting $\dot{V}O_2$ (mL.kg ⁻¹ .min ⁻¹)	3.4 (1.1)	3.1 (1.1)	0.51	3.1 (0.9)	0.730	0.9
$\dot{V}O_{2peak}$ (mL.kg ⁻¹ .min ⁻¹)	34 (9.1)	23.6 (4)	< 0.0001	30.5 (5.6)	0.001	29.1
Peak power output (Watts)	128 (41.9)	129.2 (25)	0.914	130.4 (31.9)	0.764	0.9
Time to exhaustion (sec)	675 (27.5)	677 (28.9)	0.876	675 (23.5)	0.865	-0.3

CPET: cardiopulmonary exercise testing; HR = heart rate; $\dot{V}O_2$ = oxygen uptake. At admission, *P* values refer to Eutrophic vs. Obese comparisons. At 3 months, *P* values refer to Obese pre- vs. post-intervention comparisons.

Table 3. Mean (SD) values for CPET outcomes at GET and HRVT in obese and eutrophic groups at baseline and after recreational soccer intervention.

	At Admission			After 3-months					
	GET	HRVT	<i>P value</i>	GET	HRVT	<i>P value</i>	%Δ GET	%Δ HRVT	<i>P value</i>
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Obese (n = 25)									
$\dot{V}O_2$ (mL·kg ⁻¹ ·min ⁻¹)	12.8 (2.8)	13.3 (3.1)	0.233	14.7 (1.9)	15.6 (2.4)	0.167	14.8 (2.1)	17.3 (3.9)	0.712
% $\dot{V}O_2R$	65 (22)	68 (22)	0.198	53.8 (14) #	57.1 (18) #	0.445	-17.2 (2.7)	-16.0 (4.2)	0.789
HR (bpm)	164.5 (10.9)	169.3 (12.2)	0.567	166.3 (12.3)	170.2 (14.5)	0.199	1.1 (0.2)	0.5 (0.1)	0.882
Power output (Watts)	37.8 (1.6)	35 (3.9)	0.345	45.2 (3.6) €	43.9 (6.3) €	0.902	19.6 (3.4)	25.4 (10.2)	0.098
Eutrophic (n= 10)									
$\dot{V}O_2$ (mL·kg ⁻¹ ·min ⁻¹)	13.2 (4.1)	14.1 (4.0)	0.177	NE	NE	NE	NE	NE	NE
% $\dot{V}O_2R$	46 (15)*	49 (15)*	0.389	NE	NE	NE	NE	NE	NE
HR (bpm)	138.1 (9.1) £	141 (7.5) £	0.134	NE	NE	NE	NE	NE	NE
Power output (Watts)	36 (2.3)	38 (4.2)	0.234	NE	NE	NE	NE	NE	NE

$\dot{V}O_2$ = oxygen uptake; % $\dot{V}O_2R$ = percentage of oxygen uptake reserve; HR = heart rate; GET = gas exchange threshold; HRVT = heart rate variability threshold; *: Difference compared to the obese in % $\dot{V}O_2R$ ($P=0.016$). £: Differences compared to the obese at admission in HR ($P<0.021$). #: Differences compared to the obese at admission in % $\dot{V}O_2R$ ($P=0.041$). €: Differences compared to the obese at admission in power output ($P=0.036$). NE = not evaluated.

Figure 2 shows Bland-Altman plots, ICC, and SEE between $\dot{V}O_2$ -GET vs. $\dot{V}O_2$ -HRVT and $\% \dot{V}O_2R$ -GET vs. $\% \dot{V}O_2R$ -HRVT. Correlations between $\dot{V}O_2$ and $\% \dot{V}O_2R$ at the GET and HRVT were above $r = 0.8$ and $r = 0.9$, and SEE was lower than 5 and 4 mL.kg⁻¹.min⁻¹, in obese and eutrophic groups, respectively. Figure 3 shows Bland-Altman plots and ICC for the test-retest reliability of $\dot{V}O_2$ -HRVT and $\% \dot{V}O_2R$ -HRVT. The reproducibility for $\dot{V}O_2$ was lower [ICC within 0.59 and 0.72 and SEE within 1.96 and 2.1 mL.kg⁻¹.min⁻¹ in obese and eutrophic groups, respectively] than for $\% \dot{V}O_2R$ [ICC within 0.79 and 0.82 and SEE within 7.1 and 9 % in obese and eutrophic groups, respectively].

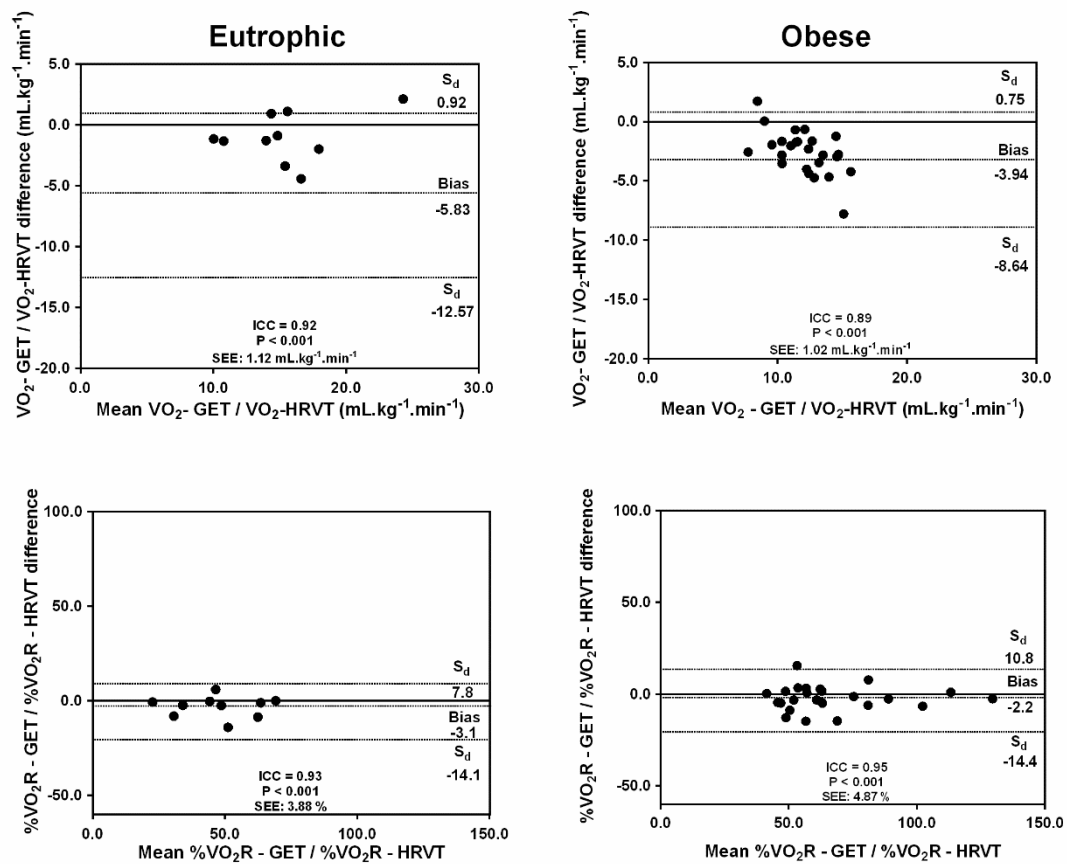


Figure 2. Bland-Altman plots, ICC and SEE between $\dot{V}O_2$ -GET vs. $\dot{V}O_2$ -HRVT and $\% \dot{V}O_2R$ -GET vs. $\% \dot{V}O_2R$ -HRVT in obese (n = 25; right side) and eutrophic (n = 10; left side) groups. ICC = intra-class correlation; SEE = standard errors of the estimate; $\dot{V}O_2$ = oxygen uptake; $\% \dot{V}O_2R$ = percentage of oxygen uptake reserve; GET = gas exchange threshold; HRVT = heart rate variability threshold.

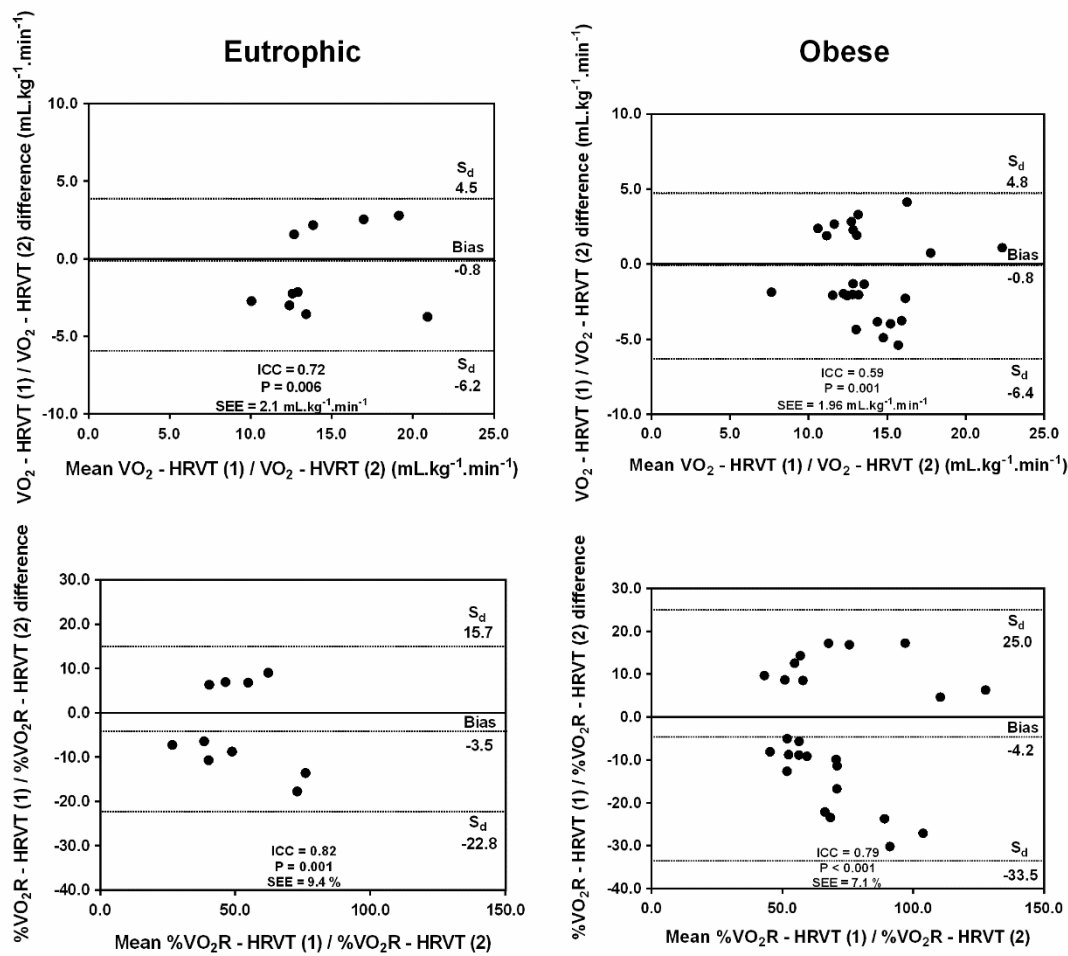


Figure 3. Bland-Altman plots and ICC for the test-retest reliability of $\dot{V}O_2$ -HRVT and $\% \dot{V}O_2R$ -HRVT in obese and eutrophic groups. ICC = intra-class correlation; $\dot{V}O_2$ = oxygen uptake; $\% \dot{V}O_2R$ = percentage of oxygen uptake reserve; GET = gas exchange threshold; HRVT = heart rate variability threshold.

DISCUSSION

The main purposes of this study were: (i) to compare the $\dot{V}O_2$, $\% \dot{V}O_2R$, HR, and power output assessed by the GET and HRVT methods, in obese and eutrophic adolescents during maximal CPET; and (ii) to verify whether the HRVT method would be useful to detect improvements in cardio-respiratory fitness in obese adolescents after a 3-month recreational soccer program. Additionally, the reproducibility and level of agreement in $\dot{V}O_2$ and $\% \dot{V}O_2R$ at the GET and HRVT

were calculated. The major findings were: (i) No significant difference was found between the GET and HRVT methods with regard to $\dot{V}O_2$, $\%\dot{V}O_2R$, HR, and power output; (ii) GET and HRVT methods were equally capable of detecting improvements in cardio-respiratory fitness in obese adolescents following a three months soccer intervention; and iii) in both obese and eutrophic groups, $\dot{V}O_2$ and $\%\dot{V}O_2R$ determined at the HRVT were strongly correlated and reproducible.

The use of the HRVT to detect vagal withdrawal during exercise and its relationship with the anaerobic threshold has been documented in healthy and unhealthy adults [137, 175, 194, 195, 197, 198, 202, 210, 211]. However, few studies have investigated this issue in overweight or obese children and adolescents [201-203]. Brunetto et al. [201] compared the $\dot{V}O_2$ obtained by the HRVT and GET during incremental exercise, using the SD1 method and non-linear Poincaré plots. The relative $\dot{V}O_2$ was shown to be lower at the GET in obese vs. eutrophic adolescents, but no difference between groups was detected when the GET was determined by means of HRVT. In the present study, both methods produced lower GET values in obese vs. eutrophic groups, which is theoretically consistent and somehow expected.

These controversial results could be explained by the fact that in the study by Brunetto et al. (12), the HRVT was determined using SD1 instead of rMSSD. The SD1 method has been previously applied to determine the HRVT in healthy adults [193-195, 212, 213], but not in obese adolescents. The SD1 method consists of a non-linear analysis of the HRV, providing information limited to width and length of Poincaré plots. In other words, this approach lacks temporal information, and it is well accepted that Poincaré plots of similar SD1 might have different underlying temporal dynamics [214]. Hence, the use of a time-domain marker of HRV, as the rMSSD seems to be more suitable than SD1 Poincaré plots to estimate variables that are influenced by temporal drifts, and such is the case for the GET along incremental exercise. Furthermore, as shown in Table 3, obese adolescents have higher HR values corresponding to GET and HRVT, due to chronic sympathetic overstimulation and increased catecholamine levels [173].

Another related issue concerns the gold-standard method adopted by previous studies to investigate the agreement between GET and HRVT. For instance, the present study has adopted the combined method (i.e. V-slope, ventilatory equivalents, and end-tidal gas tensions methods) proposed by Gaskill et al. [209] that seems to be more reliable than using any of these methods separately. Indeed, the findings of Gaskill et al. [209] showed that the combined method not only results in fewer rejected data but also improves the accuracy of the GET determination and greatly reduced the number of large errors when compared with individual methods of ventilatory threshold determination. With the exception of two previous studies [193, 194], most studies adopted individual methods to evaluate the ventilatory threshold [195-198, 203]. Therefore, it is not difficult to understand that such inherent error would have important practical consequences for the validity and reliability of HRVT method from the evaluation for determining the GET.

Paschoal and Fontana [202] compared the $\dot{V}O_2$ at the HRVT among pre-adolescents classified as eutrophic, and morbidly obese. The morbidly obese group exhibited the lowest $\dot{V}O_2$ at the HRVT, followed by obese and eutrophic pre-adolescents ($10.8 < 12.0 < 30.1 \text{ mL.kg}^{-1}.\text{min}^{-1}$, respectively). Quinart et al. [203] have demonstrated that GET determined by means of time-domain HRV analysis was able to detect an increase of 13.5% in power output at the HRVT, in obese adolescents after chronic aerobic training. Our findings concur with these previous studies, since the HRVT method proved to be capable of detecting differences between $\dot{V}O_2$, $\% \dot{V}O_{2R}$, HR, and power output at GET, when comparing obese vs. eutrophic adolescents. In addition, after three months of recreational soccer, improvements of approximately 30% in power output were detected in the obese group, while $\% \dot{V}O_{2R}$ at HRVT decreased by approximately 15%. These results might be considered as evidence that the HRVT method would be useful to assess and classify cardio-respiratory fitness in normal and overweight pre-adolescents, as well to ascertain gains due to chronic aerobic training.

The reproducibility and validity of the HRVT during exercise have been investigated in middle age and older adults. Guijt et al. [215] also have reported good to excellent test-retest reliability for rMSSD assessed during cycle ergometer exercise in healthy adults (mean ICC of 0.84). Albeit using a different HRVT approach (SD1 Poincaré Plots), sample (middle-aged and older adults), and exercise mode (incremental shuttle walk test), Dourado and Guerra [196] also reported good HRVT reliability (ICC = 0.82 to 0.96) when estimating GET. The present study provides original information, and probably the first to verify the reproducibility and agreement of $\dot{V}O_2$ and $\% \dot{V}O_2R$ at the GET obtained by the HRVT in obese and eutrophic adolescents. Good-to-excellent reliability was observed for rMSSD to detect HRVT (ICC values between 0.59 and 0.72; SEE between 1.96 and 2.1 mL.kg⁻¹.min⁻¹, for obese and eutrophic, respectively) during incremental CPET.

Limitations to the present study must be acknowledged. Firstly, there is some subjectivity when the anaerobic threshold is determined only by GET evaluation. Unfortunately, it was not possible to compare the GET obtained through the HRVT with a quantitative peripheral marker, like blood lactate assessment. Furthermore, the inclusion of a non-exercise control group of obese adolescents and an intervention group of normal weight adolescents would certainly improve the internal and external validity of this experimental trial. Additional research is therefore warranted to confirm our findings.

In conclusion, The HRVT method proved to be reliable to estimate both $\dot{V}O_2$ and $\dot{V}O_2R$. The GET and HRVT methods produced similar values in obese and eutrophic adolescents within maximal CPET. On the other hand, as expected, both the GET and HRVT produced higher $\% \dot{V}O_2R$ and HR values, and lower power output in obese vs. eutrophic adolescents. Finally, the HRVT and GET showed to be equally capable of detecting improvements in power output and $\dot{V}O_2R$ in obese adolescents after participation in a recreational soccer program. These findings provide original information and reinforce the usefulness of the HRVT to estimate exercise intensity when prescribing aerobic training for overweight or obese adolescent populations.

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Capítulo IV

Discussão

1. Discussão geral

O conjunto de estudos que constituem a presente dissertação procuraram analisar o efeito da prática regular de Futebol recreativo em variáveis metabólicas, hemodinâmicas, função endotelial, modulação autonômica cardíaca, composição corporal, biomarcadores e aptidão cardiorrespiratória em adolescentes obesos. Destacam-se como resultados mais relevantes o efeito positivo que a prática recreativa de Futebol parece ter em alguns fatores de risco cardiovascular de adolescentes obesos, como a melhoria na vasodilatação endotélio-dependente, redução na pressão arterial sistólica e dos componentes simpáticos da VFC, massa corporal, percentual de gordura, IMC, frequência cardíaca de repouso, proteína C reativa e do HOMA-IR, além de um aumento do componente parassimpático da VFC, e do VO_2 de pico após três meses de intervenção. Adicionalmente, também investigamos métodos mais acessíveis e de baixo custo para a avaliação da variabilidade da frequência cardíaca, assim como métodos de prescrição e controle de treino de fácil aplicação nesta população [107].

No que tange ao efeito de programas de atividade física sobre os diferentes componentes da composição corporal os resultados da literatura ainda são muito controversos [40]. Os diferentes métodos de avaliação da composição corporal e pontos de corte distintos para classificar o excesso de peso e a obesidade na infância e na adolescência têm contribuído para esta inconsistência [107]. A utilização do IMC como indicador de obesidade é igualmente uma das razões para esta ausência de consensualidade [59, 107]. No entanto, é importante ressaltar que estudos mais recentes, utilizando métodos mais fiáveis e sofisticados para avaliar a composição corporal (como por exemplo: absorciometria de dupla energia de raios-X – DXA), demonstraram, a exemplo deste estudo, uma diminuição significativa na massa gorda e no percentual de gordura após a participação em programas de atividade física [110, 111].

No presente estudo foi igualmente identificada uma diminuição significativa dos valores da pressão arterial sistólica após 12 semana de treino de Futebol. Embora estes resultados sejam concordantes com os observados em pesquisas anteriores [216, 217] a magnitude da diminuição após a prática recreativa de Futebol foi superior à verificada em outros programas de atividade física (corrida ou ciclismo) [84, 93, 96]. Este resultado pode ser justificado pelo fato de o Futebol ser um desporto intermitente [45], que exige dos seus participantes uma alternância de esforços de alta intensidade com outros de intensidade mais baixa [218]. A diminuição da pressão arterial sistólica pode ainda ser explicada pelas alterações que se verificaram na variabilidade da frequência cardíaca, uma vez que a prática de Futebol diminuiu a atividade simpática e aumentou a atividade parassimpática. Em conjunto, a diminuição da pressão arterial sistólica combinada com este impacto na variabilidade da frequência cardíaca refletem uma melhoria na função autonômica cardíaca, o que pode ser considerado como um efeito cardioprotetor do programa de Futebol recreativo [141]. Em nossa opinião esta é uma das contribuições importantes desta dissertação, pois a variabilidade da frequência cardíaca reflete as mudanças batimento a batimento da frequência cardíaca, expressando a interação simpato-vagal obtida pela variação do ciclo cardíaco [178]. O comprometimento da variabilidade da frequência cardíaca pode ser explicado por uma menor atividade parassimpática ou por uma maior atividade simpática, e tem sido associada ao desenvolvimento de algumas patologias, nomeadamente a hipertensão [157, 158], a síndrome metabólica [151], os acidentes vasculares cerebrais [152], a fadiga crônica [153], e a obesidade [155, 156]. Outro aspeto a salientar prende-se com o fato de até ao momento, e tanto quanto julgamos saber, nenhum outro estudo mostrou alterações positivas na variabilidade da frequência cardíaca de adolescentes obesos submetidos a programas de atividade física, especialmente com Futebol.

Na literatura consultada não existe unanimidade relativamente ao efeito de programas de atividade física na aptidão cardiorrespiratória de adolescentes obesos [83, 101]. Uma das possíveis razões para esta inconsistência poderá ter a ver com as metodologias que têm sido utilizadas para avaliar a aptidão cardiorrespiratória [101, 219]. Na generalidade dos estudos esta aptidão é

avaliada recorrendo a testes submáximos, não permitindo por isso o contraste dos resultados com os obtidos em testes máximos. Para além deste aspeto é igualmente importante referir que a generalidade dos estudos que procuraram avaliar a eficácia de programas de atividade física na aptidão cardiorrespiratória em adolescentes obesos, adotaram, em sua maioria, atividades monótonas e repetitivas (por exemplo, exercícios na esteira ou no cicloergômetro) [83]. São escassas as pesquisas que utilizaram atividades motivadoras e variadas (por exemplo os jogos desportivos coletivos) [121]. Faude et al investigaram o efeito de um programa de Futebol recreativo em crianças (8 a 12 anos de idade; 3 vezes por semana durante 6 meses) com excesso de peso e obesidade não tendo registado um aumento significativo no VO_2 pico [7]. Contrapondo os resultados encontrados por Faude e colaboradores, a presente dissertação demonstrou que houve um aumento significativo no VO_2 de pico de adolescentes obesos, após um programa de intervenção de Futebol recreativo com três meses de duração. O que pode explicar a diferença dos resultados encontrados entre as duas pesquisas é a metodologia adotada. Enquanto no estudo de Faude et al. as sessões de treino consistiam em: aquecimento (10% do tempo total), jogos reduzidos (50% do tempo total), exercícios técnicos (20% do tempo total), e treino de deslocamento com bola (20 % do tempo total), na presente pesquisa, o programa teve mais tempo dedicado aos jogos reduzidos (70% do tempo total), e consequentemente os praticantes estiveram mais tempo a realizar atividade de moderada a alta intensidade [220], o que pode explicar a melhoria no pico de VO_2 destes sujeitos.

A presente dissertação teve igualmente como propósito estudar o impacto do Futebol recreativo no perfil lipídico, na proteína C-reativa, na glicemia de jejum, na insulina e no índice HOMA-IR. Alguns estudos recentes demonstraram a importância da atividade física na melhoria dos valores da lipoproteína de alta densidade (HDL colesterol), da insulina e da glicose [38, 84, 96]. No entanto, o aumento nos níveis de HDL foi maior na presente dissertação do que quando comparado ao efeito de programas de atividade física mais tradicionais [87, 96]. O que pode ser compreendido por ser um esporte de moderada a alta intensidade e que devido ao seu carácter recreativo promove nos praticantes uma

sensação de menor esforço [50], enquanto que programas de atividade aeróbica quando realizados em intensidades semelhantes são mais fatigantes e monótonos [38, 45].

No presente estudo foi possível perceber uma redução significativa nos níveis de proteína C-reativa e HOMA-IR em adolescentes obesos. Estes biomarcadores são particularmente importantes, pois traduzem um estado pró inflamatório e estão geralmente aumentados em adolescentes obesos. Estudos anteriores utilizando programas de treino aeróbico de moderada a alta intensidade encontraram diminuições semelhantes na proteína C-reativa [88]. O fato da intervenção realizada ter sido baseada na prática de Futebol recreativo através da realização de jogos reduzidos, parece ter contribuído para este resultado, pois como referido anteriormente, os jogos reduzidos são caracterizados por ações intermitentes de elevada intensidade [218]. Por outro lado, estudos que recorreram a programas de atividade física de baixa intensidade não tiveram o mesmo sucesso no que diz respeito a redução dos níveis de proteína C-reativa. [84, 85]. Este achado é de extrema importância para a saúde de adolescentes obesos. A proteína C-reativa é um forte indicador do início de um processo inflamatório crônico, e devido ao fato do Futebol ser uma atividade lúdica e motivadora, pode ser mais fácil sensibilizar os adolescentes obesos a realizarem atividades de alta intensidade por meio da prática de esportes de equipe como o Futebol.

Ainda neste contexto, vale ressaltar que a redução nos níveis de HOMA-IR está frequentemente associada à prática regular de atividade física [87] nomeadamente ao treino aeróbico [96]. Embora se exija a realização de novas pesquisas, os resultados encontrados permitem perceber que a resistência à insulina em adolescentes obesos pode ser melhorada através da participação em programas de Futebol recreativo.

A função endotelial está igualmente comprometida em adolescentes com excesso de peso e obesidade [117]. São escassos os estudos localizados na literatura que reportem benefício de programas de atividade física sobre a saúde do endotélio em adolescentes obesos [81, 84, 97]. Este efeito benéfico da

atividade física na função vascular, poderá ser resultado de um aumento da biodisponibilidade de óxido nítrico resultante da tensão de cisalhamento durante a atividade [120]. Os resultados da presente dissertação são consistentes com a literatura demonstrando que os adolescentes que participaram neste programa melhoraram os valores de condutância vascular pós a isquemia e diminuíram a resistência vascular, ao passo que após ser provocada uma vasodilatação endotélio independente com nitroprussiato a alteração não foi significativa. Demonstrando assim, que o programa de Futebol recreativo promoveu um efeito benéfico no endotélio e não no vaso sanguíneo. Estes resultados sugerem que a disfunção endotelial frequentemente observada em adolescentes obesos [221], foi, pelo menos em parte, neutralizada pela participação neste programa. O fato de não ter havido melhoria na função endotelial com a utilização do nitroprussiato após o programa de Futebol recreativo, indica que provavelmente as paredes externas dos vasos sanguíneos ainda eram saudáveis em nossa coorte de adolescentes obesos [138]. Tanto quanto julgamos saber, este foi provavelmente um dos primeiros trabalhos a investigar os efeitos de um programa de Futebol recreativo na função endotelial em adolescentes obesos, sendo por isso difícil contrastar os seus resultados com outras pesquisas. Os estudos que conseguimos localizar mostraram que o exercício aeróbio pode melhorar a função endotelial em crianças e adolescentes que estavam com excesso de peso ou obesos [81, 222]. Contudo, estes estudos aplicaram programas de exercício individualizados, como correr, andar de bicicleta, ou treinamento em circuito, o que pode em certa medida ser menos motivador para adolescentes quando comparados com os esportes de equipe [9].

A presente dissertação teve ainda como propósito investigar fidedignidade e reprodutibilidade de novos métodos de controle e prescrição do exercício físico para adolescentes obesos. Tem sido uma preocupação constante a determinação da capacidade aeróbia máxima ($VO_2\text{max}$) para esta população. Porém como se sabe, crianças e adolescentes com excesso do peso e obesidade são mais propensas a evidenciar um inferior $VO_2\text{max}$, devido à fadiga periférica relacionada com a necessidade de mover um corpo maior e mais pesado durante o exercício [189]. Além disso, novos métodos foram criados para

controlar e prescrever a atividade física com um custo mais baixo em comparação com os métodos utilizados convencionalmente (por exemplo, limiar de lactato ou limiar ventilatório). Estudos recentes, utilizando a variabilidade da frequência cardíaca tanto no domínio do tempo como no da frequência têm sido propostos com base na ocorrência de um limiar de variabilidade da frequência cardíaca (LiVFC) que pode ser correlacionado com o ventilatório (VT) determinado pela análise de gases e o limiar de lactato (LT) determinado pelo sangue [204]. Essas evidências sugerem que LiVFC poderia ser uma ferramenta confiável e simples [162, 223]. Na verdade, o LiVFC foi sugerido para ser uma ferramenta útil e apropriada para quantificar as melhorias induzidas por sessões de exercícios crônicos no desempenho físico [197].

No entanto até ao momento não existia nenhum estudo que tivesse verificado a concordância e a reprodutibilidade da variabilidade da frequência (VFC) cardíaca avaliada por diferentes métodos em adolescentes obesos. Estudos anteriores demonstraram associações positivas entre os índices de VFC avaliados pelo eletrocardiograma (ECG) e os obtidos a partir de monitores cardíacos [163, 164], ou entre ECG e fotoplestímetro (PPG) [88, 165]. Para além disso, estas pesquisas concluem que a concordância das variáveis da VFC pode ser dependente das características da população avaliada. Por exemplo, Wallen et al. (2012) compararam a VFC avaliada por ECG e Polar RS800CX, e foi observado uma boa concordância entre os homens jovens, mas não em mulheres com mais de 45 anos de idade [169]. Do ponto de vista prático, estes autores concluem que o Polar RS800CX, apesar de ser um instrumento mais acessível, pode não ser o instrumento mais adequado para a avaliação de VFC em diferentes populações.

A maioria dos estudos que investigaram a concordância e confiabilidade das diferentes técnicas para medir a VFC foi realizado em adultos saudáveis [164, 171]. Na literatura e particularmente em adolescentes obesos são escassas as pesquisas sobre a concordância e reprodutibilidade dos índices de VFC avaliados por diferentes técnicas. Levando-se em conta a relevância clínica da avaliação da VFC em populações com risco potencial para a função autonômica cardíaca desequilibrada (ou seja, redução da atividade parassimpática e

aumento da atividade simpática) [223], uma descoberta relevante desta pesquisa foi que os índices de VFC derivadas Polar RS800CX e PPG quando comparados com o sinal de ECG tinham níveis de concordância considerados de moderado a excelentes.

Em relação à reprodutibilidade das variáveis da VFC, nenhum outro estudo havia analisado esta população. Os presentes resultados de reprodutibilidade, tanto para o Polar RS800cx como o PPG, estão de acordo com os resultados obtidos no ECG e com o estudo de Pinna et al. (2007) que em adultos saudáveis, encontraram os mesmos níveis de reprodutibilidade para todos os aparelhos [179]. Nesse sentido, pode-se assumir que os dois equipamentos (Polar RS800cx e PPG) são tão confiáveis quanto o ECG para a avaliação da VFC nesta população.

A validação de um instrumento acessível para avaliação da VFC como é o caso do Polar permitiu avançar no conhecimento de aplicações práticas para controle e prescrição de treino através deste método. Tem sido demonstrado que as crianças e adolescentes obesos são mais propensas a ter uma menor capacidade aeróbica (VO_{2max}) [189, 224]. Além disso, a maior capacidade aeróbica parece ter um efeito protetor independente sobre o risco de desenvolver doença cardiovascular, ou seja, quanto mais apto for o indivíduo menor a chance de desenvolver doença cardiovascular [225]. Em outras palavras, os indivíduos obesos que estão aptos têm menor risco de desenvolver doença cardiovascular em comparação com aqueles com menor capacidade aeróbica, o que tem sido referido como o paradigma do "gordo, porém apto" [190]. Desta maneira parece ser importante, devido à dificuldade desta população em realizar teste máximo para avaliação do VO_{2max} , encontrar meios de avaliar, controlar e prescrever o treino baseado em métodos submáximos [38]. Neste sentido, até o momento não tinha sido encontrado na literatura estudos anteriores investigando a concordância entre limiar anaeróbio determinado pelo método ventilatório e o método do LiVFC e em adolescentes obesos e com sobrepeso. Isso seria importante, já que a disfunção autonômica cardíaca precoce tem sido relatada em crianças que são obesas [162, 204].

Desta forma, a presente dissertação investigou a concordância e reprodutibilidade do limiar de variabilidade da frequência cardíaca (LiVFC – Polar RS800cx) em adolescentes obesos e não obesos. Além disso, verificou se o método LiVFC é sensível para detectar alterações na aptidão física em adolescentes obesos inscritos no programa de Futebol recreativo. Os resultados encontrados não permitiram encontrar diferenças significativas entre os adolescentes obesos e não obesos nas diferentes variáveis da VFC em repouso, frequência cardíaca de pico e potência de pico. No entanto, os adolescentes obesos revelaram um consumo de oxigênio de pico mais baixo que os não obesos. Não foram igualmente encontradas diferenças significativas entre os métodos de limiar ventilatório e LiVFC em relação ao VO_2 , VO_2 de reserva, frequência cardíaca e potência no limiar anaeróbio. Tanto os métodos de limiar ventilatório como o LiVFC foram adequados para detectar maiores valores de consumo de oxigênio e frequência cardíaca no grupo de obesos que praticou Futebol recreativo, quando comparado com o grupo que não praticou. Contudo, o método LiVFC parece ser adequado para detectar as melhorias da aptidão física após três meses de programa de Futebol recreativo em adolescentes obesos.

Capítulo V

Conclusões

1. Conclusões

Com base nas conclusões gerais de cada um dos estudos que constituem esta dissertação, é possível apresentar as seguintes conclusões:

- Apesar da diversidade de delineamentos de pesquisa, dimensões amostrais, metodologias e programas de intervenção analisados pelos estudos revisados nesta dissertação, foram detectadas tendências importantes sobre os efeitos dos programas de atividade física para o tratamento e prevenção do excesso de peso e obesidade em uma idade precoce. Intervenções incluindo programas de atividade física são muito propensos a induzir adaptações favoráveis na composição corporal e aptidão física de adolescentes com excesso de peso e obesidade. Mesmo que as evidências neste sentido permaneçam inconclusivas, nossos resultados sugerem que os programas de atividade física também podem melhorar variáveis bioquímicas, marcadores inflamatórios e função endotelial nesta população.
- Uma intervenção de Futebol recreativo de 12 semanas foi capaz de melhorar marcadores de saúde de adolescentes obesos. Efeitos favoráveis foram observados na massa corporal e nos constituintes da composição corporal, pressão arterial, atividade autonômica cardíaca, aptidão física, marcadores bioquímicos e função endotelial. Estes resultados reforçam a importância da prática de esportes para adolescentes com sobrepeso e obesidade.
- A avaliação da VFC de curto prazo obtidos a partir Polar RS800CX e do fotoplestímetro parece ser um método preciso para avaliar o controle autonômico da frequência cardíaca de adolescentes obesos em repouso, indicando níveis de concordância significativa com ECG. Assim como, a confiabilidade teste-reteste de ambos Polar RS800CX e fotoplestímetro mostrou-se muito similar a reprodutibilidade do ECG.
- Os achados reforçam a utilidade do método LiVFC na prática diária da reabilitação e programas de perda de peso para população de jovens obesos. Sendo assim, o método é considerado fiável e também sensível as alterações provocadas por um programa de três meses de Futebol recreativo.

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