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JOÃO CARLOS LOCATELI

EFEITOS DO EXERCÍCIO INTERVALADO DE ALTA INTENSIDADE E DO EXERCÍCIO CONTÍNUO DE INTENSIDADE MODERADA SOBRE A FUNÇÃO VENTRICULAR ESQUERDA E DEFORMAÇÃO MIOCÁRDICA EM MULHERES OBESAS

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Prof. Dr. **Wendell Arthur Lopes**
(Orientador)

Anche ad essere si impara.”

Italo Calvino

DEDICATÓRIA

Dedico essa dissertação à minha família, cujo valores e princípios ensinados foram imprescindíveis na minha formação pessoal, me proporcionando também o aporte necessário para a conclusão dessa etapa importante de minha trajetória profissional. Dedico essa dissertação ao esforço de meus pais, que forneceram todas as condições possíveis para que eu seguisse meu sonho, abdicando muitas vezes de seus próprios objetivos. Com certeza passarei para frente essa lição de carinho, bondade e amor que vocês tão espontaneamente me transmitiram.

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RESUMO

Introdução: A obesidade é uma doença crônica não transmissível caracterizada pelo acúmulo excessivo de tecido adiposo. Sua alta e crescente prevalência desperta a preocupação dos principais órgãos de saúde mundial, que preconizam que medidas para o combate dessa pandemia devem ser tomadas em caráter emergencial. Estima-se que o excesso de peso afeta 1,9 bilhões de pessoas, sendo que destas, 603,7 milhões já apresentam índice de massa corporal (IMC) correspondente à obesidade. Além disso, a obesidade é considerada um fator de risco para o desenvolvimento de doenças cardiovasculares (DCVs), que estão intimamente associadas a disfunção do ventrículo esquerdo (VE). A função do VE é avaliada por meio da fração de ejeção (FE), técnica essa ainda muito difundida na cardiologia. No entanto, a avaliação da FE apresenta limitações quanto a sua sensibilidade em identificar alterações cardíacas subclínicas. Dessa forma, uma nova técnica tem emergido como uma alternativa para a avaliação da função ventricular. O *strain* longitudinal global (SLG) tem se mostrado superior na predição de eventos cardíacos em indivíduos assintomáticos, que ainda apresentam FE preservada. Por meio da técnica *speckle-tracking*, padrões no tecido do miocárdio são rastreados, sendo o *strain* caracterizado como a média relativa de deformação entre dois pontos ao longo das direções pré-definidas relativas aos valores normativos de deformação miocárdica. Os efeitos provenientes da prática de exercício físico na prevenção e tratamento de DCVs têm sido exaustivamente estudados na literatura. É consenso o papel benéfico do mesmo na diminuição da chance de desenvolvimento de eventos cardíacos. No entanto, ainda falta esclarecimento acerca dos efeitos de diferentes modalidades de exercício no sistema cardiovascular sobre a deformação miocárdica. Evidências sugerem que a obesidade exerce um impacto negativo na função cardíaca, apresentando também alteração na deformação miocárdica, sendo que indivíduos obesos são mais expostos ao desenvolvimento de comorbidades cardiovasculares em comparação aos seus pares eutróficos, no qual o SLG pode se destacar como um marcador subclínico nessa população. Sendo assim, os objetivos da presente dissertação foram: i) revisar os efeitos de diferentes modalidades de exercício físico sobre a deformação miocárdica em indivíduos saudáveis e com doenças crônicas; e ii) verificar os efeitos agudos do HIIT e do MICT sobre a função ventricular esquerda e deformação miocárdica em mulheres obesas.

Métodos: Para a consecução da dissertação, foram realizados dois delineamentos de pesquisa, uma revisão sistemática com meta-análise e uma pesquisa experimental com design crossover. A revisão sistemática com meta-análise teve como estratégia de pesquisa a busca por artigos originais publicados em periódicos indexados nas bases de dados eletrônicas *Pubmed/Medline, Web of Science, Cochrane, Lilacs e Scielo* sobre os efeitos do treinamento físico sobre a função do VE pela avaliação do SLG em indivíduos saudáveis e com doenças crônicas. Para a meta-análise, os dados foram inseridos em um *software* apropriado para a agrupamento dos resultados dos estudos incluídos na meta-análise. Foi utilizado a diferença média estandardizada, com intervalo de confiança de 95% para a determinação do tamanho de efeito. O modelo de efeitos randômicos foi aplicado com o objetivo de minimizar a influência da heterogeneidade dos estudos incluídos. Também foram conduzidas análises de sensibilidade

examinando os individuais de cada estudo no resultado final da meta-análise. Ademais, foram realizadas análises de subgrupos. O nível de significância estabelecido foi p≤0.05.
Para o delineamento experimental de design *crossover*, compuseram a amostra 15 mulheres, com idade entre 18 e 35 anos e diagnosticadas com obesidade grau I (IMC entre 30 e 40 kg/m^2). As participantes foram submetidas a três protocolos experimentais distintos, sendo um protocolo de exercício intervalado de alta intensidade (HIIT), um de exercício contínuo de intensidade moderada (MICT) e controle (GC). Medidas antropométricas, de composição corporal e de espessura médio-íntimal da carótida foram coletadas com a finalidade de caracterização da amostra do estudo. As variáveis relacionadas à função ventricular esquerda, assim como de deformação miocárdica foram coletados imediatamente antes e depois de cinco (t5) e 35 min (t35) após a realização de cada protocolo experimental. O tamanho da amostra foi calculado atráves do *software* específico G Power® 3.1. As variáveis contínuas são apresentadas em média e desvio-padrão. A comparação entre as condições e momentos foi feita por meio da ANOVA para medidas repetidas, seguido do teste de comparações múltiplas de Sidak. Utilizou-se o *software* SPSS, versão 23 e o nível de significância adotado foi p≤0.05.
Resultados: Vinte e seis estudos compuseram a revisão sistemática, em que 18 estudos com 1288 indivíduos foram incluídos na meta-análise. A análise de efeitos aleatórios mostrou que o exercício aeróbico melhorou o GLS (SMD -0,33 [IC 95%, -0,56 a -0,10], p = 0,007, I^2 = 63%) em comparação ao GC. O HIIT foi superior ao MICT na melhora do GLS (SMD -0,25 [IC 95%, -0,48 a - 0,02], p = 0,04, I^2 = 23,4%) e FEVE (SMD 0,76 [IC 95%, 0,22 a 1,30], p = 0,006, I = 69%). O treinamento resistido realizado isoladamente ou combinado com o treinamento aeróbico não mudou significativamente o GLS nem a FEVE. Observou-se no artigo original uma interação significativa para as variáveis onda E (p = 0,019), onda A (p = 0,050), relação E/A (p = 0,006) e E 'septal (p = 0,032). Foi observado um declínio significativo na onda E em t5 após as condições HIIT (p = 0,003) e MICT (p = 0,049), assim como o HIIT mostrou uma redução significativa em relação à linha de base. O SLG apresentou efeito de grupo, no qual a condição controle diferiu da condição HIIT em t5 (p = 0,010), sendo o mesmo reduzido após o HIIT nesse tempo.
Conclusão: Com a revisão sistemática com meta-análise constatou-se que o exercício aeróbico promove alterações salutares na deformação miocárdica, representadas pelo GLS, nas quais o HIIT pareceu apresentar efeitos superiores no GLS e na FEVE em comparação com o MICT, tanto para indivíduos saudáveis quanto para pacientes crônicos. O artigo original revela que de forma aguda foi verificada alteração na função sistólica, diastólica e deformação miocárdica após o HIIT, entretanto, tais mudanças são rapidamente reestabelecidas aos valores de *baseline*, indicando mudanças transientes na função cardíaca e deformação miocárdica induzida pelo HIIT em mulheres obesas.

Palavras-Chave: Strain longitudinal global. Deformação miocárdica. Função do ventrículo esquerdo. Exercício físico. Obesidade. Mulheres.

LOCATELI, João Carlos. **EFFECTS OF HIGH-INTENSITY INTERVAL TRAINING VERSUS MODERATE INTENSITY CONTINUOUS TRAINING LEFT VENTRICULAR FUNCTION AND PARAMETERS OF MYOCARDIAL DEFORMATION IN OBESE WOMEN**. 2019. 122f. Dissertation (Masters in Physical Education) – Health Sciences Center. State University of Maringa, Maringá, 2019.

ABSTRACT

Introduction: The obesity is a non-communicable chronic disease defined by the excessive accumulation of fat tissue. Its high and increasing prevalence is object of concern of the major health organizations worldwide. These organizations are nowadays spreading the importance of tacking this disease in an urgent matter. It is estimated that the weight excess affects approximately 1.9 billion people, in which 603.7 million of these already present high levels of body mass index (BMI) indicating obesity. Moreover, the obesity is a risk factor for the development of cardiovascular diseases (CVD), in which the latter is narrowly related to left ventricle (LV) dysfunctions. The LV function is assessed by the ejection fraction (EF), a still widespread technique in cardiology. However, the evaluation of the EF present several limitations in terms of its ability to identify subclinical alterations. Therefore, a new technique is arising for the assessment of LV function as well as myocardial deformation. The global longitudinal strain (GLS) has showed a superior predictive capacity of cardiac events in asymptomatic patients, even when the individuals have a preserved EF. The positive effects of physical exercise on cardiovascular system has been widely explored on literature. It is already well known that the regular practice of physical exercise diminished the risk of the development of CVD. Nevertheless, there is still a lack of consensus as regards to the effect of different exercise modalities in the cardiovascular system, more specifically in the parameters related to myocardial deformation and LV function. Considering that the obese individuals are more exposed to the risk of CVD development than its normal-weight counterparts, it is imperative to study this phenomenon in this specific population. Thus, the aim of the present study was to verify the effects of different modalities of physical exercise (high-intensity interval training vs. moderate-intensity continuous training) on the LV ventricular function and myocardial deformation in obese women.

Methods: To achieve the dissertation requirements, two study designs were performed. The systematic review with meta-analysis had as search strategy the search for original articles published in journals indexed in the electronic databases Pubmed / Medline, Web of Science, Cochrane, Lilacs and Scielo on the effects of physical training on LV function by the evaluation of GLS in healthy and chronically diseased individuals. For the meta-analysis, data were inserted in an appropriate software, in which data were presented in standardized mean differences (SMD). The random-model effects was used in order to minimize the influences of heterogeneity from the included studies. Forest plots were created to quantify the effect of different exercise modalities vs. control group. Additionally, subgroup analyses were performed regarding the effects of age, pathologies, exercise intensity and volume on the main outcome. The original article aimed to verify the acute effects of different modalities of aerobic exercise (HIIT and MICT) on cardiac function in obese women. Fifteen women aged between 18 and 35 years and at bodu mass index levels indicating obesity composed the sample of the present study, which had an experimental crossover design. The participants underwent three different experimental conditions. In a randomized order, all participants have performed a high-intensity interval training (HIIT), a moderate-intensity continuous training (MICT), and a control condition (CG). Anthropometric, body composition, and intima-media carotid thickness measurements were obtained for the purpose of sample characterization. The LV function-related and myocardial deformation variables were collected at baseline and five (t5), 35 (t35), and 65 minutes (t65) after the performance of each experimental protocol. All measurements were performed according to previously validated assessment protocols. Data were expressed as mean with standard deviation. Comparisons between groups and times were made via ANOVA two-way for repeated measures, followed by the Sidak multiple comparisons tests. Data were analysed using the SPSS, version 23.

Results: Twenty-six studies comprised the systematic review, in which 18 studies with 1288 subjects were included in the meta-analysis. Random effects analysis showed that aerobic exercise improved GLS (SMD -0.33 [95% CI, -0.56 to -0.10], p = 0.005, I^2 = 14%) compared to CG. HIIT was superior to MICT in the improvement of GLS (SMD -0.25 [95% CI, -0.48 to-0.02], p = 0.04, I^2 = 23.4%) and LVEF (SMD 0,76 [95% CI, 0.22 to 1.30], p = 0.006, I = 69%). Resistance training performed alone or in combination with aerobic training did not change significantly in GLS or LVEF. A significant interaction was observed in the original article for the variables E wave (p = 0.019), A wave (p = 0.050), E / A ratio (p = 0.006) and E 'septal (p = 0.032). A significant decline in E wave at t5 was observed after HIIT (p = 0.003) and MICT (p = 0.049) conditions, as well as HIIT showed a significant reduction from baseline. The SLG presented group effect, in which the control condition differed from the HIIT condition in t5 (p = 0.010) and t65 (p = 0.019).

Conclusion: The systematic review with meta-analysis showed that aerobic exercise promotes salutary changes in LV systolic function, represented by GLS, in which HIIT appeared to have superior effects on GLS and LVEF compared to MICT for healthy individuals as well as for chronic patients. The original article revealed that HIIT had an acute transient negative effect on diastolic and systolic function, with a significant worsening in GLS after this exercise modality. However, these effects are rapidly cessed and values returned to baseline conditions at t35. Hence, HIIT promoted no negative effects on cardiac function in obese women. However, further studies are needed to better elucidate the effects of different aerobic exercise modalities on LV function.

Keywords: Global longitudinal strain. Myocardial deformation. Left ventricle function. Physical exercise. Obesity. Women.

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LISTA DE SIGLAS E ABREVIATURAS

A	Velocidade Diastólica Tardia
AO	Artéria Aorta
CC	Circunferência de Cintura
DC	Debito Cardíaco
DCV'S	Doenças Cardiovasculares
E	Velocidade Diastólica Inicial
EMI	Espessura Médio-Intimal
EST	Estatura
FC	Frequência Cardíaca
FE	Fração de Ejeção
GC	Grupo Controle
GHIIT	Grupo Treinamento Intervalado de Alta Intensidade
GMICT	Grupo Treinamento Contínuo de Intensidade Moderada
GPHARV	Grupo de Pesquisa em Hipertensão Arterial Sistêmica, Rigidez Arterial e Envelhecimento Vascular
HUM	Hospital Universitário de Maringá
IMC	Índice de Massa Corporal
MC	Massa Corporal
NPC	Núcleo de Pesquisa Clínica
OMS	Organização Mundial da Saúde
SLG	Strain Longitudinal Global
TCLE	Termo de Consentimento Livre e Esclarecido
UEL	Universidade Estadual de Londrina
UEM	Universidade Estadual de Maringá
VDF	Volume Diastólico Final
VE	Ventrículo Esquerdo
VSF	Volume Sistólico Final

SUMÁRIO

1 INTRODUÇÃO

Caracterizada pelo acúmulo excessivo de tecido adiposo, causado principalmente pelo desbalanço energético entre um alto consumo de calorias e um baixo dispêndio energético, a obesidade é considerada um dos principais fatores de risco para o desenvolvimento de doenças crônicas não transmissíveis, tais como diabetes do tipo II, hipertensão arterial, dislipidemias, certos tipos de cânceres e doenças cardiovasculares (DCVs). Tornando-se, dessa forma, motivo de preocupação substancial dos principais órgãos de saúde pública mundiais (OMS, 2018). Estima-se que a obesidade quase triplicou nas últimas décadas, atingindo alarmantes taxas de prevalência. Evidências recentes mostram que 1,9 bilhões de pessoas apresentam índice de massa corporal (IMC) em níveis que indicam sobrepeso, enquanto que 603,7 milhões de pessoas já foram diagnosticas com obesidade (OMS, 2018; Abarca-Gómez et al., 2017). No Brasil, dados epidemiológicos apontam que mais da metade da população (54%) tem excesso de peso, sendo que desses, 18,9% são obesos. Além disso, um alto índice de excesso de peso também foi encontrado nas mulheres, no qual 51,2% apresentaram sobrepeso, e destas, 16,7% apresentaram obesidade (VIGITEL, 2017). Além disso, embora os homens serem mais suscetíveis a doenças cardiovasculares, as mulheres apresentam maior risco de doenças relacionadas à inflamação, assim como redução na qualidade de vida em decorrência da obesidade (CRIMMINS et al., 2019; CHOO et al., 2014).

Já está bem estabelecida na literatura a relação entre obesidade e DCVs, sendo a obesidade relacionada ao desenvolvimento de doenças como aterosclerose, doença arterial coronariana, insuficiência cardíaca, e fibrilação atrial (MANDVIWALA et al., 2016). A influência da obesidade no aumento do risco de DCVs se dá pelo desenvolvimento ou agravamento de algumas comorbidades associadas, sendo elas hipertensão arterial, dislipidemia e diabetes tipo II. Considerando o aumento da prevalência de obesidade, juntamente com a grande prevalência de morbimortalidade advinda de eventos cardíacos, essa relação tem sido vista com ainda mais atenção (KOLIAKI et al., 2018).

As DCVs são a principal causa de morte em âmbito global (ROGER et al., 2012). Aproximadamente 173 milhões de pessoas morrem a cada ano em decorrência de doenças no sistema cardiovascular. Esse cenário já preocupante tende a piorar com a projeção de que cerca de 23,4 milhões de mortes serão causadas pelas DCVs no ano de 2030 (OMS, 2011). De acordo com a *American Heart Association*, a taxa de mortalidade das DCVs é maior do que quando comparada as mortalidades em decorrência de câncer e doenças respiratórias juntas (AHA, 2017). Não obstante, parece haver uma intrínseca relação entre as DCVs e alterações na função do ventrículo esquerdo (VE) (ARTHAM, 2009). Disfunções no VE, tais como sua hipertrofia e alterações na sua geometria estão associadas a um elevado risco de morbimortalidade em decorrências de DCVs (COHN, 2013).

A avaliação não-invasiva da função ventricular por meio da fração de ejeção (FE) é uma técnica ainda muito difundida na cardiologia (POTTER et al., 2018), sendo um parâmetro muito utilizado não somente para a avaliação, mas também para a identificação de disfunções relacionadas ao ventrículo durante a sístole, no qual uma redução no seu valor está diretamente associada a uma vasta gama de doenças cardiovasculares (KELLY & STRUTHERS, 1999), tendo uma ampla importância clínica na predição de acidente vascular cerebral e mortalidade em pacientes com insuficiência cardíaca congestiva (DI TULIO et al., 2016). Evidências científicas reportam que um decréscimo de 10% na FE corresponde a um aumento significativo na chance de desenvolvimento de insuficiência cardíaca, eventos cardiovasculares e mortalidade derivada de todas as causas (YEBOAH et al., 2012). Ademais, a FE do VE é usada para a definição e conseguinte prescrição de medicamentos assim como tratamentos para DCVs (RAHIMI et al., 2014).

No entanto, apesar do seu amplo uso, a avaliação da função ventricular sistólica apresenta algumas limitações. Primeiramente, a FE pode apresentar valores normais mesmo com a presença de disfunção ventricular. Isso ocorre por efeito da hipertrofia do ventrículo e consequente diminuição do tamanho da cavidade, resultando em uma diminuição do volume sistólico apesar de uma FE preservada (POTTER & MARWICK, 2018). Além disso, o método de imagem mais utilizado para a obtenção da FE apresenta algumas limitações relativas ao traçado da cavidade do VE e a conjectura de sua geometria. Outrossim, existiu por muito tempo uma incerteza no que diz respeito às potenciais influências que a pré- e pós-carga poderiam causar nos valores referentes à FE. Assim, sua interpretação como um índice de contratilidade é inacurada quando feita sem o conhecimento prévio das cargas do VE nos períodos de sístole e diástole (KONSTAM & ABBOUD, 2017).

Recentemente, uma nova técnica de mensuração da função do VE emergiu como uma alternativa ao método tradicional de avaliação de FE (KRISHNASAMY et al., 2014). Mensurado por meio do rastreamento de marcadores naturais do miocárdio (*speckle tracking)*, o *strain* longitudinal global (SLG) tem se tornado um método útil para a avaliação da função ventricular na prática clínica (ALCIDI et al., 2017). A técnica consiste na detecção de padrões de interferência gerados pela interação entre o feixe do ultrassom com o miocárdio, possibilitando o rastreamento de sua deformação tanto na sístole quanto na diástole (SINGH et al., 2009). Em termos gerais, o termo *strain* é definido pela deformação causada pela aplicação de força, sendo o *strain* miocárdico a mudança expressa em porcentagem da deformação do comprimento do miocárdio do momento de relaxamento até o estado contrátil (AMZULESCU et al., 2019; GOODMAN et al., 2009). O SLG tem se mostrado um preditor superior de eventos cardíacos assim como de mortalidade geral quando comparado à FE em indivíduos saudáveis (STANTON et al., 2019). Tal superioridade pode ser justificada pela maior sensibilidade do SLG em detrimento à FE para a detecção de mudanças subclínicas (SMISETH et al., 2015). Diferentes estudos têm reportado que a habilidade do SLG em identificar disfunções sistólicas no ventrículo esquerdo em diferentes cardiomiopatias em casos onde a FE permanece preservada (FENT et al., 2017). Com base nisso, vê-se como essencial a detecção precoce de condições subclínicas para que a intervenção terapêutica seja assertiva (POTTER et al., 2018).

O papel da atividade física na prevenção do desenvolvimento de doenças cardiovasculares é bem estabelecido na literatura científica, no qual altos índices de atividade física, independentemente do tipo de atividade realizada, estão associados a um risco diminuído do aparecimento de DCVs (KOOLHAAS et al., 2017; WILLIAMS et al., 2013). Segundo Kodama e colaboradores (2009), uma melhor aptidão cardiorrespiratória está associada a um risco diminuído de mortalidade geral, assim como ao desenvolvimento de doenças cardiovasculares. Em corroboração com os achados acima mencionados, um amplo estudo observacional verificou que mesmo um engajamento modesto para com a prática de atividade física foi suficiente para promover uma diminuição no risco do desenvolvimento de DCVs (LANCHMAN et al., 2018). No entanto, ainda não há um consenso sobre os benefícios da prática de atividade física nos parâmetros relacionados à função ventricular esquerda, em especial ao SLG. De maneira crônica, apesar de alguns estudos apresentarem uma melhora do SLG por consequência do exercício físico (INGUL et al, 2018; MALFATTO et al., 2017; HOWDEN et al., 2013), outros apresentaram uma estabilidade da variável perante à pratica de exercício físico, no qual o mesmo foi inefetivo para a melhora do SLG (O'DRISCOLL et al., 2018; HOWDEN et al., 2018). Em relação aos efeitos agudos do exercício no SLG, apesar da já constatada melhora aguda do SLG em decorrência do exercício (O'DRISCOLL et al., 2017), a maioria dos estudos reportaram ausência de mudanças (PIELES et al., 2015; LIU et al., 2015) ou até mesmo piora na variável após a execução de exercícios físicos (GOODMAN et al., 2008; COTE et al., 2013). No entanto, tais estudos foram desenvolvidos em populações distintas, tornando a comparação entre os resultados referentes aos efeitos do exercício no SLG inadequada. Portanto, é notável a falta de consenso na literatura acerca dos efeitos do exercício físico no SLG, sendo evidente também o entendimento superficial em relação à duração, intensidade e modalidade do exercício e suas distintas respostas no SLG (HUANG et al., 2019; INGUL et al., 2018). Além disso, diferentes repostas podem advir mediante diferentes tipos de exercício, sendo que o exercício aeróbio, mais especificamente o HIIT, tem sido uma alternativa promissora para melhora da função cardiovascular (RAMOS et al., 2015). Especificamente na função cardíaca, apenas uma meta-análise analisou a comparação de diferentes modalidades de exercícios aeróbico (HIIT vs. exercício contínuo de intensidade moderada (MICT)), sendo que ambos promoveram mudanças significativas na FE em indivíduos com insuficiência cardíaca e FE reduzida, sem diferença significativa entre HIIT e MICT (TUCKER et al., 2019).

A respeito dos efeitos do exercício físico envolvendo indivíduos obesos, população essa potencialmente exposta ao risco de desenvolvimento de DCVs (LAVIE et al., 2016), o exercício físico parece promover mudanças positivas no SLG (INGUL et al., 2018; OBERT et al., 2013). No entanto, ambos os estudos foram desenvolvidos tendo a população pediátrica como amostra (crianças e adolescentes), não sabendo, portanto, os efeitos de diferentes modalidades de exercício físico na função ventricular de mulheres obesas jovens. Levando em consideração que as doenças cardiovasculares juntas são a principal causa de morte em mulheres, e diferentemente do cenário observado na população masculina, as taxas de mortalidade em decorrência de eventos cardíacos em mulheres não apresentaram queda (STOCK et al., 2012), vê-se como crucial o entendimento do impacto de diferentes modalidades de exercício físico nos parâmetros relacionados à função ventricular, em especial no SLG, em mulheres com obesidade.

2 OBJETIVOS

2.1 Objetivo Geral

Investigar os efeitos agudo e crônico de diferentes modalidades de exercício físico sobre a função ventricular esquerda e a deformação miocárdica em mulheres obesas.

2.2 Objetivos Específicos

- Revisar os efeitos crônicos de diferentes modalidades de exercício físico sobre o *strain* longitudinal global (SLG) em indivíduos saudáveis e portadores de doenças crônico-degenerativas;
- Verificar os efeitos agudos do exercício intervalado de alta intensidade (HIIT) e do exercício contínuo de intensidade moderada (MICT) sobre a função ventricular esquerda e a deformação miocárdica em mulheres obesas.

3 MÉTODOS

3.1 REVISÃO SISTEMÁTICA E META-ANÁLISE

Para o desenvolvimento da revisão sistemática, inicialmente, as diretrizes estabelecidas pelo Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) foi rigorosamente seguido. Cinco bases de dados eletrônicas foram elencadas para a busca e extração de artigos, sendo elas: Pubmed/Medline, Web of Science, Cochrane, Lilacs e Scielo. Os termos usados na busca foram os seguintes: "*Global longitudinal strain*", "*left ventricular function*", "*myocardial deformation*", "*longitudinal strain*", "*physical exercise*" e "*exercise*", sendo que os mesmos foram aplicados individualmente por dois pesquisadores (JCL e HBR), a fim de verificar se o número de referências encontradas seria a mesma. As buscas se limitaram a língua inglesa, compreendendo do período de início das publicações de artigo acerca do tema, até o mês de julho de 2019. Além disso, uma busca manual nas referências dos artigos aceitos foi feita para a identificação de outros estudos relevantes. Somente estudos com design longitudinal foram considerados elegíveis.

Os estudos foram considerados para inclusão desde que atendenssem os seguintes critérios de eligibilidade: (1) possuir medidas pré e pós intervenção; (2) ter realizado qualquer tipo de exercício físico (aeróbico, combinado ou resistido); (3) possuir um delineamento de estudo crônico; (4) populações saudáveis ou com alguma doença crônico-degenerativa. As referências da busca inicial foram organizadas em um *software* especifico de gerenciamente de referências (Mendeley®), para a seleção dos estudos. Dois pesquisadores conduziram independentemente a seleção dos estudos (JCL e HBR). Os estudos cujo objetivos eram indubitamente incompatíveis com o objetivo do estudo foram excluídos, assim como as referências duplicadas, foram removidas. Sequentemente, foram analisados os títulos e resumos dos artigos, e, se compatíveis com o objetivo do estudo, o texto na íntegra. Em caso de desacordo em os dois pesquisadores, a opinião de um terceiro (VHSM) foi requisitada para que se estabelecesse uma decisão final. Após isso, os dados referentes ao objetivo, população, protocolo de exercício físico e resultados foram extraídos dos artigos incluídos na revisão sistemática e meta-análise e organizados em uma planilha eletrônica. Ademais, a qualidade metodológica dos estudos incluídos foi feita por meio de uma ferramenta previamente validada.

3.2 ESTUDO EXPERIMENTAL COM DESIGN *CROSSOVER*

3.2.1 Seleção e caracterização da amostra

O tamanho da amostra para o presente estudo foi calculado pelo programa G Power® 3.1 utilizando a formula para o cálculo de amostra de medidas repetidas. Foram estipulados um poder estatístico de 83%, nível de significância de 5%, tamanho do efeito de 0,65. Deste modo, o número mínimo de indivíduos foi definindo em 15.

Após recrutamento por meio de divulgação nas mídias sociais seguido de reunião para possíveis esclarecimentos acerca dos procedimentos previstos no estudo, 17 mulheres com idade entre 18 e 35 anos, provenientes da cidade de Maringá e região metropolitana e diagnosticadas com obesidade (IMC≥ 30-40 kg/m^2) ingressaram no presente estudo.

Os seguintes critérios de inclusão foram pré-estabelecidos para a seleção da amostra: 1) Mulheres com idade entre 18 e 35 anos; 2) IMC: ≥ 30-40kg/m^2 de acordo com os pontos de corte propostos pela OMS (OMS, 1995); 3) Massa corporal (MC) estabilizada há pelo menos 12 semanas. Os critérios de exclusão adotados foram os seguintes: 1) Participação prévia em programas que tivessem como foco a redução de peso; 2) Apresentar cardiomiopatias, diabetes e/ou hipertensão e doenças endócrinas; 3) fazer uso regular de tabaco; 4) Fazer uso de medicamentos que possam provocar alterações nos sistemas cardiorrespiratório e neuromuscular; 5) Não participação integral nas avaliações; 6) Não completar o protocolo experimental.

A amostra inicial consistiu na alocação aleatória de 17 participantes. No entanto, duas participantes não completaram o protocolo completo de avaliação e foram consequentemente excluídas do estudo (Figura 1). Dessa forma, a amostra final foi composta por 15 mulheres, sendo alocadas aleatoriamente em três condições distintas: Condição Controle (GC) (n = 15); Condição Treinamento Intervalado de Alta Intensidade (GHIIT) (n = 15); Condição Treinamento Contínuo de Intensidade Moderada (GMICT) (n = 15).

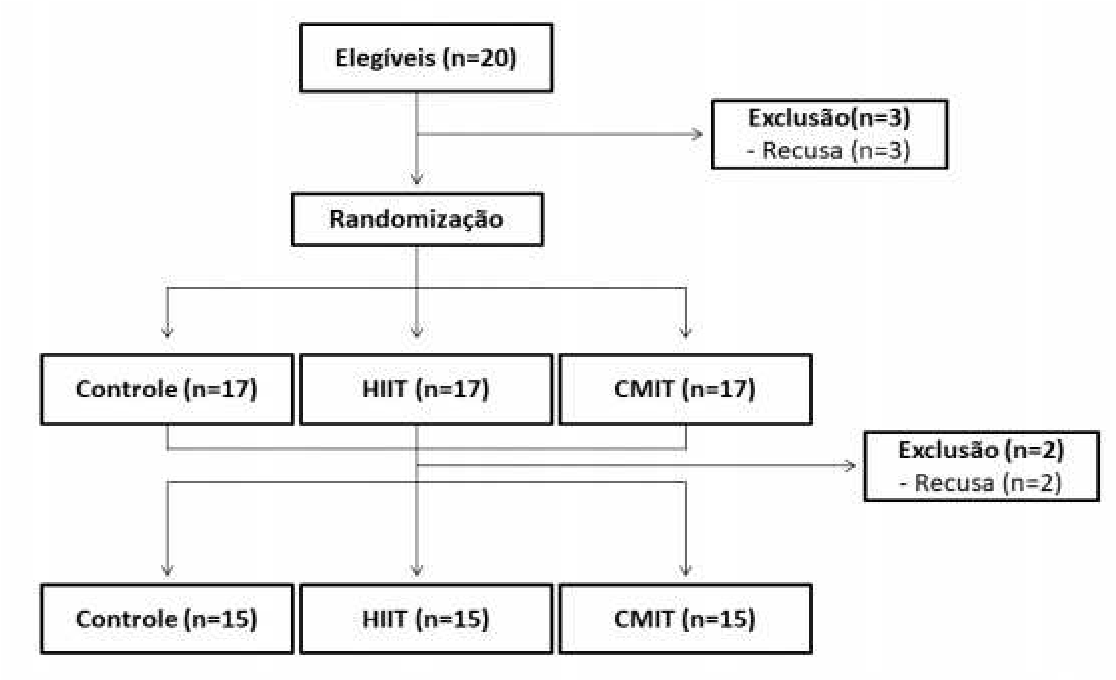

Figura 1. Fluxograma do estudo.

Precedentemente a coleta de dados, as voluntárias foram informadas quanto aos procedimentos metodológicos do estudo, e após os devidos esclarecimentos, assinaram o Termo de Consentimento Livre e Esclarecidas- TCLE (APÊNCIDE 1). O projeto foi previamente submetido e aprovado no Comitê de Ética da Universidade Estadual de Maringá – UEM sob o Parecer nº 3.268.455 (ANEXO 1).

3.2.2 Delineamento experimental

O presente estudo teve duração de 10 semanas, sendo dividido em sete visitas. A primeira visita consistiu na realização de uma reunião de caráter informativo, com o intuito de esclarecer os procedimentos previstos na pesquisa. Ao fim da referida reunião, foi obtido o consentimento das voluntárias para com a participação das mesmas na pesquisa por meio da assinatura do TCLE. A avaliação médica e o exame físico foram realizados na segunda visita do estudo. Após a assinatura do TCLE, as voluntárias que manifestaram interesse em participar da pesquisa foram sujeitas a uma triagem para a verificação do risco cardiovascular, a fim de garantir que as voluntárias estão aptas para a prática de exercício físico. Na terceira visita do estudo, foram realizadas as avaliações antropométricas e de composição corporal para fim de caracterização da amostra. A quarta visita do estudo compreendeu a realização de um teste incremental máximo em esteira ergométrica com a finalidade de definir os valores referentes a frequência cardíaca máxima (FCmáx) das voluntárias. A quinta visita do estudo consistiu na realização da familiarização, etapa na qual as voluntárias se adaptam ao local e equipamentos utilizados na pesquisa. A sexta e sétima visitas do estudo basearam-se na avaliação da condição controle (GC) e execução dos protocolos de treinamento. De maneira randômica, as voluntárias foram alocadas nas condições HIIT e MICT em dias aleatorizados respeitando sempre o intervalo mínimo de 72 horas entre a execução dos protocolos. A randomização foi feita através de um software eletrônico específico. As avaliações cardiovasculares foram conduzidas antes e após a realização de cada um dos três protocolos experimentais. A coleta de dados foi realizada no Núcleo de Pesquisa Clínica (NPC), do Hospital Universitário de Maringá (HUM) e na clínica BioCor. Todas as avaliações do presente estudo foram realizadas por profissionais experientes integrantes do Grupo de Pesquisa em Hipertensão Arterial Sistêmica, Rigidez Arterial e Envelhecimento Vascular (GPHARV). Os procedimentos executados estão detalhados na figura 2.

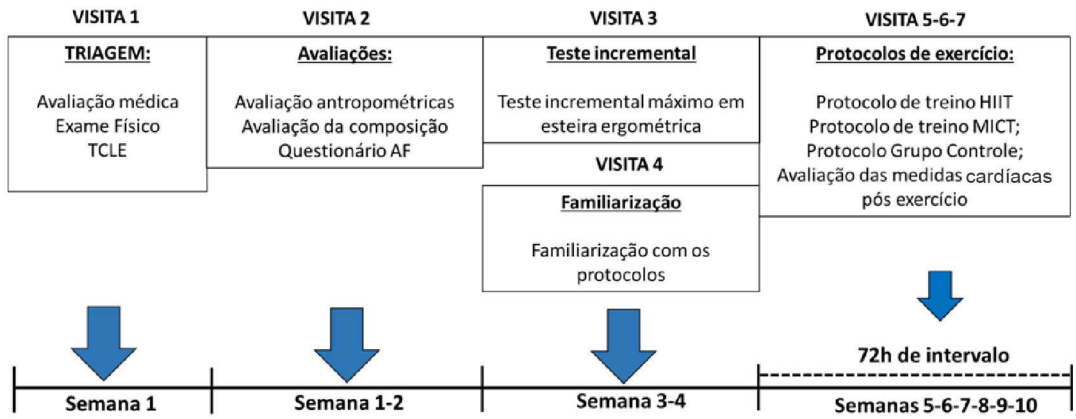

Figura 2. Representação das visitas.

3.3 INSTRUMENTOS E AVALIAÇÕES

3.3.1 Avaliação das Variáveis Antropométricas e de Composição Corporal

A massa corporal (MC) foi aferida por meio de uma balança antropométrica mecânica (Finizola®), com precisão de 0.1 kg e capacidade máxima de 150 kg. A estatura foi aferida a partir de um estadiômetro acoplado a balança mecânica, com precisão de 0.1 cm e amplitude de 220 cm. Para a avaliação das variáveis previamente citadas, as participantes permaneceram em posição ortostática, descalças, com os braços relaxados ao longo do corpo, pés ligeiramente afastados, cabeça voltada para a frente e glúteos e ombros corretamente posicionados, em concordância com o plano de Frankfurt.

O IMC das voluntárias foi calculado a partir da divisão da massa corporal (MC) pela estatura (EST), em metros (m), ao quadrado ($IMC=MC/EST^2$) e classificado de acordo com os pontos de corte propostos pela OMS (OMS, 1995). A circunferência de cintura (CC) foi mensurada com a ajuda de uma fita métrica inelástica (Sanny®), com resolução de 0.1 cm e amplitude de 2 m. Anteriormente à avaliação, foi verificada se a participante estava em posição ortostática correta para a aferição da medida. Assim, o valor referente ao ponto médio entre a última costela e a crista ilíaca foi coletado (LOHMAN; ROCHE; MARTORELL, 1988).

Para a avaliação da composição corporal, foi utilizado o aparelho de bioimpedância, modelo BF-900 (Maltron®, Reino Unido), seguindo estritamente as recomendações propostas por Heyward (2001). A avaliação foi realizada com o indivíduo em decúbito dorsal, posicionado em uma superfície plana, as pernas ligeiramente afastadas e sem portar nenhum objetivo metálico. Os eletrodos foram posicionados nas articulações da mão e do punho direito, e do pé e dos dedos dos pés. As participantes que estavam em seus respectivos ciclos menstruais tiveram sua avaliação remarcada, para que fossem evitadas possíveis influências hormonais sobre as variáveis coletadas.

3.3.2 Teste Incremental Máximo

A aptidão cardiorrespiratória das participantes foi avaliada mediante a realização de um teste incremental máximo, utilizando o protocolo de Bruce, em esteira ergométrica, objetivando a definição dos valores correspondentes a FC_{max}, variável essa utilizada para a determinação das cargas de treino. O protocolo começou a uma velocidade de 2,7 km/h e 10% de inclinação, ocorrendo aumentos progressivos tanto na velocidade quanto na inclinação (2%) a cada três minutos. Nos estágios 2, 3, 4, 5 e 6 a velocidade foi alterada para 4,0, 5,4, 6,7, 8,0 e 8,8 km/h respectivamente (BRUCE, 1971). O teste era interrompido no momento em que a fadiga volitiva era atingida. O VO_{2max} foi estimado por meio de uma equação obtida através de um software específico (Micromed®, São Paulo, Brasil). Além disso, a frequência cardíaca foi constantemente monitorada através de um monitor cardíaco (Polar®, Kempele, Finlândia).

3.3.3 Protocolos de Treinamento

De forma aleatória, todas as participantes realizaram todos os procedimentos experimentais, respeitando um intervalo de recuperação de pelo menos 72 horas entre a execução de cada protocolo. Os protocolos de treinamento foram ajustados segundo as recomendações do *American College of Sports Medicine* (GARBER et al., 2011). Tais recomendações preconizam a prática de atividades aeróbias de intensidade moderada por no mínimo 30 minutos, 5 vezes por semana, ou atividades de alta intensidade, por 20 minutos, 3 vezes por semana ou a combinação de ambas.

As voluntárias foram instruídas a manter suas dietas e atividades rotineiras, além da recomendação para que as mesmas não iniciassem nenhum programa de exercícios físicos durante o período de realização do estudo. Não foi realizado nenhum controle dietético no presente estudo. Entretanto, foi obtido um recordatório alimentar de 24h a fim de controlar a ingestão calórica do dia precedente ao da execução dos protocolos experimentais. Ademais, foi recomendado que as participantes não ingerissem alimentos num período de duas horas antecedentes ao período da coleta, para que fosse evitado qualquer tipo de desconforto gastrointestinal.

O protocolo de exercício intervalado de alta intensidade (HIIT) consistiu na execução de caminhada/corrida em uma esteira ergométrica. Inicialmente, foi realizado um aquecimento de 10 minutos, sendo os cinco primeiros a uma frequência de 55 a 65% da $FC_{máx}$ e os cinco minutos finais entre 65 e 75% da $FC_{máx}$. Sequencialmente, foram realizados 4 estímulos de quatro minutos cada a uma intensidade entre 85 e 95% da $FC_{máx}$, sendo alternados por períodos de recuperação ativa de 3 minutos na intensidade entre 65 e 75% da $FC_{máx}$. Ao final do protocolo, um desaquecimento de 5 minutos foi conduzido, sendo os três primeiros minutos a uma intensidade entre 65 e 75% da $FC_{máx}$, seguidos de dois minutos com intensidade entre 55 e 65% da $FC_{máx}$. O protocolo teve uma duração total de 40 minutos (Figura 3).

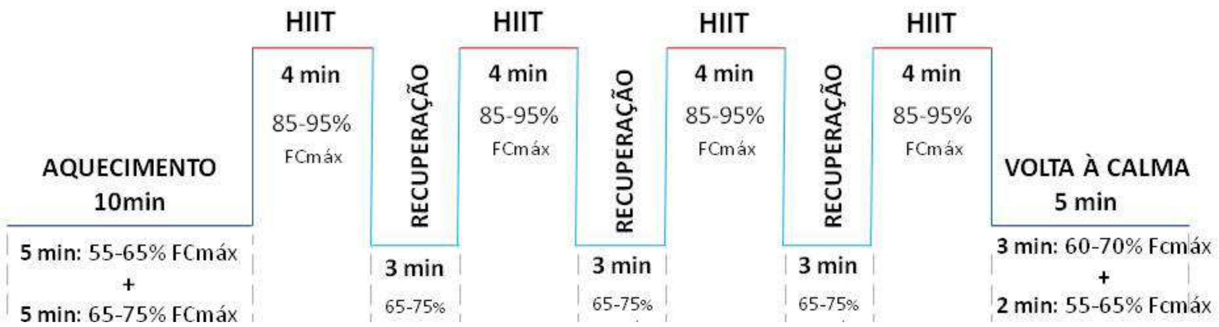

Figura 3. Ilustração do protocolo de exercício HIIT.

O protocolo de exercício contínuo (MICT) também consistiu na execução da caminhada/corrida em uma esteira ergométrica. Inicialmente, foi realizado um aquecimento de cinco minutos com intensidade entre 55 e 65% $FC_{máx}$, seguidos de 41 minutos com intensidade entre 65 e 75% da $FC_{máx}$ e dois minutos de volta a calma com intensidade entre 55-65% da $FC_{máx}$. O protocolo total teve duração de 48 minutos (Figura 4).

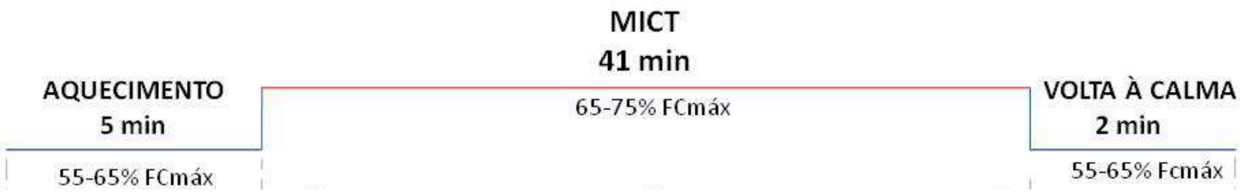

Figura 4. Ilustração do protocolo de exercício contínuo.

A condição controle (GC) foi realizada com os indivíduos permanecendo sentados por um período de 30 minutos. Todas as condições experimentais foram constantemente monitoradas por um médico especializado e um profissional de educação física experiente.

3.3.4 Avaliação dos parâmetros ecocardiográficos

Os testes ecocardiográficos foram realizados antes, cinco e 35 minutos após a execução das condições experimentais. As análises foram feitas com os indivíduos em posição semi-supina voltada para o lado esquerdo, em decúbito lateral de aproximadamente 60º em uma maca adequada para a realização do exame. Os exames foram feitos por meio de um aparelho de ecocardiografia (Vivid E95, General Eletric Medical Systems, Milwaukee, WI, Estados Unidos).

Para caracterização da amostra, a mensuração da espessura médio-intimal (EMI) foi realizada através da ultrassonografia de alta resolução, com o auxílio de um transdutor digital com foco variável. A EMI foi obtida pela medida da distância entre duas linhas ecogênicas representadas pelas interfaces lúmen-íntima e média-adventícia da parede da artéria.

A função ventricular esquerda foi avaliada por ecocardiografia bidimensional: modo – M, Doppler pulsátil, com mapeamento de fluxo de cores e tecidual, de acordo com as diretrizes propostas pela Sociedade Americana de Ecocardiografia. Os seguintes parâmetros foram coletados: diâmetro da aorta (AO), fração de ejeção (FE), débito cardíaco (DC), e volumes sistólico (VSF) e diastólico (VDF) final do ventrículo esquerdo, obtidos nos planos paraesternal eixo curto e longo. Além disso, o corte apical de quatro câmaras permite a verificação do fluxo de sangue pelas valvas atrioventriculares. Dessa forma, a velocidade diastólica inicial (E) e tardia (A) das valvas mitral e tricúspide, assim como a razão E/A, o pico de velocidade diastólica (e’), e a velocidade sistólica anular das paredes septais (s’ sep) e (s’ lat) foram coletadas objetivando a avaliação da função sistólica e diastólica do ventrículo esquerdo.

O SLG foi coletado por meio da técnica baseada no rastreamento de pontos específicos do miocárdio (speckle-tracking) pela ecocardiografia bidimensional (2D-STE). Marcadores acústicos naturais, denominados *speckles*, refletem padrões do tecido no miocárdio. Assim, por meio de um software acoplado ao 2D-STE, os pontos são identificados e os movimentos são consequentemente rastreados em todas as direções, no qual o *strain*, é avaliado baseado na comparação dos padrões quadro a quadro. Por conseguinte, o *strain* é caracterizado como a média relativa da deformação entre dois pontos ao longo das direções pré-definidas relativas aos valores normativos de deformação miocárdica.

3.4 ANÁLISE ESTATÍSTICA

Para a meta-análise, os dados dos estudos incluídos foram inseridos em um *software* específico, no qual os resultados foram agrupados para análise. Os dados são apresentados em diferença média estandardizada, sendo que o modelo de efeitos randômicos foi utilizado com o intuito de minimizar a heterogeneidade entre os estudos. *Forest Plots* foram criados para quantificar os efeitos de diferentes modalidades de exercício em comparação ao grupo controle no SLG e na FE. Análises de sensibilidade examinando os efeitos de cada estudo individualmente no efeito geral das comparações também foram conduzidas. Outrossim, foram feitas análises de subgrupo a fim de identificar se os efeitos das análises se diferiam em relação a idade (jovem, adulto e idoso), período de intervenção (< ou ≥ de 12 semanas de intervenção), intensidade do exercício (moderada ou alta), volume do exercício (<150 ou ≥150 minutos) e patologias (condições cardíacas, metabólicas, renais, pacientes com câncer, além de indivíduos saudáveis). A heterogeneidade dos estudos foi verificada por meio do teste I^2, no qual os valores 25%, 50% e 75% foram utilizados para indicar baixa, moderada ou alta heterogeneidade, respectivamente. *Funnel plots* foram criados e a verificação do risco de viés foi feita mediante inspeção visual. O teste de Egger foi aplicado para a verificação de risco de viés na publicação.

Para o delineamento experimental, foi utilizada estatística descritiva para a análise dos dados. A normalidade dos dados foi atestada a partir do teste de Shapiro-Wilk. Os dados foram apresentados em forma de média e desvio padrão. Para a comparação entre as condições experimentais (GC, HIIT e MICT) e entre os momentos de coleta (Pré, 5 e 35 min) aplicou-se o teste ANOVA *two way* para medidas repetidas, seguido do teste de comparações múltiplas de Sidak. Correlação de Pearson foi utilizada para verificar a relação das mudanças entre pré e pós (5 min) nas condições HIIT e MICT para as variáveis ecocardiográficas e hemodinâmicas. O nível de significância estatística adotado em todas as análises foi de $p \leq 0{,}05$. O pacote estatístico utilizado para as análises foi o SPSS versão 23.0.

4 RESULTADOS

Artigo 1

THE EFFECTS OF DIFFERENT EXERCISE TRAINING MODALITIES ON GLOBAL LONGITUDINAL STRAIN IN HEALTHY AND CHRONICALLY DISEASED INDIVIDUALS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Background

Constituted by the heart, arteries, veins and capillaries, the cardiovascular system has the function of providing enough blood supply to keep itself appropriately functioning, as well as other human body systems. The heart is the key-element of this system. It is a powerful pump responsible for propelling blood, nutrients and oxygen throughout the entire body, being a matter of interest since the earliest development of medicine, in ancient Greek society [1].

Nowadays, the cardiovascular system is still an enthralling topic of scientific discussion, since cardiovascular diseases (CVDs) are the leading cause of death worldwide [2,3]. It is estimated that CVDs are responsible for 17.3 million deaths per year, and this worrisome scenario tends to become even worse with the estimation of approximately 23.6 million deaths by 2030 [4]. The latest statistical update from the American Heart Association reported that one in every three deaths are accounted for CVDs in United States, which is a higher mortality rate than that of cancer and respiratory diseases together [5].

Impairments on the left ventricle (LV), such as LV hypertrophy (LVH) and alterations on LV geometry, are associated with CVD morbidity and mortality [6–8]. Expressed as the characterization of LV function, LV ejection fraction (LVEF) is a broadly used parameter for the assessment and targeting of LV systolic function, and its reduction is closely associated with a range of cardiac diseases [9]. Data from a wide multi-ethnic study reported that a decrease of 10% in LVEF was associated with significant increase in congestive heart failure (CHF), CVD events and all-cause mortality [10].

Despite being a traditional marker of LV function, LVEF presents noteworthy limitations. Firstly, it is influenced by both preload and afterload, and thus its interpretation as a contractile index is inaccurate when made without previous knowledge of LV loads [11]. Secondly, myocardial structural changes that alter LV end-diastolic volume may strongly affect LVEF. Additionally, its suboptimal reproducibility and ineptitude to reflect regional LV function are other issues to be considered when analyzing the reliability of LVEF as a parameter to assess LV function [12].

Recently, a novel technique for the assessment of LV function has arisen as an interesting alternative to the traditional evaluation of LVEF [13]. Obtained by means of speckle-tracking echocardiography (STE), the global longitudinal strain (GLS) has become a useful tool for LV systolic function evaluation in clinical practice [14]. The STE technique consists in interference patterns generated by the interaction between the ultrasound beam and the myocardium, allowing the tracking of its deformation in systole and diastole [15]. Precisely, strain is the deformation caused by the application of a force, whereas myocardial strain is reported as the deformation, expressed in percentage, of myocardial length from relaxed to before contraction periods [12,16].

GLS is more sensitive in detecting changes in LV systolic function than LVEF [17]. Robust scientific evidence has reported that GLS was able to detect subclinical LV systolic function in many cardiomyopathies while LVEF was still preserved [17,18]. GLS has also been proved to be a superior predictor of cardiac events as well as all-cause mortality when compared to LVEF in healthy individuals [19]. Moreover, it is also a reliable prognostic marker for patients after myocardial infarction, cardiac surgery, cardiomyopathy, and aortic stenosis [20–23]. Russo and colleagues [24] reported in a cohort study that while 4.2% of the individuals were diagnosed with impaired LVEF, 16.8% already presented abnormal values of GLS, reiterating the importance of this variable in identifying subclinical changes in LV systolic function.

The role of exercise in the prevention of CVDs is well explored in literature, according to which higher levels of exercise, regardless of modality, are closely associated with a diminished risk of CVD development [25–27]. In the meta-analysis by Kodama et al. [28], better cardiorespiratory fitness was associated with lessened risk of all-cause mortality, chronic heart disease (CHD) and CVD development. Regarding the relationship between LV function and physical exercise, there is a lack of consensus on whether physical exercise has a positive or negative effect [29,30].

While some studies have reported that physical exercise promoted favorable functional and morphological adaptations to the LV, others, at odds, have shown LV dysfunction after exercise [31–35]. Moreover, the vast majority of studies assessing the effects of exercise on LV function measuring the GLS were conducted in athletes. Considering that LV responses to exercise in athletes may differ considerably from those in healthy and chronically diseased, it is not reasonable to reproduce the outcomes reached in athletes to the entire population [36].

Recent studies assessing the effects of physical exercise on GLS have reported a lower longitudinal myocardial deformation in athletes with higher levels of exercise [37]. In addition, a recently published meta-analysis corroborates the aforementioned evidence by documenting a global reduction in LV systolic and diastolic function following prolonged endurance exercise [38]. However, while the unravelling of the effects of exercise on myocardial deformation in athletes has already begun, the same effects in healthy non-athlete, as well as populations with chronic medical conditions, are still a matter of enthralling debate due to the paucity of studies and the absence of systematization of the existent knowledge on this issue.

Having in mind the importance of understanding the effects of exercise on LV systolic function, measured by GLS, in healthy and chronically diseased individuals, since they could present subclinical impairments on LV systolic function, the aim of the present systematic review and meta-analysis was to systematize the existent knowledge surrounding the effects of exercise training on LV function by the assessment of GLS in healthy and chronically diseased individuals, analyzing the effects of different exercise modalities on GLS.

Materials and methods

The present systematic review and meta-analysis was carried out following strictly the guidance proposed in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [39]. The analysis methods and inclusion criteria were specified in advance and documented in the International Prospective Register of Systematic Reviews (PROSPERO), with the registration number CRD128299.

Search strategy

The search for potential references comprised five electronic databases (Pubmed/Medline, Web of Science, Cochrane, Lilacs and Scielo), in all of which the same key terms were uniformly applied by two researchers (JCL, HBR) independently, in order to verify if the same number of references was found. The terms used on the searches were the following: “Global longitudinal strain”, “left ventricular function”, “myocardial deformation”, “longitudinal strain”, “physical exercise”, “aerobic exercise”, and “exercise”. Searches were restricted to English-language from inception to July 2019. Additionally, a manual search from the reference list of the included studies was performed for the identification of other relevant studies. Only studies with longitudinal design were considered for inclusion.

Eligibility criteria

Studies were considered for inclusion since they met the previously established eligibility criteria, which comprise the following concerning topics: (1) baseline and post intervention measures of GLS; (2) any type of physical exercise intervention (e.g. aerobic, resistance, or combined exercise training); (3) chronic design intervention; and (4) healthy and chronically diseased populations. Studies with athletes and non-athletes groups with stratified data that underwent the same physical exercise program were also considered eligible for inclusion. Studies using exercise to induce myocardial stress in order to assess the quality of the GLS measurement rather than its effects on the variable itself were excluded.

Study screening and data extraction

The references from the initial search were systematized with the aid of a specific reference management software (Mendeley®) for reference screening. Two authors individually conducted studies screening (JCL, HBR). Studies whose scopes were undoubtedly out of the aim of the current review, as well as duplicate data, were removed. Title and abstract analyses were performed for the remaining references with the purpose of selecting studies for full-text assessment. Thereafter, the full-text assessment was meticulously performed, while the eligibility criteria were applied equally for all potential references. In case of disagreement, the two authors tried to reach consensus by explaining their points of view. If the conflict persisted, a third author's (VHSM) opinion was requested to reach a final decision.

Sequentially from the full-text screening, data concerning objective, population and groups, exercise training protocol and results were extracted from the included studies and arranged in an electronic spreadsheet. This procedure was also conducted by two researchers (CFS, GHO) and compared after all.

Quality assessment of included studies

The assessment of the methodological quality of the included studies was made with the aid of a validated tool [40]. This assessment consists of 14 questions that fully deal with the methodological issues that could represent potential risk of bias in a scientific report. The questions allow five different answers (e.g. yes, no, not reported, not applicable, not reported, and cannot determine). For each question whose the answer is yes, a score of one is assigned. Global scores range from zero to 14, the latter being the best achievable score (i.e. best methodological quality and diminished risk of bias). The aforementioned assessment tool was applied individually to all included studies. This nature of assessment is a reliable method to verify the strength of scientific evidence by identifying the likelihood of risk of bias. Nevertheless, it was not used as an exclusion criterion. Hence, even the articles with poor methodological quality remained for further analysis and discussion.

Meta-analysis

Data were inserted in an appropriate software (Review Manager®, version 5.3, Cochrane collaboration, Oxford, UK) and the outcomes of the comparable studies were pooled into the meta-analysis. Weighted mean differences between interventions and 95% confidence intervals (95% CIs) for unitless effect sizes were also determined, weighted by the inverse variance of each study. The random-effects model was used in order to minimize the influences of heterogeneity from the included studies. Corresponding forest plots were created to quantify the effect of different exercise modalities vs. control group (CG) on GLS and LVEF. Sensitivity analyses examining the individual effect of each study on the overall effect of subgroup comparisons were also conducted. A moderator analysis was carried out to determine whether the intervention effects on the main outcomes have differed regarding age group (youth, adult or elderly), intervention period (<12 or ≥12 weeks of intervention), exercise intensity (moderate or high) and volume (<150 or ≥150 minutes per week), and pathologies (cardiac conditions, metabolic impairments, renal and cancer patients, and healthy individuals). A significance level of $p \leq 0.05$ was adopted. The heterogeneity was assessed using the I^2 statistic, in which values of 25%, 50% and 75% were considered to indicate low, moderate and high heterogeneity, respectively [41]. Funnel plots were used with the aim of verifying potential risk of bias by visual inspection, and the Egger's linear regression test was applied in order to verify the publication risk of bias [42]. A leave-one-out sensitivity analysis was conducted by removing one of the included studies at a time to assure that the findings of the present study were not driven by any particular study.

Results

Literature search

Initial searches on the electronic databases retrieved 4174 potential references. After adjusting for duplicates, 3777 references remained. Following title and abstract screening, 46 studies were selected for full-text screening. Of those, 26 and 18 studies met the eligibility criteria and were included in the systematic review and meta-analysis, respectively. The entire inclusion procedure is described in figure 1.

Quality assessment of selected studies and publication bias

The methodological quality assessment revealed a wide variance among the included studies. The study scores ranged from three to 12, in which the overall rating was eight. Twenty-five studies (96%) reported the use of valid and reliable measures, implementing them consistently throughout the study. In addition, the vast majority of the studies (77%) identified their subgroups and main outcomes before

the analyses were carried out, as well as verified a drop-out rate lower than 20% (88%). Also, 20 out of 26 studies reported a high adherence to the protocol (77%). Nevertheless, only four studies (15%) conducted a sample size calculation, and three studies (12%) performed an analysis regarding intention-to-treat. The other methodological aspects kept a moderate rate. Some studies were unsuccessful in reporting all the methodological issues considered in this assessment tool due to the robustness of this methodological quality assessment tool. For this reason, some studies received a low rating. However, it does not necessarily represent poor methodological quality, but particular strategies adopted by authors that partially differed from the criteria of the assessment tool. Moreover, it is important to emphasize that no exclusion criterion was settled concerning the methodological quality of the included studies. Instead, its application had the aim of verifying the quality of the methodological procedures from the selected studies by means of a valid tool with a good acceptance in literature, indicating some potential risk of bias.

The visual inspection did not verify any abnormality on the funnel plots, wherein the Egger's linear regression tests did not indicate risk of bias. Moreover, the leave-one-out sensitivity analysis showed that the exclusion of a single study did not exert effect on the results for any of the evaluated outcomes.

Table 1. Quality assessment of the included studies

	Study ID												
Criteria	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**
1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	Y	N	Y	N	N	NR	N	N	Y	Y	Y	Y	Y
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	NR	N	Y	N	N	NR	N	N	Y	Y	NR	Y	Y
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	NR	N	Y	N	N	NR	NR	NR	Y	Y	NR	Y	Y
4. Were study participants and providers blinded to treatment group assignment?	NR	N	Y	N	NR	NR	NR	NR	Y	NR	Y	NR	NR
5. Were the people assessing the outcomes blinded to the participants' group assignments?	Y	N	CD	Y	Y	NR	NR	Y	Y	NR	Y	Y	Y
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	Y	Y	Y	Y	Y	Y	NR	Y	N	Y	Y	Y	Y
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	N	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y
9. Was there high adherence to the intervention protocols for each treatment group?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NR
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	Y	Y	Y	NR	N	Y	NR	NR	NR	NR	Y	NR	NR
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	Y	N	Y	N	N	Y	NR	NR	NR	NR	NR	NR	NR
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	N	NR	NR	N	N	N	NR	NR	NR	NR	NR	Y	NR
Total score	**09**	**07**	**12**	**07**	**07**	**08**	**04**	**07**	**10**	**09**	**10**	**10**	**09**

(Continued)

Criteria	Study ID												
	14	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**
1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	N	Y	Y	Y	N	Y	Y	Y	Y	NR	Y	Y	N
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	N	Y	Y	Y	N	Y	NR	NR	Y	NR	Y	Y	N
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	N	Y	Y	Y	N	Y	NR	NR	Y	NR	Y	Y	N
4. Were study participants and providers blinded to treatment group assignment?	N	NR	Y	Y	NR	NR	NR	NR	NR	NR	Y	NR	NR
5. Were the people assessing the outcomes blinded to the participants' group assignments?	N	Y	Y	Y	N	Y	NR	NR	Y	NR	Y	Y	Y
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	Y
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	N	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	NR	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9. Was there high adherence to the intervention protocols for each treatment group?	Y	Y	Y	Y	Y	Y	Y	NR	NR	NR	Y	NR	NR
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	NR	NR	Y	N	Y	NR	NR	NR	NR	NR	NR	NR	Y
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	NR	NR	N	Y	N	NR	NR	NR	NR	NR	NR	NR	NR
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	NR	Y	N	Y	Y	Y	Y	NR	Y	NR	Y	Y	NR
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	NR	Y	N	N	N	NR	Y	NR	NR	NR	NR	N	NR
Total score	**03**	**11**	**11**	**12**	**07**	**10**	**08**	**03**	**08**	**03**	**10**	**09**	**06**

Description of included studies

Twenty-six studies met the eligibility criteria and consequently composed the current systematic review, reaching, altogether, 1288 subjects [32,43-67]. With respect to the population assessed, six studies had healthy individuals as sample [43,47,51,54,58,65]. The other 20 studies assessed individuals with some chronic medical condition [32,44-46,48–50,52,53,55-57,59–64,66,67]. From these, five studies were conducted in type II diabetes mellitus patients [48–50,55,60], four with heart failure individuals [46,57,61,67], in which the patients had preserved LVEF in three of them [57,61,67], three with obese youth [53,59,63], two with myocardial infarction individuals [44,64], two with renal patients (i.e. one with renal transplant patients and one with chronic kidney disease patients) [52,62], one with metabolic syndrome patients [45], one with coronary artery disease [66], one with women with early stage breast cancer [68], and one with heart transplant recipients [56].

Concerning changes in GLS, this variable improved in 11 studies [44,45,63,50–53,55,59,61,62] and remained unaltered in 15 [32,43,46–49,54,56–58,60,64,65,67]. No study reported the worsening of GLS following exercise performance. As regards to LVEF, five studies verified an increase in LVEF [44,45,51,59,63], while 18 studies did not observe significant changes in this variable [43,46, 47,49,50,52,53,55–62,64–67]. Only one study reported a decrease in LVEF following exercise intervention protocols [32].

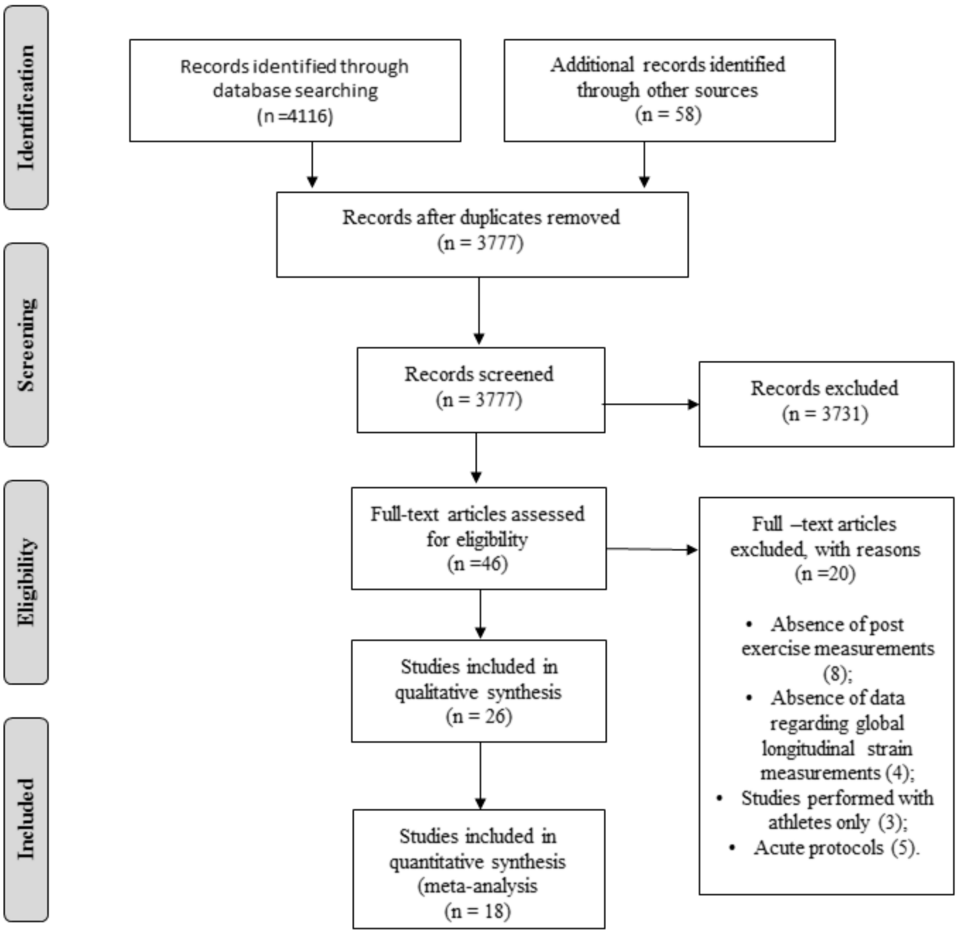

Figure 1. Inclusion procedures of the current systematic review and meta-analysis.

Table 2. Main clinical characteristics of studies included in the systematic review and meta-analysis (26 studies).

References	*Objective*	*Population/ Groups*	*Exercise Training*	*Results*
Huang et al. 2019	To examine how HIIT and MICT affects by 6 week architecture and mechanics of LV rest and during exercise	N=54/21.8±0.5 yrs Sedentary males HIIT (n=18) MICT (n=18) CG (n=18)	6 weeks-5x per week HIIT (33 min): 3-min warm-up (30% of VO_{2max}) followed by 5 bouts of 3 min (80% of VO_{2max}) interspersed by 3 min of active recovery (40% of VO_{2max}). The protocol finishes with a 3-min cool-down (30% of VO_{2max}). MICT (30 min): 3-min warm-up (30% of VO_{2max}) followed by a 30-min one bout of exercise (60% of VO_{2max}). The protocol finished with a 3-min cool down (30% of VO_{2max}). CG: no exercise intervention was provided.	**HIIT/ MICT/CG** ↔ GLS ↔ LVEF
Oxborough et al., 2019	To asesss the impact of 24 weeks of closely supervised and centre-based endurance and resistance training on LV mechanics in healthy untrained male participants.	N=23/27.5±1.75 yrs Healthy untrained men Aerobic training (AT) (n=10) Resistance training (RT) (n=13)	24 weeks AT: Three training-phases divided into eight 3-week mesocycles. In mesocycle one to four, hard-load week was followed by an easy week and in the last four mesocycles, two weeks were hard-loaded, in which he third one acted as a recovery week. RT: Olympic style weightlifting and associated exercises. The programme consisted of three training-phases divided into six 4-week mesocycles. Each mesocycle commenced with three weeks progressive loading, peaking in the third week, followed by one week of recovery.	**AT/RT** ↔ GLS
Santoso et al. 2019	To test the hypothesis that exercise training might improve the longitudinal intrinsic LV function in HFPEF patients.	N= 30/ 65.3±6.2yrs (17 males and 13 females) Heart failure with preserved ejection fraction	4 weeks/ 3-5x per week (90 min per session): Supervised ambulatory training program. Endurance training (cycling and walking) + relaxation.	↑ GLS ↔ LVEF
Enrico et al. 2018	To evaluate the myocardial strain pattern changes in a group of renal transplant recipients who were participating in a year-long, supervised exercise program.	N=30/38.6±13.1 yrs Renal transplant recipients patients Combined training (CT) (n=30)	12 months/3x per week (1 hour each session) CT: Aerobic and strength exercise according to the recommendation of the American College of Sports Medicine. The protocol consisted in strength exercises including eight muscle groups allied with 15 min of stationary cycling.	**CT** ↑ GLS ↔ LVEF

Howden et al. 2019	To determine whether a structured exercise training program would attenuate reductions in VO2peak and whether exercise cardiac imaging is a more sensitive marker of cardiac injury than the current standard of care resting LVEF	N=28/47.0±10.5 yrs Women with early stage breast cancer CT (n=14) CG (n=14)	12 weeks- 3x per week: CT: 2x per week: 30 min of aerobic exercise + 30 min of resistance exercises; 1x per week: unsupervised session of 30-60 min of home-based aerobic exercise. CG: medical care.	**CT** ↔ GLS ↓ LVEF **CG** ↔ GLS ↔ LVEF
Ingul et al. 2018	To compare the effects of twelve weeks of HIIT, MICT, and nutrition advice on resting systolic cardiac function in children with obesity. In addition, they aimed to compare the effect of the three interventions on LV and right ventricular resting diastolic cardiac function, GLS, and strain rate during rest, peak exercise and recovery	N=99/12.0±2.3 yrs (46 boys and 53 girls) Obese children HIIT (n=33) MICT (n=32) CG (n=34)	12 weeks- 3x per week HIIT (40 min): 10 min of warm-up (60-70% HRmax) followed by 4 bouts of 4 min each (85-95% HRmax) interspersed by 3 min of recovery (50-70% HRmax). The protocol finishes with a 5-min cool-down (60-70% HRmax). MICT (44 min): 1 bout (60-70% HRmax). Control: Nutritional counselling.	**HIIT/ MICT** ↑ GLS ↑ LVEF **CG** ↔ GLS ↔ LVEF
Mcgregor et al. 2018	To exploratory study was to examine the effect of exercise training on LV longitudinal strain and twist in myocardial infarction patients.	N= 36/ 55.5±10.6 yrs Males with myocardial infarction Intervention Group (IG) (n= 18) CG (n= 18)	10 weeks: Gym based cardiovascular exercise 2x per week (25–40 min each session): 10-min warm-up on progressive treadmill or cycle followed by a resistance programme in a training machine (1 set, 12 repetitions, 5 upper and 2 lower body exercises). The protocol finished with a 5--min cool down walking (60–80% VO2peak). CG: no exercise intervention was provided.	**IG/CG** ↔ GLS ↔ LVEF
O'Driscoll et al. 2018	To perform a randomised cross-over controlled study in a large cohort of physically inactive and highly sedentary young adults following 2 weeks of HIIT and record alterations in functional capacity, arterial blood pressure, non-invasive cardiac autonomic modulation and a comprehensive assessment of cardiac function and mechanics	N=40/21.0±1.7 yrs Sedentary healthy males HIIT (n=40) CG (n=40)	2 weeks-3x per week: Cross-over design HIIT: 5-min warm-up followed by 3 Wingate tests separated by a 2-min active (unloaded) recovery period. The protocol finishes with a 5-min cool-down CG: the control assessments were performed after a 4-week wash out period.	**HIIT/ CG** ↔ GLS ↔ LVEF

Van de Heyning et al. 2018	To investigate whether aerobic interval training and aerobic continuous training differ regarding their impact on left ventricular geometry and parameters of systolic and diastolic function.	N= 132/ 58.5±9 yrs (180 males and 20 females) Coronary artery disease HIIT (n=67): 91 males + 9 females MICT (n=65): 89 males + 11 females	3 months: Aerobic training on bicycle HIIT: 3x per week of 38-min cycling period: 10-min warm-up at 60–70% of peak HR + 4 bout of 4min at 85–95% of peak HR with 4 bouts of 3-min active pauses at 50–70% of peak HR. MICT: 3x per week of 47-min cycling: 5-min warm-up at 60–70% of peak HR, followed by 37-min continuous at minimum 70–75% of peak HR, and ending with a 5-min cool-down at 60–70% of peak HR.	**HIIT/MICT** ↔ GLS ↔ LVEF
Angadi et al. 2017	To explore the changes in right and LV-GLS and global longitudinal systolic strain rate following 1 month of HIIT in comparison to MICT, examining also the relationship between change in LV and right ventricular strain parameters and change in cardiorespiratory fitness.	N= 19/ 70±18.3 yrs Heart failure with preserved ejection fraction HIIT (n= 17): 8 males + 9 females MICT (n= 13): 4 males + 9 males	4 weeks- 3x per week HIIT: 4 bouts of 4-min each at 85–90% peak HR, interspersed by 3-minute active recovery periods. MICT: 30-min at 70% peak HR.	**HIIT/ MICT** ↔ GLS ↔ LVEF
Malfatto et al. 2017	To evaluate short- and long- term effects of exercise training on left ventricular systo-diastolic function in a specific population of low-risk patients with normal left ventricular ejection fraction, using conventional echocardiography and newer echocardiographic tools.	N= 55/ 61.5±10.5 yrs Myocardial infarction Rehab-group (n= 34): 27 males + 7 males CG (n= 21): 15 males + 6 females	6 months Cardiopulmonary rehabilitation program: 45-min of aerobic exercise on a bicycle or treadmill corresponding to the intensity of the first aerobic threshold. CG: Received counselling regarding life habits.	**Rehab-group** ↑ GLS ↑ LVEF **CG** ↔ GLS ↔ LVEF
Serrano-Ferrer et al. 2016	To determine the effect of lifestyle intervention on LV regional myocardial function in patients with metabolic syndrome and investigate the relationships of the changes in myocardial function to changes in epicardial adipose tissue, inflammatory profile and metabolic syndrome components.	N= 87/ 59.19.±4.6yrs (38 males and 49 females) Metabolic syndrome	CT: 30-70% of 1RM and moderate-endurance +aerobic activities at 30-70% of peak oxygen take.	**CT** ↑ GLS ↑ LVEF

Benda et al. 2015	To examine whether 12-weeks of MICT or HIIT is effective and feasible for heart failure patients, and whether this HIIT-protocol leads to superior effects on fitness, cardiovascular function and quality of life compared to MICT.	N= 20/ 64±8 yrs Heart failure HIIT (n=10): 9 males + 1 females MICT (n=10): 10 males	12-weeks - 2x per week: Intervention in a rehabilitation setting or hospital HIIT: 10-min warm-up at 40% of maximal workload + 10 periods of 3.5-min (1 min at 90% of maximal workload and 2.5 min at 30% of maximal workload) + 5-min cool-down at 30% of maximal workload. MICT: 10-min warm-up at 40% of maximal workload + 30 min at 60–75% of maximal workload + 5-min cool-down at 30% of maximal workload.	**HIIT/ MICT** ↔ GLS ↔ LVEF
Scharf et al. 2015	To evaluate whether short-term HIIT induces detectable morphological cardiac changes untrained men in cardiovascular magnetic resonance imaging.	N= 84/ 43.2±5.1 yrs Sedentary healthy males HIIT (n=42) CG (n=42)	16 weeks- First month: 2x per week Second month: 2-3x per week Last two months: 3-4x per week HIIT: 95–105% of individually calculated HR at the anaerobic threshold during 90s–12 min, alternated with active recovery 1–3 min jogging or fast walking (65%–70% HRmax) + HIIT + a continuous high-intensity running session every fifth session (range, 25–45 min; 85% HRmax). CG: no exercise intervention was provided.	**HIIT/ CG** ↔ GLS ↔ LVEF
Hollekim-Strand et al., 2014	To compare the effects of HIIT and MICT according to current guidelines and other cardiovascular risk factors in patients with type II diabetes mellitus and diastolic dysfunction.	N=37/55.9±6 yrs Type II diabetes mellitus and diastolic dysfunction (23 males and 14 females) HIIT (n=17) MICT (n=20)	12 week, 3x per week HIIT: (4 bouts of 4 minutes each at 90 to 95% of maximal heart rate. Total exercise time: 40 minutes. MICT: according to current guidelines (≥10 min/bout, 210 min/week).	**HIIT/MICT** ↔ GLS
Ofstad et al., 2014	To test the hypothesis that an overall reduction in cardiovascular risk factors type II diabetes mellitus patients during a 2-year multi-intensive intervention would improve LV systolic and diastolic function.	N=89/58±13.5 (63 males and 26 females) Type II diabetes mellitus Concurrent training (CONT) (n=44) CG (n=45)	24 months CONT: Did not report any further detail.	**CONT** ↔ GLS ↔ LVEF **CG** ↑ GLS ↔ LVEF

Sacre et al., 2014	To evaluate the impact of a 6-month exercise intervention on cardiac autonomic function and VO_{2peak}.	N=49/59.5±9.5 yrs (23 males and 26 females) Type II diabetic patients with non-ischemic subclinical left-ventricular dysfunction CT (n=24) CG (n=25)	6 months CT: 2x/week – 20-40 minutes of aerobic exercise and 6-12 minutes of resistance exercises, and home-based exercise prescriptions. Target exercise intensity (moderate to vigorous) was controlled by rating of perceived exertion as well as intermittent verification using heart rate monitors.	**CTP/CG** ↑ GLS ↔ LVEF
Schmidt et al. 2014	To examine the cardiovascular effects of a 1-year intervention consisting of either football training or strength training in elderly, healthy and untrained men	N=26/68.2±3.3 yrs Elderly healthy men Football training (FT) (n=9) Strength training (ST) (n=9) CG (n=8)	1 year: First 4 months: 2x per week Last 8 months: 3x per week FT: first 3 months: 15 min of low-intensity warm-up followed by 3 bouts of 15-min exercise periods interspersed by 2-min rest periods. Last 9 months: shorter warm-up followed by 4 bouts of 15-min exercise periods interspersed by 2-min rest periods. ST: 5-min low intensity warm-up followed by 5 strength training exercises. At the end of each session, the subjects performed 5 min of core training. From the first 3 months: 3 sets per exercise with 1.5-min rest periods between each set. From 4 to 12 months: 4 sets per exercise with 1.5-min rest periods between each set.	**FT/ ST** ↑ GLS ↑ LVEF **CG** ↔ GLS ↔ LVEF
Howden et al. 2013	Investigate the effect of exercise training and lifestyle intervention on CRF, and assess the effect on cardiovascular risk factors, cardiac function, arterial stiffness, and ventricular-vascular interaction in CKD.	N= 72/ 58.9±9.4 yrs (45 males and 27 females) Patients with stage 3–4 CKD Lifestyle intervention (LI) (n=36): 24 males + 12 females CG (n= 36): 21 males + 15 females	12 weeks LI: 2-3x/ week - 150 min: warm-up 20–30 min of aerobic activity using a treadmill, stationary bike, or rowing ergometer + whole-body resistance training with machines and free weights + 4 week Home-based program (booklet depicting resistance exercise using Thera-Bands and a Swiss ball, lifestyle modification facilitated by a dietitian and psychologist).	**LI/ CG** ↑ GLS ↔ LVEF
Obert et al. 2013	To investigate whether lifestyle intervention is able to favourably impact these obesity-related myocardial abnormalities and whether improvements are related to changes in insulin resistance and cardiac remodelling.	N= 48/ 14.5±1.5 yrs (17 boys and 31 girls) Severe obese adolescents Aerobic training (AT) (n=28) CG (n=20)	9 months AT: 3x per week: 9 bouts of 5min each with 4 min of moderate (50% VO2max) and 1 min of intense exercise (85% VO2max). Additionally: moderate physical activities were performed 2x per week during the first 2 months and then 5x per week during the following 7 months. Physical education lessons on how to incorporate exercise into their daily life and how to reduce sedentary behaviours were held. Total daily calorie intake was 2300-2500 kcal (30% fat, 14% proteins, and 56% carbohydrates).	**AT** ↑ GLS ↔ LVEF

Schmidt et al., 2013	To evaluate the effects of a 24-week soccer training group (STG) in pysically inactive men with type II diabetes mellitus on myocardial function, exercise capacity, and blood pressure.	N=17/50±8.1 yrs Type II diabetes mellitus STG (n=8) CG (n=9)	24 week, 2x per week STG: the subjects played five 10-minute games interspersed by two minutes of passive recovery. The average intensity for all training protocol was 82% ± 6% of HR_{max} (145 ±10 bpm)	**STG** ↑ GLS ↔ LVEF **CG** ↑ GLS ↔ LVEF
Rustad et al., 2014	To investigate whether HIIT improved cardiac function and exercise capacity in stable heart transplant recipients by use of comprehensive rest- and exercise-echocardiography and cardiopulmonary exercise testing.	N=48/57±19-72 yrs (33 males and 15 females) Heart transplant recipients HIIT (n= 24) CG (n= 24)	24 weeks HIIT: 3x/week – 38 min: 10-minute warm-up followed by 4 bouts of 4 minutes each at 85-95% of peak HR, separated by 3-minute active pauses. CG: requested to maintain pre-inclusion exercise patterns.	**HIIT/CG** ↔ GLS ↔ LVEF
Smart et al., 2012	To evaluate the effect of exercise training in functional capacity, cardiac function, and quality of life in heart failure with preserved ejection fraction patients.	N=38/64±8 yrs (13 males and 25 females) Heart failure with preserved ejection fraction AT (n=19) CG (n=19)	16 week, 3x per week AT: 60 rpm, 30 minutes with a workload corresponding to a heart rate equivalent to an initial intensity of 60% to 70% peak oxygen.	**AT/CG** ↔ GLS ↔ LVEF
Spence et al., 2011	To examine the "Morganroth hypothesis" using a prospective randomised trial of distinct and controlled training interventions using MRI.	N=23/27.5±1.6 yrs Healthy males AT (n=10) RT (n=13)	24 weeks AT: eight three week mesocycles with the program divided into three training phases. The first four mesocycles consisted of low-moderate intensity exercise. The second phase increased running intensity and included elements of hill running and short intervals. In the last phase intensity was maintained but volume was somewhat reduced. RT: four week mesocycles with a focus on muscular strength, including elements of Olympic weightlifting. The first phase consisted aimed to condition the body and develop correct lifting technique. Each mesocycle was progressively overloaded so that the volume and load peaked in the third week with the fourth week acting as a recovery week.	**AT/RT** ↔ GLS ↔ LVEF

Ingul et al., 2010	To measure cardiac function before and after three months of aerobic interval training in obese adolescents and to compare the findings with those in lean counterparts	N=20/14.8±1.2 Obese adolescents (12 males and 8 females) HIIT (n=10) CG (n=10)	13 weeks, 2x per week HIIT: warm-up period of 10 minutes as 70% of the maximal heart rate followed by an interval of 4 minutes at 90% to 95% of the maximal heart rate and then 3 minutes of active recovery at 70% of the maximal heart rate, for a total of 4 intervals. The training session ended with a 5-minute cool-down period. The total training time was 40 minutes.	**HIIT** ↑ GLS ↑ LVEF
Hordern et al., 2009	To identify the effects of a one-year exercise intervention on myocardial dysfunction in patients with type II diabetes mellitus.	N=176/55.5±10.1 Adults with type II diabetes (64 males and 112 females) LI (n=88) CG (n=88)	16 weeks LI: first 4 weeks consisted in a supervised, gym-based exercise program, followed by home-based training (12 weeks) with the aim of reaching a minimum of 150 minutes of at least moderate-intensity exercise each week. CG: Individuals have received standard risk factor intervention for type II diabetes mellitus, including support to maintain a target blood pressure at normal levels, smoking cessation, and attainment of lipid targets.	**LI/CG** ↔ GLS ↔ LVEF

LV, left ventricle; HIIT, high-intensity interval training; MICT, moderate-intensity continuous training; CG, control group; VO_2, oxygen uptake; GLS, global longitudinal strain; LVEF, left-ventricle ejection fraction; HFPEF, heart failure with preserved ejection fraction; HR, heart rate; RM, maximum repetition; CRF, cardiorespiratory fitness; CKD, chronic kidney disease.

Quantitative outcomes

Thirteen studies were excluded from the meta-analysis for not providing enough data for group comparison. Thereupon, 18 trials were included in the meta-analysis [43,44,46,48–52,55-57,60,63–67].

Effects of different exercise modalities on global longitudinal strain (GLS)

The pooled analysis showed that aerobic exercise improved GLS significantly (SMD -0.33 [CI 95%, -0.56 to -0.10], p = 0.005) compared to the CG (Fig 2.a). Low heterogeneity was detected for this analysis (I^2 = 14%; p = 0.31). No significant difference was observed for combined training (SMD -0.35 [CI 95%, -0.84 to 0.15], p = 0.17) (Fig 2.b), in which a high heterogeneity between studies was reported (I^2 = 83%; p < 0.001). Resistance training did not change GLS (SMD -0.60 [CI 95%, -1.59 to 0.38], p = 0.23) (data not shown). However, only one study with this exercise modality was included in this analysis.

	Experimental			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
a. Aerobic vs Control								
Huang et al. 2019a	0.1	0.58	18	0.1	0.82	9	4.8%	0.00 [-0.80, 0.80]
Huang et al. 2019b	0.3	0.72	18	0.1	0.82	9	4.8%	0.26 [-0.55, 1.06]
Ingull et al. 2018a	-1.6	3.44	23	-0.1	3.72	11	5.3%	-0.41 [-1.14, 0.31]
Ingull et al. 2018b	-0.8	3.83	26	-0.1	3.72	11	5.5%	-0.18 [-0.89, 0.53]
Malfatto et al. 2017	-2.2	4.06	34	0.9	4.23	21	6.7%	-0.74 [-1.30, -0.18]
O´Driscoll et al. 2018	-0.8	2.87	40	0.1	2.78	40	7.8%	-0.32 [-0.76, 0.13]
Rustad et al., 2012	-0.4	2.84	24	0	2.86	24	6.6%	-0.14 [-0.70, 0.43]
Schimidt et al. 2014	-1.5	2.22	9	0.5	3.05	8	3.7%	-0.72 [-1.71, 0.27]
Schmidt el al. 2013	-1.5	0.94	8	0.5	1.5	9	3.2%	-1.49 [-2.61, -0.38]
Smart et al. 2012	1.7	8.46	19	3	6.55	19	6.0%	-0.17 [-0.81, 0.47]
Subtotal (95% CI)			**219**			**161**	**54.5%**	**-0.33 [-0.56, -0.10]**
Heterogeneity: Tau² = 0.02; Chi² = 10.48, df = 9 (P = 0.31); I² = 14%								
Test for overall effect: Z = 2.82 (P = 0.005)								
b.Combined vs Control								
Hordern et al. 2009	0.7	2.8	88	0.7	3.1	88	9.1%	0.00 [-0.30, 0.30]
Howden et al. 2013	0.4	0.67	36	1.3	0.5	36	7.0%	-1.51 [-2.03, -0.98]
Howden et al. 2018	0.1	2.56	14	0.9	2.02	14	5.2%	-0.34 [-1.08, 0.41]
McGregor et al. 2018	0.3	3.82	18	0	3.37	18	5.9%	0.08 [-0.57, 0.74]
Ofstad et al. 2014	1.8	6.7	44	1	4.29	45	8.0%	0.14 [-0.27, 0.56]
Sacre et al. 2014	4.3	0.94	24	4.8	0.96	25	6.6%	-0.52 [-1.09, 0.05]
Subtotal (95% CI)			**224**			**226**	**41.7%**	**-0.35 [-0.84, 0.15]**
Heterogeneity: Tau² = 0.31; Chi² = 29.86, df = 5 (P < 0.0001); I² = 83%								
Test for overall effect: Z = 1.37 (P = 0.17)								
Total (95% CI)			**443**			**387**	**100.0%**	**-0.34 [-0.59, -0.10]**
Heterogeneity: Tau² = 0.15; Chi² = 40.77, df = 15 (P = 0.0003); I² = 63%								
Test for overall effect: Z = 2.71 (P = 0.007)								
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.87), I² = 0%								

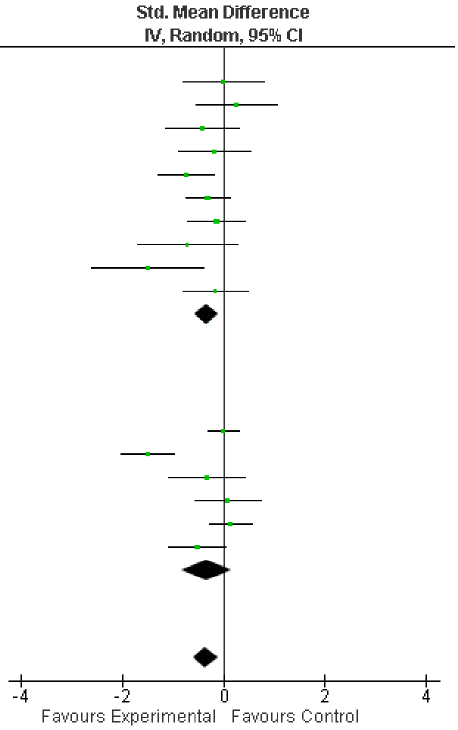

Fig 2. Meta-analysis’ forest plot with random-effect model for the comparison of the effect of training vs control group on global longitudinal strain.

Considering the effects of HIIT versus MICT on GLS, we observed significant superior effects following HIIT than MICT (SMD -0.25 [CI 95%, -0.48 to -0.02], $p = 0.04$). Low heterogeneity was reported for this analysis (I^2 = 23.4%; $p = 0.78$) (Fig. 2).

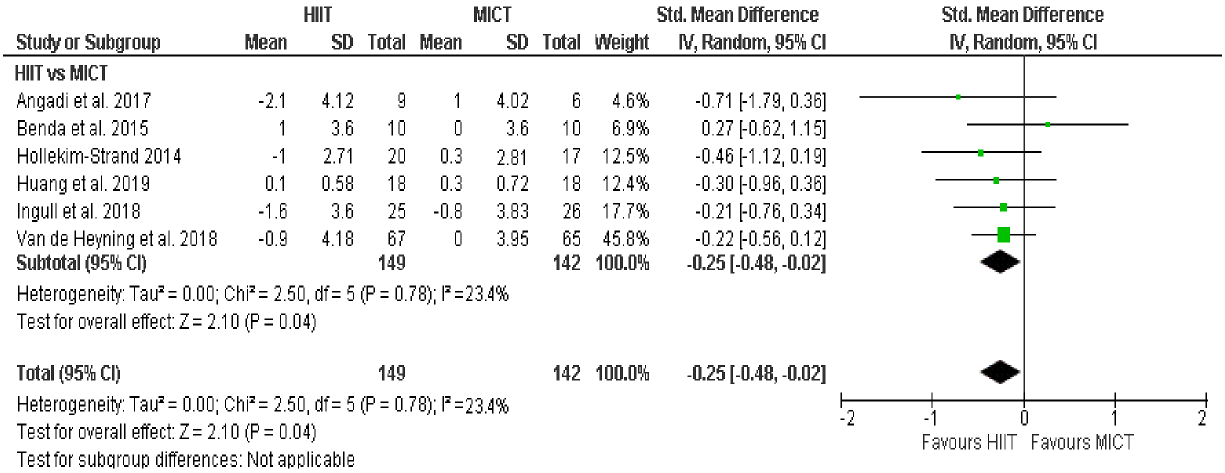

Fig 3. Meta-analysis' forest plot with random-effect model comparing the effects of high-intensity interval training vs. moderate-intensity continuous training on global longitudinal strain.

Effects of different exercise modalities on left ventricular ejection fraction (LVEF)

Regarding the comparison between exercise training vs. CG on LVEF, the analysis according to exercise modality has shown that neither aerobic (SMD 0.22 [CI 95%, -0.05 to 0.50], $p = 0.12$) (Fig 4.a) nor combined training (SMD -0.05 [CI 95%, -0.74 to 0.64], $p = 0.88$) (Fig 4.b) reported any significant change, in which moderate (I^2 = 50%; $p = 0.03$) and high (I^2 = 81%; $p < 0.001$) heterogeneity between studies were observed, respectively. Resistance training induced a significant increase on LVEF (SMD 2.22, [CI 95%, 0.94 to 3.50], $p <$ .001). However, only one study was included in this analysis (data not shown).

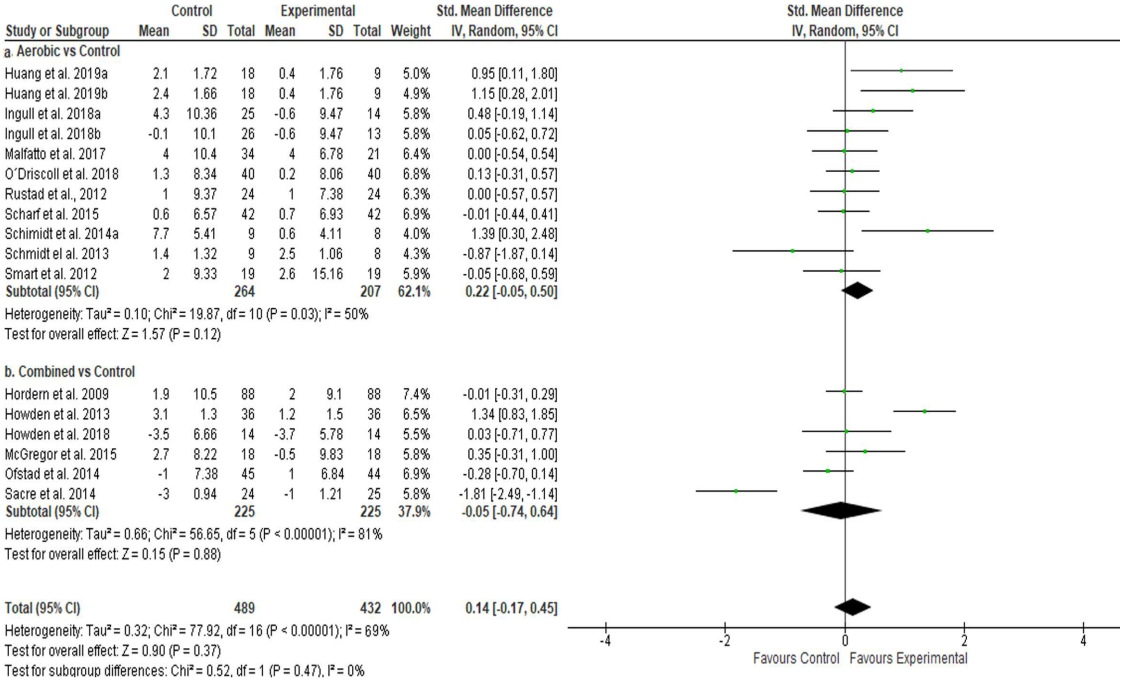

Fig 4. Meta-analysis' forest plot with random-effect model comparing the effect of exercise training vs. control group on left ventricular ejection fraction.

Comparing the effects of HIIT and MICT on LVEF, HIIT presented a superior effect of positively changing LVEF (SMD 0.76 [CI 95%, 0.22 to 1.30], p = 0.00) (Fig. 5), in which a moderate heterogeneity was reported (I^2 = 69%; p = 0.01).

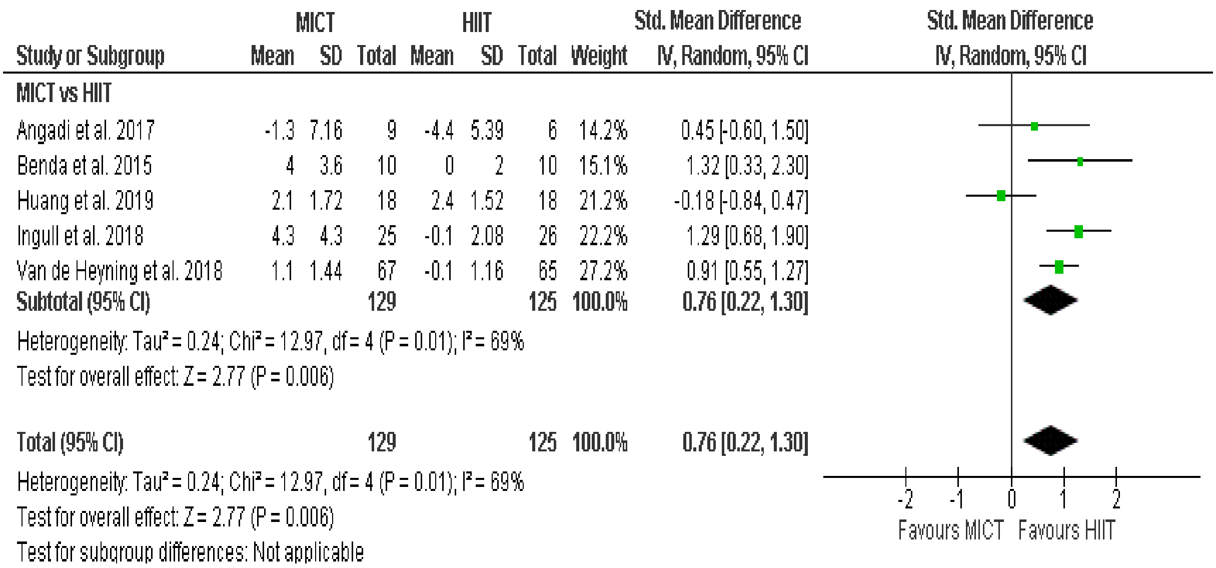

Figure 5. Meta-analysis' forest plot with random-effect model comparing the high-intensity interval training vs. moderate-intensity continuous training on left ventricular ejection fraction.

Effects of different exercise modalities on subgroup analyses

The subgroup analyses of the effects of physical exercise on GLS have demonstrated that physical exercise induced a greater improvement of GLS in adults and elderly (SMD -0.40[CI 95%, -0.61 to -0.19], and SMD -0.40[CI 95%, -0.75 to -0.05], respectively). Although interventions with 12 weeks or less still reported significant changes in GLS (SMD -019[CI 95%, -0.37 to -0.01]), intervention periods that lasted longer than 12 weeks presented superior effects on GLS (SMD -0.55[CI 95%, -0.78 to -0.32]). As regards to exercise intensity, both moderate and high intensities promoted equivalent effects on GLS (SMD -0.38[CI 95%, -0.62 to -0.14] and SMD -0.37[CI 95%, -0.54 to -0.19], respectively). Similar results were verified for exercise volume, in which changes in GLS occurred regardless of the exercise volume (e.g. <150 or ≥150 min/week) (SMD -0.29[CI 95%, -0.46 to -0.12] and SMD -0.37[CI 95%, -0.65 to -0.08], respectively). Regarding the individuals' pathological characteristics, it was observed that patients with metabolic impairments had a greater response of GLS following physical exercise (SMD -0.60[CI 95%, -0.91 to -0.29]). However, physical exercise also presented a tendency to induce positive changes in GLS for cardiac and renal patients, besides healthy individuals.

Table 3. Subgroup analyses of the effects of physical exercise on global longitudinal strain

	GLS (%)		
	References	**n**	**Std. Mean Difference (95% CI)**
AGE GROUP			
Youth	[43,53,59,63,65]	163	-0.26[-0.59, 0.06]
Adult	[45,48-50,52,54–56,58, 60,62,64,66,68]	587	-0.40 [-0.61, -0.19]
Elderly	[44,46,51,57,61,67]	136	-0.40 [-0.75, -0.05]
INTERVENTION PERIOD			
≤12 weeks	[32,43,46,48,52,61,63–67]	429	-0.19 [-0.37, -0.01]
> 12 weeks	[44,45,49-52,54-60,62]	459	-0.55 [-0.78, -0.32]
EXERCISE INTENSITY			
Moderate	[44-46,48,52,60,63,66,67]	369	-0.38 [-0.62, -0.14]
High	[46,48,51,53,56,59,63-67]	258	-0.37 [-0.54, -0.19]
EXERCISE VOLUME			
< 150 min/week	[46,48,51,53,55-57,59,63-67]	401	-0.29 [-0.46, -0.12]

≥150 min/week	[32,43-45,48-50,52,54,58,60-62]	498	-0.37 [-0.65, -0.08]
MEDICAL CONDITIONS			
Cardiac conditions	[44,46,56,57,61,64,67]	292	-0.24 [-0.49, 0.04]
Metabolic conditions	[45,53,59,63]	375	-0.60 [-0.91, -0.29]
Healthy	[43,51,54,58,65]	139	-0.29 [-0.61, 0.03]
Renal patients	[52,62]	66	-0.41 [-1.01, 0.18]
Cancer patients	[32]	14	0.05 [-0.69, 0.79]

Discussion

The main finding of our systematic review and meta-analysis was that aerobic training improved GLS significantly in comparison with the CG. Besides that, HIIT promoted superior improvement in GLS when compared to MICT. However, resistance training alone or combined with aerobic training does not improve GLS significantly. LVEF does not change significantly with aerobic training alone or combined with resistance training. These findings demonstrate that GLS is a more sensitive measurement of exercise-induced changes when compared to LVEF, and that HIIT appears to be more effective than MICT in inducing changes in cardiac mechanics when compared to other types of training.

There is a considerable and up-to-date body of evidence supporting the positive effects of aerobic exercise on cardiac function [68-72]. In fact, aerobic exercise improves diastolic function by reducing early transmitral filling velocity (E)/early relaxation tissue velocity (E’) (E/E’) and deceleration time, which represents an improvement in LV filling pressures [69-71]. Also, it increases LVEF, considered an important marker of systolic function [68, 72]. However, the prognostic value of LVEF has been questioned [12]. Although the LVEF measurement is a validated method that has been widely used for decades, the assessment of myocardial deformation with GLS has shown greater sensitivity in evaluating the LV systolic function when compared to the LVEF measurement, being capable of identifying even subclinical subtle alterations [12]. The findings of the present meta-analysis revealed that aerobic exercise training was effective in improving GLS in chronically diseased as well as in healthy individuals, promoting an effect size of -0.33 (CI 95%, -0.56 to -0.10) in GLS. Although apparently modest, this may be considered a compelling improvement, given the fact that a change of 1% in GLS represents an increase of 7% of all-cause mortality and 18% of cardiovascular events risk [73]. Moreover, it is still not clear whether pharmacological treatment can promote the same benefits as aerobic exercise in patients with isolated abnormal GLS [24], reinforcing the importance of aerobic exercise in reversing LV systolic function subtle abnormalities.

The noteworthy benefits that aerobic exercise can induce in LV systolic function may be essentially attributed to the reduced afterload. It occurs via the reduction of LV pressure which, combined with an optimized cardiac output due to the performance of aerobic exercise, suggests a decrease in vascular resistance and, in consequence, reduced afterload [74]. In addition to that, there is an increase in the stroke volume coupled to an unchanged end-diastolic volume but reduced end-systolic volume, representing improved cardiac contractility and reduced afterload [75]. This results in an improved vascular function, causing a lightened impact on afterload, and consequently enhancing LV systolic function [65,76]. Howbeit, although predominantly affected by afterload, preload conditions seem to play a role on LV systolic function [38]. Studies that have induced an increase in preload by saline infusion and passive leg elevation found significant positive associations between an increase in preload and improvements in GLS [77,78]. The improvement in GLS, as a consequence of an improved preload condition, may be attributed to an increase in end-diastolic volume, which augments the stretch of LV fibers [78]. This greater stretch due to a preload increase drives to an increase in the contraction force and velocity, as expressed by the Frank-Starling mechanism [79].

There are some other possible factors that may explain the improvement of GLS by aerobic training, such as the reduction of cardiac lipotoxicity, inflammation (e.g. by reducing the serum levels of TNF-α and IL-6 and increasing the plasma levels of IL-10), and calcium-related abnormalities [53]. Subendocardial myofibers, which are arranged parallel to the LV long axis, are primarily responsible for longitudinal function [80,81]. These myofibers are most vulnerable to cardiac events, being also more affected by oxidative stress than other layers [82]. Thus, the improvements in inflammatory profile and oxidative stress induced by aerobic exercise [83] diminished the vulnerability of these myofibers to ischemia, thus improving the longitudinal cardiac function.

Moreover, the exercise-induced changes in cardiac autonomic modulation by an increase in heart rate variability, via augmented parasympathetic and decreased sympathetic activity [84], accounts for improvements in LV function. The reflex inhibition of central sympathetic activation leads to an acute resensitization of adrenergic receptors, which may induce improvements in cardiac mechanics and, consequently, in GLS [85].

Although HIIT has been shown to provide superior effects in vascular function and cardiorespiratory fitness, having also a tendency to elicit greater effects in other health-related variables, such as traditional CVD risk factors, oxidative stress, inflammation and insulin sensitivity when compared to MICT [86–88], this difference is less clear in terms of LV systolic function. Recently, Tucker and colleagues [68] did not find significant differences between HIIT and MICT in improving LVEF in heart failure patients with reduced EF (HFrEF), since both aerobic training protocols induced approximately 3.7% increase in LVEF. On the contrary, our meta-analysis showed the superiority of HIIT over MICT in improving GLS -0.25 (CI 95% -0.48 to -0.02) and LVEF 0.76 (CI 95% 0.22 to 1.30). The discrepancy of these findings may be related to differences in the populations included in the studies. The present study included not only HFrEF but also other chronic conditions (e.g. metabolic, renal, cancer and other cardiac conditions), which could be more responsive to HIIT in comparison to MICT, considering that most of these conditions have preserved LVEF.

As regards to the superior effects of HIIT on improving cardiac function, HIIT rather than MICT is able to increase blood capillary density [74]. It improves oxidative metabolism, being this improvement not limited to the skeletal muscle, but also expanded to the heart [74,89]. Moreover, HIIT induced a greater load on the central circulation, inducing preeminent cardiac adaptations due to modifications in intracellular calcium regulation [65]. Interestingly, peripheral adaptations in the vasculature may play a role in improving cardiac health following HIIT [74]. Considering that GLS is mainly affected by afterload conditions [90], it is pertinent to infer that a lessened afterload impact, caused by the performance of HIIT, is able to improve GLS values.

Concerning the effects of combined exercise, the meta-analysis has shown that no significant differences were found regarding this exercise modality on both GLS and LVEF. These findings go hand in hand with two other meta-analyses [68, 72], which reported that no significant improvements in LVEF were verified after combined or resistance training. In resistance training, there is an intermittent increase in blood pressure, causing a pressure overload to the left ventricle, also increasing the cardiomyocyte cell diameter and left ventricular wall thickening caused by the addition of sarcomeres within cardiomyocyte [91]. This concentric cardiac hypertrophy can be understood as a compensatory mechanism that occurrs in order to stabilize the imbalance caused by the afterload. Thus, the performance of resistance training leads to higher afterload, causing LV hypertrophy and promoting dysfunction in LV systolic function, subtly identified by a decreased in GLS [92,93]. Nonetheless, despite no significant difference was observed for combined training on GLS and LVEF, recent evidence has reported that combined training provides more favorable effects on CVD risk factors than the performance of aerobic or resistance training alone [94,95]. Aerobic exercise promotes greater improvements in cardiorespiratory and cardiometabolic parameters. Meanwhile, resistance exercise exerts positive effects on muscular strength, body composition, such as waist circumference, and insulin sensitivity [94,96], reiterating the importance of this exercise modality. Therefore, the findings of the present study should not be misinterpreted and the combined training should not be overlooked, since it provides noteworthy benefits for CVD risk factors. With respect to resistance training, our meta-analysis demonstrated that resistance training did not change GLS, but promoted a substantial increase in LVEF. However, given the fact that only one study with resistance training was included in the analysis, we decided to not generalize the results, avoiding any discussion on this specific topic due to the potential risk of bias.

We have also performed subgroup analysis with the aim of identifying potential variables that could exert some influence on the effects of exercise on GLS. As a result, we have observed that physical exercise promotes more substantial effects on GLS in adults and elderly than in youth. The natural aging process might be the most reasonable justification for this outcome. There is natural artery stiffening throughout life, which means that the older an individual is, the stiffer his arteries are. This arterial stiffness increases the afterload and consequently affects GLS negatively [97]. Thus, physical exercise causes vasodilation of the peripheral arteries, reducing therefore the afterload, promoting salutary effects on GLS [98]. Also, since there is a progressively impairment of GLS throughout lifetime, it is pertinent to assume that GLS values in adults and elderly are worse than in youth. In such wise, physical exercise would be able to better affect a worse and slightly impaired condition in comparison with an unaltered one [99].

Regarding exercise variables, our findings have shown that longer periods of exercise exposure (> 150 min/week) promote better results on GLS. Moreover, regardless of the exercise modality, both moderate and high exercise intensities similarly improved GLS. Our findings support the groundwork tenet of the physical exercise guidelines, which recommend at least 150 minutes of moderate or 75 minutes of vigorous physical activity per week. Furthermore, it is pivotal to reiterate that greater amounts of physical exercise result in additional health benefits [100-102]. However, it is noteworthy the dearth of studies with low-intensity exercise protocols. For this reason, it is unclear whether low intensity physical exercise would be able to promote positive effects on GLS. In addition, our findings have demonstrated that individuals with metabolic dysfunctions tended to respond better to physical exercise interventions, improving GLS. Likewise, there was a tendency for improvements in GLS following physical exercise performance in individuals with cardiac comorbidities. Physical exercise induces improvements in cardiac and inflammatory markers, which are altered in individuals with metabolic and cardiac comorbidities and are closely associated with an increase in cardiac afterload [91]. Taking this into consideration, the physical exercise salutary effects on inflammatory markers, lessening their impaired condition, affect also the afterload and, consequently, GLS.

To our knowledge, this is the first study that has systematized and quantified the current knowledge about the effects of exercise training on GLS in a wide range of healthy and chronically diseased subjects, clarifying also how different exercise modalities and intensities affect the LV systolic function. Nevertheless, the present study has several limitations that need to be mentioned. Firstly, although the number of studies assessing the effects of aerobic and combined exercises on GLS is satisfactory, there is a clear paucity of studies analyzing the effects of resistance exercise on this variable, which is why the effects of this exercise modality on GLS are still poorly understood. Secondly, the high heterogeneity found in some analysis is an assumed limitation of this study. Nevertheless, for the main analysis of the present study (e.g. aerobic exercise vs. control on GLS), the heterogeneity reported was low (14%). Thirdly, we chose to verify the effects of exercise training on GLS in view of its closer association with CVD mortality when compared to other variables of cardiac function. Yet, significant alterations in other cardiac strains (e.g. circumferential and rotational), as well as twist mechanics, could occur, as evidenced by Beaumont and colleagues [103] in a meta-analysis carried out in athletes, which must be explored in more depth. Lastly, despite the methodological strictness of the present systematic review and meta-analysis, which rigidly followed the PRISMA guidance, it is possible that some potential reference has been erroneously disregarded during the paper screening process.

In summary, aerobic exercise was able to promote salutary changes in LV systolic function, represented by GLS. HIIT seemed to present superior effects on this variable in comparison with MICT. Notwithstanding, the scarcity of studies concerning resistance training hampers the analysis of the effects of this exercise modality on GLS. Thus, more studies are imperative in order to better elucidate this issue. Additionally, provided that aerobic exercise has been proved to be effective on the improvement of GLS, studies aiming to verify the impact of low-intensity aerobic exercise are required since the effects of this intensity of aerobic exercise are still underexplored.

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Artigo 2

Acute effects of high-intensity interval training and moderate-intensity continuous training on left ventricular function and myocardial mechanics in obese women

Introduction

Nowadays, approximately 1.9 billion and 609 million adults have body mass index (BMI) at levels indicating obesity and overweight, respectively, in a worldwide worrisome scenario (CHOOI et al., 2019). This alarming prevalence represents nearly a third of the entire world population, placing obesity as one of the biggest societal health care burden (GBD, 2015). Obesity is the cornerstone for a wide range of physiological impairments (CHOOI et al., 2019), increasing also the risk for developing cardiovascular disease (CVD) (MANDVIWALA et al., 2016), which are the leading cause of death around the globe (WHO, 2017).

The increase of CVD risk as a consequence of obesity occurs due to changes in body composition, that can affect negatively hemodynamics, altering heart structure and hampering cardiac function (CARBONE et al., 2019; BELLO et al., 2016; VASAN, 2003). Greater obesity-related anthropometric parameters seem to be associated with impaired left ventricle (LV) dimension, such as LV walls, mass and cavity size independently of the sex (BELLO et al., 2016). However, there is a higher likelihood for obese women to present abnormal LV geometry (BELLO et al., 2016).

In terms of cardiac function, it is suggested that obesity negativelly affects both LV diastolic and systolic functions (ALPERT et al., 2016). The same author in a recent published study has demonstrated impairments in mitral A-wave velocity, mitral E'-wave velocity, and the ratio of early diastolic transmitral velocity (E) to early diastolic tissue velocity (E') (E/E'ratio), all parameters of diastolic function (ALPERT et al., 2018). These findings corroborate with previous evidence that has found that obese individuals presented lessened cardiac systolic and diastolic function (DIAS et al., 2017; ALP et al., 2014). Additionally, loading conditions seem to play a crucial role in the development of obesity-related LV dysfunction. Evidence suggests that LV end-diastolic volume

(LVEDV) is positively correlated with obesity, mostly due to a left atrial enlargement, which generates a volume overload (TURKBEY et al., 2010; ALPERT et al., 2016). Regarding LV systolic function, obesity also exerts a negative influence on LV systolic function parameters (GERDTS et al., 2013). Conflicting evidence makes unclear the association between obesity and LV ejection fraction (LVEF) (TURBKEY et al., 2010; BELLO et al., 2016; BLOMSTRAND et al., 2019), wherein a normal or supra-normal LVEF in obese subjects has been shown. Nevertheless, a growing body of evidence points to the closer association between weight excess and global longitudinal strain (GLS) (HALLAND et al., 2019; CAÑON-MONTAÑEZ et al., 2017; BELLO et al., 2016), a new and reliable tool for LV systolic function assessment (SINGH et al., 2019). A plenty of studies have demonstrated abnormal GLS in asymptomatic obese individuals in speckle-tracking echocardiography assessment. Interestingly, Bello and colleagues (2016) have found an association between obesity and both LV systolic and diastolic functions in women, whilst the same associations were not verified in men, indicating that this population could be more exposed to cardiac dysfunctions.

The role of aerobic exercise in improving both systolic and diastolic functions has been extensively debated in literature, wherein contrasting outcomes emphasize the lack of consensus on whether aerobic training elicits a positive effect on cardiac function (TUCKER et al., 2019; FUKUTA et al., 2019; PEARSON et al., 2017). The meta-analysis conducted by Tucker et al. (2019) reported that both high- (HIIT) and moderate- intensity continuous training (MICT) significantly increased LVEF. In addition, the meta-analysis carried out by Pearson and colleagues (2017) revealed that aerobic exercise was able to improve diastolic function by enhancing the E/E’ratio. On the other hand, two meta-analyses did not find an improvement on cardiac function with aerobic exercise training (FUKUTA et al., 2019; PANDEY et al., 2014). However, all the aforementioned studies were conducted in heart failure with preserved or reduced EF patients and with a chronic aerobic training protocol. Therefore, the acute effects of aerobic exercise as well as the chronic effects of aerobic training on systolic and diastolic parameters in other exposed populations is yet to be better explored.

Concerning the effects of aerobic training on cardiac function in obese individuals, longitudinal studies have reported salutary changes on both systolic and diastolic function with aerobic training protocols, whereas both HIIT and MICT seems to elicit the same (INGUL et al., 2018; OBERT et al., 2013; INGUL et al., 2010). Moreover, to our knowledge, no study has verified the acute effects of aerobic exercise on cardiac function in obese women, highlighting the evident paucity of acute protocols in this population. Having in mind that women could be more exposed to cardiac dysfunctions than men, and that obese is closely related to LV systolic and diastolic impairments, it becomes imperative to study the acute effects of aerobic exercise on this population, since it could drive to physiological adaptations that may be hazard to them. Thus, the aim of the present study was to verify the acute effects of different modalities of aerobic exercise (e.g. HIIT and MICT) on cardiac function in obese women.

Methods

Study Design

The present study has a randomized crossover design. The individuals were subjected to three experimental conditions: HIIT, MICT, and control (CO). Each condition was conducted on different days, separated by at least 72h, at the same time of the day in a quiet, temperature-controlled room. The measurements were performed immediately before and repeated at five (t5) and 35 (t35) minutes after each experimental condition.

Participants

Twenty obese women were firstly recruited from the local community. The eligibility criteria for inclusion consisted in being female, aged 38-35 years, and body mass index (BMI) between 30-40 kg/m^2. The exclusion criteria were the following: participation in weight reduction programs, weight-related surgical procedures or exercise training programs in the last six months; be physically active according to IPAQ (MATSUDO et al. 2001); physical inaptitude to perform the exercise experimental conditions; presence of endocrine, vascular, cardiac diseases or other cardiac risk factors apart from obesity; use of medications. A medical evaluation was carried out by an experienced in order to verify whether the participants could fit in any of the previously established exclusion criteria. The assessment was based on clinical history, physical examination, and cardiovascular-related exams, which included resting electrocardiogram, exercise treadmill test and transthoracic echocardiogram, and carotid Doppler ultrasonography. Those who did not complete all the experimental conditions as well as did not perform all the assessments were excluded from the analysis. This study was approved by the local ethics committee (Comitê Permanente de Ética em Pesquisa com Seres Humanos – COPEP. Protocol number: 91380218.4.0000.0104), and registered as a clinical trial on the Brazilian Clinical Trials Registry (ReBec) (RBR-3v3dqf). In addition, the present study is in accordance with the 1964 Declaration of Helsinki and its later amendments, rigorously following the requirements settled on the Resolution 466/2012 of the Brazilian National Health Council as well.

Anthropometric and body composition assessments

Body mass (BM) and stature were measure by means of a mechanical anthropometric scale with coupled stadiometer (Filizola®, São Paulo, Brazil). Waist circumference (WC) was measured positioning an inelastic metric tape (Sanny®, São Paulo, Brazil) at the bottom of the rib cage and the top of the iliac crest. BMI was calculated and classified according to the World Health Organization (WHO, 1995). Body composition was evaluated by bioelectrical impedance device (Maltron® BF-906, Rayleigh, UK).

Maximal aerobic power (VO_{2max}) and heart rate (HR_{max})

A maximum aerobic test was performed on a treadmill (Inbramed®, Porto Alegre, Brazil), to estimate VO_{2max} and maximum heart rate (HR_{max}). This exercise protocol starts at 2.7 km/h and 10% inclination, having progressive increments in both velocity and inclination each tree-minute period. The test was stopped when the participant reached volitional exhaustion (Bruce, 1971).

VO_{2max} was estimated by a software-provided equation (Micromed®, São Paulo, Brazil).

Exercise training protocols

HIIT and MICT exercise sessions were carried out on a treadmill (Movement® LX-160i-C4, São Paulo, Brazil). Participants were constantly controlled to maintain the desired HR training zone, and verbal encouragements were given when necessary. Additionally, the rate of perceived exertion (RPE) was applied throughout the exercise conditions. Both exercise protocols were standardized to guarantee that they are isocaloric (Rognmo et al., 2004).

The proposed HIIT started with 10 minutes of warming-up (e.g. five minutes at 55-65% of HR_{max} and five minutes at 65-75% of HR_{max}). Thereafter, four bouts of four minutes each were performed at 85-95% of HR_{max}, interspersed by three-minute periods at 65-75% of HR_{max}. The protocol ended with five minutes of cooling down (e.g. three minutes at 65-75% of HR_{max} and two minutes at 55-65% of HR_{max}). The exercise session had a total duration of 40 minutes. The MICT session consisted of walking/running at 65-75% of HR_{max}, with a five-minute warm-up at 55-65% of HR_{max}, ending with a two-minute cool down at 55-65% of HR_{max}. The session total time had 48 minutes. In the CO, the individuals remained seated for 30 minutes in a quiet temperature-controlled room.

Echocardiography assessments

The transthoracic echocardiography assessments were made using a phased-array transducer (GE M3S/M4S, 1.5-4 MHz) on an ultrasound system (Vivid T8, General Electric Medical Systems®, Milwaukee, WI, USA). Individuals were laid in the left lateral decubitus, maintaining this position during the whole assessment. LV systolic and diastolic function were assessed by means of 2D STE echocardiography. GLS was analysed using the semi-automatic STE algorithm in two parasternal short-axis (e.g. basal and apical) and three apical (e.g. four-chamber, two-chamber, and long-axis) methods (Nesser, 2009). A visual inspection of the endocardial borders was performed. When a poor tracking quality was achieved, the endocardial trace or width were manually adjusted in order to obtain an appropriate trace of the endocardial borders. LVEF and LV volumes at the end of systole (LVESV) and diastole (LVEDV) were determined by an automated ejection fraction measurement software (Auto- EF – General Electric Medical Systems®, Milwaukee, WI, USA).

Doppler pulse wave analysis was performed in order to determine diastolic trans-mitral blood flow velocities for peak early (E) and late (A) fillings, and the ratio of E to A wave, which is a sensitive parameter of LV diastolic function (Brun, 1992). In addition, tissue Doppler imaging was collected at the lateral and septal mitral annulus to assess peak early diastolic (E’) and peak late diastolic (A’) velocities. The echocardiography assessments were performed by an experienced investigator who was blinded to know which experimental condition the individual was about to perform.

Statistical analysis

Continuous variables are expressed as mean The sample size calculation was performed with the aid of the software G Power® 3.1, in which the statistical power was set in 83%, significance level 5%, and effect size 0.65. Comparisons between groups and moments were made via two-way repeated measures ANOVA, followed by the Sidak multiple comparisons tests. Pearson correlation coefficients were evaluated between Δ pre and t5 echocardiographic and hemodynamic parameters of exercise conditions (HIIT and MICT). Data were analysed using the Statistical Package for Social Sciences (SPSS, version 23) (IBM®, New York, USA).

Results

Fifteen volunteers completed the experimental conditions. The inclusion procedure is detailed in figure 1. The general characteristics of the participants' baseline are presented in table 1.

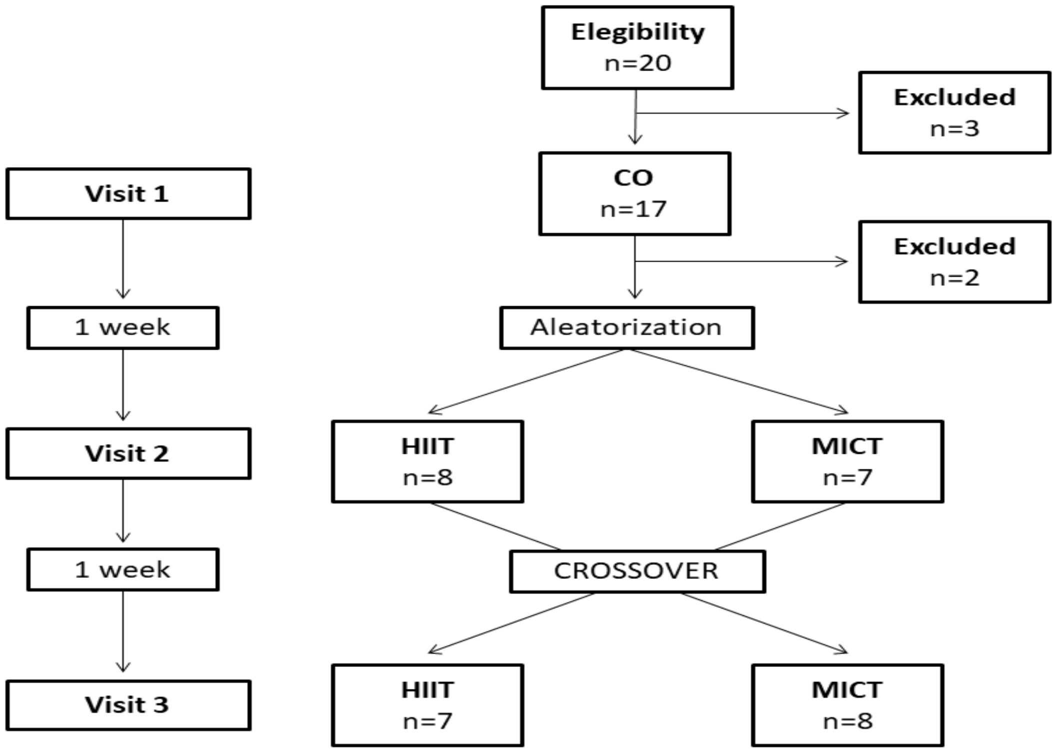

Figure 1. Flowchart of the inclusion procedure of the present study.

Table 1. Baseline sample characteristics (*n*=17).

Variables	Baseline
Age (years)	25.2±4.8
Anthropometric and body composition	
Body weight (kg)	88.2±11.5
Body mass index (kg/m²)	33.5±3.3
Waist circumference (cm)	91.1±7.2
Body fat (%)	43.4±3.7
Fat mass (kg)	38.5±7.8
Fat free mass (kg)	49.8±4.6
Physical Activity Level	
Light (min/week)	60.0(25.0-135.0)
Moderate (min/week)	90.0 (25.0-140.0)
Vigorous (min/week)	0.0 (0.0-60.0)
Cardiorrespiratory fitness	
Heart rate (beats/min)	190.5±12.0
Treadmill speed (km/h)	6.3±0.6
Treadmill gradiente (%)	15±1.0
VO_{2max} (ml/kg/min)	33.2±4.8
Hemodynamics	
Resting HR (beats/min)	72.7±13.5
Peripheral SBP (mm Hg)	124.6±12.6
Peripheral DBP (mm Hg)	74.1±8.5
Central SBP (mm Hg)	110.6±9.9
Central DBP (mm Hg)	75.1±8.6
Echocardiographic characteristics	
LVIDd (mm)	47.7±3.9
LVIDs (mm)	29.1±3.5
LVST (mm)	9.6±1.1
LVPWd (mm)	11.1±1.8

VO_{2max}, maximal oxygen intake; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVIDd, Left ventricular internal diameter in diastole; LVIDs, Left ventricular internal diameter in systole; LVST, left ventricular septal thickness; LVPW, left ventricular posterior wall.

Regarding exercise protocols characteristics, HR was higher in HIIT (179.7 ± 10.5 bpm) than MICT (137.3 ± 8.3 bpm) (Figure 2), and RPE was also higher in HIIT (15.0 ± 2.3) in comparison with MICT (11.0 ± 2.6). Although MICT presented a higher covered distance (3.9 ± 0.5 vs. 3.2 ± 0.3 km, p= <0.001), the total energy expenditure was similar between both exercise protocols (HIIT = 386 ± 38.5 vs. MICT = 379.9 ± 35.2 kcal, p = 0.631).

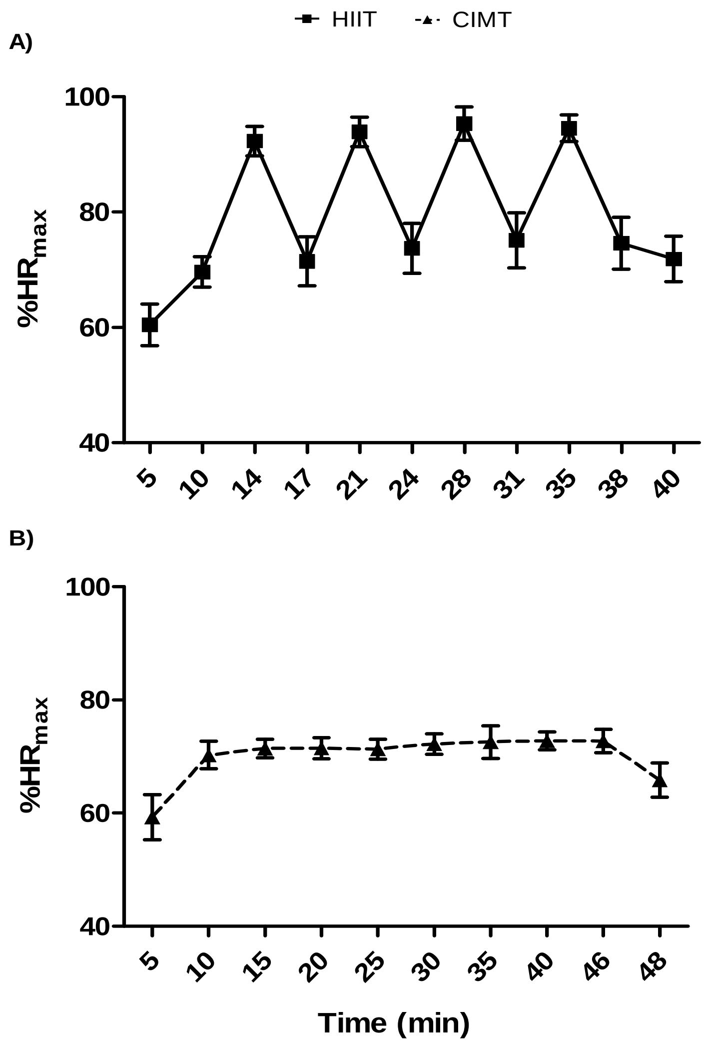

Figure 2. (a) Heart rate (HR) during high-intensity interval training (HIIT); (b) HR during moderate-intensity continuous training (MICT).

The pattern of the LV diastolic (e.g. E/A ratio and EDV), and systolic (e.g. GLS and LVEF) parameters before and after the experimental sessions are shown in Figure 3. Significant time and group interactions were observed for E/A ratio ($p = 0.006$), LVEDV ($p = 0.007$), GLS ($p = 0.040$) and LVEF ($p = 0.028$). At t5, LVEF presented a significant difference after HIIT in comparison to CO ($p = 0.010$) and baseline ($p = 0.017$). Considering LVEDV, a significant reduction was observed for HIIT in comparison to CO at t5 ($p = 0.048$). GLS showed a significant worsening for HIIT in comparison to MICT ($p = 0.013$), and E/A ratio showed a significant reduction after HIIT when compared to MICT ($p = 0.027$) at t5. HIIT also presented worsened GLS ($p = 0.002$) and reduced E/A ratio ($p = <0.001$) in comparison to CO at this time. In addition, all parameters showed a significant difference in the HIIT condition at t5 when compared to baseline values. Only E/A ratio showed a significant reduction for HIIT when compared to baseline (p = 0.001), as well as to MICT (p = 0.008) and CO (p = 0.001) at t35.

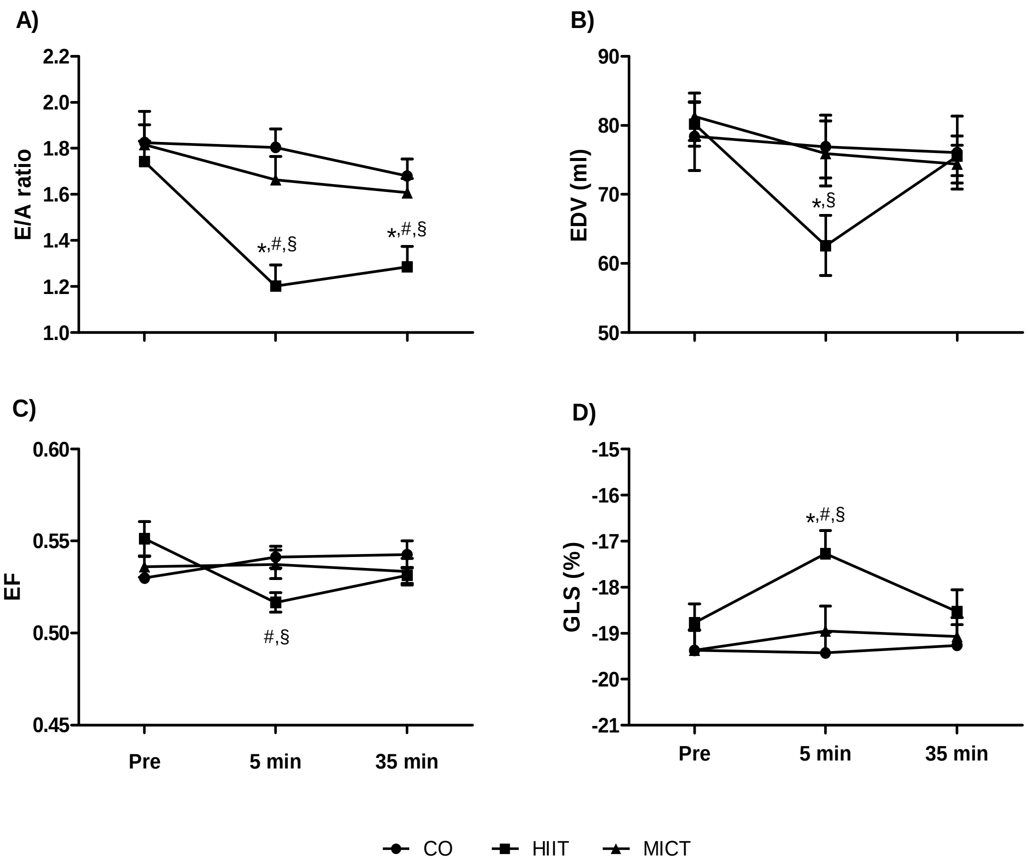

Figure 3. a) The ratio between E and A waves (E/A ratio); b) Left ventricular end-diastolic volume (LVEDV); c) Left ventricular ejection fraction (LVEF); d) Global longitudinal strain patterns according to experimental conditions.
*Difference to control group; #Difference to exercise group; §Difference to baseline.

Table 2. Echocardiographic parameters at baseline and post (t5 and t35) experimental conditions.

		Pre	Post				ANOVA		
			5 min		35 min				
		MD	MD	ES	MD	ES	Time	Trial	Time x Trial
E	***CO***	0.87±0.15	0.88±0.12		0.82±0.02				
(m/s)	***HIIT***	0.85±0.12	0.69±0.14*§	1.79	0.71±0.11	0.75	<0.001	0.007	<0.001
	MICT	0.82±0.11	0.77±0.13	0.89	0.78±0.11	0.10			
A	***CO***	0.49±0.09	0.49±0.06		0.49±0.07				
(m/s)	***HIIT***	0.49±0.07	0.60±0.12*#§	1.01	0.58±0.13*#§	0.93	0.012	0.001	0.015
	MICT	0.46±0.07	0.48±0.07	0.26	0.49±0.05	0.35			
E´septal	***CO***	0.12±0.01	0.12±0.01		0.12±0.02				
(m/s)	***HIIT***	0.12±0.01	0.11±0.03	0.46	0.10±0.02*§	1.04	0.001	0.118	0.031
	MICT	0.12±0.02	0.11±0.02§	1.04	0.11±0.02§	0.65			
E´lateral	***CO***	0.18±0.02	0.18±0.02		0.18±0.02				
(m/s)	***HIIT***	0.19±0.03	0.16±0.05	0.82	0.16±0.04	0.65	0.149	0.067	0.051
	MICT	0.18±0.03	0.18±0.02	0.00	0.18±0.03	0.00			
E/E´septal	***CO***	7.26±1.19	7.27±1.33		6.89±1.71				
	HIIT	7.03±1.48	6.65±1.73	0.30	7.37±2.42	0.37	0.603	0.799	0.360
	MICT	6.75±1.09	6.83±0.93	0.08	7.01±1.13	0.53			
E/E´ lateral	***CO***	4.99±0.97	4.91±0.83		4.57±0.93				
	HIIT	4.63±0.86	4.66±1.36	0.03	4.83±2.10	0.34	0.799	0.307	0.695
	MICT	4.46±0.69	4.39±0.79	0.15	4.32±0.64	0.23			
Average	***CO***	5.89±1.02	5.83±0.90		5.43±0.98				
E/e´	***HIIT***	5.89±1.01	5.41±1.37	0.05	5.76±2.19	0.41	0.872	0.409	0.448
	MICT	5.39±0.63	5.29±0.67	0.07	5.32±0.66	0.47			
	CO	36.26±8.30	35.46±8.45		34.93±10.18				
ESV (ml)	***HIIT***	36.07±7.28	30.26±8.38§	0.75	35.60±6.09	0.13	0.032	0.510	0.139
	MICT	37.86±6.41	34.93±8.24	0.33	34.66±5.02	0.26			
	CO	42.13±11.10	41.46±10.18		41.13±10.58				
SV	***HIIT***	44.13±6.15	32.33±8.56*#§	2.89	40.00±5.31§	0.47	0.002	0.337	<0.001
	MICT	43.40±7.46	41.00±10.51	1.90	39.73±6.46	0.34			

	CO	72.73±13.51	73.13±11.93		70.26±11.97				
HR (bpm)	***HIIT***	76.66±12.22	100.13±8.94$^{*\#\S}$	2.89	93.66±10.87$^{*\#\S}$	3.29	<0.001	<0.001	<0.001
	MICT	77.00±11.22	86.13±10.45$^{*\#\S}$	1.11	77.60±9.85$^{*\#}$	0.47			

Difference to control group; $^{\#}$Difference to exercise group; §Difference to baseline. Values are means ± SD. E and A waves, diastolic trans-mitral blood flow velocities for peak early and late fillings, respectively; GLS, global longitudinal strain, EF, ejection fraction; E/A, E and A waves ratio; E´, mitral annular tissue velocity ESV, end-systolic volume; EDV, end-diastolic volume; SV, Stroke Volume, HR, heart rate. ES, Effect Size. Cohen´s *d*, negligible effect (>= -0.15 and <.15); small effect (>=.15 and <.40); medium effect (>=.40 and <.75), large effect (>=.75 and <1.10), very large effect (>=1.10 and <1.45), huge effect >1.45.

Correlations between Δ pre and t5 echocardiographic and hemodynamic parameters of exercise conditions (e.g. HIIT and MICT) are expressed in table 2. Very strong significant correlations were observed between LVEDV and both LVESV (p <0.001) and SV (p <0.001). Central MBP showed strong correlations with central DBP (p <0.001) and central SBP (p <0.001). Moderate negative correlations were observed between GLS and LVEF (p = 0.016), LVEDV (p = 0.024), SV (p = 0.002), and between LVESV and SV (p <0.001). Moderate positive correlations were verified between SV and E/A ratio (p = 0.021). Weak but significant correlations were reported between LVEF and both LVESV (p = 0.032) and SV (p = 0.046). Additionally, a weak correlation was found between LVEDV and E/A ratio (p = 0.033). Finally, SV presented a weak correlation with HR (p = 0.046).

Table 3. Pearson correlation coefficients compared to Δ pre and t5 echocardiographic and hemodynamic parameters of exercise conditions (HIIT and MICT).

	1	2	3	4	5	6	7	8	9	10	11
1. GLS (%)	-										
2. LVEF (%)	-0.436*	-									
3. EDV (ml)	-0.411*	0.004	-								
4. ESV (ml)	-0.207	-0.393*	0.912**	-							
5. SV (ml)	-0.534**	0.367*	0.926**	0.690**	-						
6. E/A ratio	-0.178	0.143	0.389*	0.291	0.420*	-					
7. Average E/e´	-0.078	0.112	0.258	0.218	0.256	0.128	-				
8. Central SBP	-0.222	0.054	0.162	0.108	0.187	0.108	0.057	-			
9. Central DBP	0.103	0.094	-0.006	-0.048	0.033	0.176	-0.018	0.443*	-		
10. Central MBP	-0.001	0.006	0.062	0.045	0.068	0.122	-0.101	0.731**	0.878**	-	
11. HR (bpm)	0.245	-0.158	-0.337	-0.247	-0.367*	-0.277	-0.141	-0.275	-0.027	-0.019	-

*Correlation is significant (p ≤0.05); **Correlation is significant (p ≤0.01); GLS, global longitudinal strain, EF, left ventricle ejection fraction; ESV, end-systolic volume; EDV, end-diastolic volume; SV, Stroke Volume; E/A, E and A waves ratio, SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure, HR, heart rate.

The pattern of the echocardiographic parameters following the experimental conditions are presented in table 2. Significant time and group interactions were observed for E wave ($p < 0.001$), A wave (p 0.015), E/A ratio ($p = 0.006$), E 'septal (p 0.031), SV ($p < 0.001$) and HR ($p < 0.001$).

There is a significant decline in E wave at t5 after HIIT in comparison to baseline ($p = 0.001$) and CO ($p = 0.003$). A significant increase in A wave was observed after HIIT in relation to CO ($p = 0.032$; $p = 0.034$) and MICT ($p = 0.019$; $p = 0.039$) at t5 and t35, respectively. These changes in HIIT condition were significant compared to baseline at both t5 ($p = 0.011$) and t35 ($p = 0.019$). Regarding E'septal, a reduction was observed after MICT compared to baseline at t5 ($p = 0.040$), whilst at t35 this difference was observed for both MICT ($p = 0.007$) and HIIT ($p = 0.006$) in comparison to baseline values. Moreover, E'septal was significantly reduced after HIIT in comparison to CO at t35 ($p = 0.039$).

A significant reduction in LVESV was observed after HIIT when compared to baseline at t5 ($p = 0.050$). As regards to SV, it was significantly reduced following HIIT in comparison to baseline at t5 ($p < 0.001$) and t35 ($p = 0.050$), as well as it was significant reduced in comparison to both MICT ($p = 0.038$) and CO ($P = 0.013$) at t5. Finally, HR was significantly increased after HIIT when compared to MICT ($p < 0.001$, $p < 0.001$) and CO ($p < 0.001$, $p < 0.001$) at t5 and t35, respectively. In addition, HR values at HIIT were significant different from baseline at t5 ($p < 0.001$) and t35 ($p < 0.001$), whereas MICT only showed a significant difference at t5 in comparison to baseline ($p = 0.002$).

Discussion

The present study analysed the acute effects of HIIT and MICT on LV function and myocardial mechanics in obese women. The main finding of this study was that a single bout of HIIT promoted transient reductions in LV diastolic and systolic function parameters as well as myocardial mechanics, represented by GLS, in obese women, wherein the same effect was not reported after MICT.

Regarding LV diastolic function parameters, temporary reductions in the E and E/A ratio, as well as an increase in A wave were documented following HIIT. It is known that physical exercise promotes a promptly increase in HR, which remains elevated after exercise performance for a certain short period, even more in deconditioning individuals (BUCHHEIT & GINDRE, 2006). This elevation in HR causes a shortened diastolic filling time, and a subsequent decline in E wave (GEORGE et al., 2010). A significant rise in A wave was reported and might be explained mostly due to the amount of blood remained in left atrium in consequence of a shortened early filling (e.g. E wave). In addition, there is also a reduction in diastasis and late filling time (DONALDSON et al., 2019). However, the increase in A wave not sufficiently compensate the lessened early filling, causing hence a decrease in E/A ratio and LVEDV. Previous evidence reported that E/A ratio is inversely proportional to HR (GALDERISI et al., 1993), supporting the findings of the present study. Having in mind that HIIT promotes a substantial increase in HR due to its higher intensity than MICT, which was seen to be higher in the current study, this could explain why this transient impact in LV diastolic function was observed following HIIT and not MICT nor CO. Accordingly, a recent meta-analysis conducted by Donaldson et al. (2019) predicted a reduction of 0.03 on the E/A ratio for each increase of one bpm in HR. The aforementioned higher HR due to exercise increases the magnitude of the post-exercise alteration in the LV diastolic filling. In addition, further mechanisms that could explain these changes on LV diastolic filling include the downregulation of the B1-adrenergic receptors, mediated by the increased number of catecholamines during the exercise (EYSMANN et al., 1996). The catecholamines support the sympathetic system in altering the blood flow during exercise, increasing also the HR, contractile force and cardiac output by the stimulation of the B1-adrenergic receptors (WATCHER et al., 2012). Despite the transient reduction aforementioned, the LV diastolic function values rapidly return near to baseline values. According to Middleton and colleagues (2006), the prompt return of any alteration induced by exercise on the diastolic filling proposes that the clinical impact of this phenomenon is minimal.

The newest guidelines of the American Society of Echocardiography as well as the European Association of Cardiovascular Imaging showed new recommendations to lessen the false-positive diagnostic of diastolic dysfunction, giving a critical importance to the septal and lateral early mitral annular velocities (e.g. e’septal and e’lateral) as well as the average E/e’ratio. The obesity is an independent predictor of heart failure incident (KENCHAIAH et al., 2012; LOEHR et al., 2009). It is also an important factor for the decline of diastolic function, in which lower values of both e' septal and lateral, and the average E/e' ratio were observed for obese individuals in comparison with the normal-weight counterparts (RUSSO et al., 2011; KIM et al., 2016). The exercise drives to an increase in HR and cardiac output with a consequently reduction on the diastolic LV filling due to a shorter diastolic time (GOODMAN et al., 2008). However, the effects of post-exercise recovery on these new diastolic parameters in not properly elucidated. Our results showed that both HIIT and MICT presented a significant reduction in the e'septal at t35 in comparison to baseline values, but only HIIT presented a significant reduced value when compared to CO at this time. These findings still need further clarification since both exercise modalities induced the same pattern of the variable. It emphasizes the importance of basing the diagnoses in more than a single diastolic parameter in order to avoid an erroneous interpretation, using these variables only to have initial evidence on a potential diastolic dysfunction (MITTER et al., 2017).

A transient decrease in LV systolic function following aerobic exercise have been reported in previous studies (ASHLEY et al., 2006; TULLOH et al., 2006; SHAVE et al., 2004), corroborating with the findings of the present study. This decrease in LV systolic function, mainly in SV, might be elucidated by the decrease in LVEDV. It is well reported the close association of LVEDV and SV (FUKUTA & LITTLE, 2008). A decrease in LVEDV drives to a small amount of blood in LV right before systole. Thus, there is a clear reduction in SV, even though physiological heart mechanisms try to compensate it by increasing the contractile force, reducing therefore the LVESV (DAVIDSON & GIRAUD, 2012). This goes hand in hand with our findings, which reported a very strong correlation between LVEDV and SV, and a moderate negative correlation between LVESV and SV. Moreover, the maintenance of high levels of catecholamines may play a role in the diminished left ventricular systolic function after endurance aerobic exercise (COTE et al., 2013). It is reported that high levels of circulating catecholamines due to demanding exercise drives to decreased functional activity of B1-adrenergic receptors, concomitant with sustained increases in sympathetic activation (DOUGLAS et al., 1987; LEFKOWITZ et al., 2000). Initially, this mechanism was thought to be motivated by exercise duration, specifically endurance exercise (WHYTE et al., 2000). However, the intensity of exercise is also a determining factor to be considered, provided it also influences ventricular function (BANKS et al., 2010), endorsing the findings of the present study, since HIIT is an aerobic exercise modality in which high intensities are achieved.

Regarding changes in myocardial mechanics, our study showed a transient worsening in GLS after HIIT. More recent evidence suggested the same decrease when analyzing specifically the GLS, in diverse populations (COTE et al., 2013; HAUSER et al., 2013; PIELES et al., 2015; STEWART et al., 2017). The recent study of Lembo and colleagues (2019) reported an independent association between LVEDV, in conjunction with other diastolic indices such as E/e', and GLS. The reduced of LVEDV due to the higher HR and consequent shorter diastolic filling period leads to a lessened myocardial deformation by virtue of less amount of blood on LV, explaining the worsening in GLS after HIIT performance. Moreover, a moderate negative correlation was verified between GLS and LVEDV, emphasizing the narrow relationship between those parameters. Interestingly, this transient reduction in myocardial mechanics is rapidly adjourned by a restoration of the baseline GLS values. Stewart and colleagues (2017) reported that is improbable that a single acute bout of exercise is able to induce cardiac dysfunctions, promoting consequently adverse remodeling. Instead of that, it seems that repeatedly bout of exercise could elicit this response, especially when recovery time is not sufficient, driving to structural changes in the LV.

The debate that surrounds the HIIT and MICT aerobic exercise modalities on what could elicit greater health benefits makes evident that this issue still requires further elucidation (HUSSAIN et al., 2016). Additionally, it is still not clear the difference of these exercise modalities on the cardiovascular parameters following exercise performance in obese women. A plenty of studies in special populations have demonstrated an enhancement of the cardiac parameters following HIIT rather than MICT in chronical experiments. Cassidy and colleagues (2015) showed that 12 weeks of HIIT enhanced the systolic parameters in adults with type II diabetes. Other studies showed that HIIT also promoted improvements on the cardiovascular parameters in individuals with hypertension and heart failure (MOLMEN, 2012; WISLOFF et al., 2007). The ACSM 2014 guideline recommends the practice of intense or moderate aerobic exercise aiming the maintenance of cardiovascular health, showing that HIIT may be an excellent alternative due to its time-efficiency in comparison to MICT. Therefore, although our results showed reductions on both LV systolic and diastolic functions, this phenomenon seems to be transitional and not hazard to the cardiovascular health of obese women.

To our knowledge, the present study is the first to investigate the acute effects of HIIT and MICT on LV systolic and diastolic function as well as LV cardiac geometry in obese women. However, our study is limited by a small sample and included only female participants. The GLS measurement has already been shown to be consistent and with good reproducibility compared to the circumferential and radial strain measurements, as well as the echocardiographic apparatus used has been compared previously and has been shown to allow comparison of deformations in different ultrasound systems (RISUM et al. al. 2012). However, myocardial strain measurements are highly dependent on the choice of imaging equipment and analysis software, and levels of disagreement are beyond the intrinsic variability of measurements of any of the tested hardware and software combinations (GAYAT et al. 2011). There are likely to be varying degrees of out-of-plane movement observed in various views due to the complex orientation of myocardial fibers, and no specific type of tension currently understood can explain this (RISUM et al. 2012). Furthermore, it is not yet known whether the highlighted acute responses translate into sustained cardiac adaptations.

Conclusion

In summary, despite a transient reduction in both LV diastolic and systolic functions following HIIT and well as a worsening in myocardial mechanics, these impairments are rapidly reestablished to baseline values, indicating that this exercise modality did not seem to elicit any negative effect on both LV systolic and diastolic function in obese women acutely. Thus, provided HIIT can elicit more beneficial cardiac chronic adaptations than MICT, not promoting acute hazard for obese women, this aerobic exercise modality should be highly recommended. However, more studies are required in order to better elucidate the effects of different aerobic exercise modalities on LV function.

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5 CONSIDERAÇÕES FINAIS

Em suma, conclui-se com a realizaçao do presente trabalho que, de forma crônica, o exercício aeróbio é capaz de promover melhoras significativas na deformação miocárdica em indivíduos saudáveis e com doenças crônico-degenerativas, sendo estas melhoras superiores após o HIIT comparado ao MICT. De forma aguda, o HIIT promove uma redução transitória da função sistólica, diastólica e na deformação miocárdica alguns minutos após a sessão, mas que logo após ela é reestabelecida. Sendo assim, tendo em vista os efeitos crônicos positivos que o exercício aeróbio, em especial o HIIT, promove na função ventricular esquerda assim como na mecânica miocárdica em mulheres obesas, esta modalidade se mostra segura e promissora na melhora da deformação miocárdica nesta população.

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ANEXOS

ANEXO A – PARECER CONSUBSTANCIADO DO CEPE ADENDO I

UEM UNIVERSIDADE ESTADUAL DE MARINGÁ Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DA EMENDA

Título da Pesquisa: EFEITOS AGUDOS HIGH INTENSITY INTERVAL TRAINING (HIIT) VERSUS TREINAMENTO CONTÍNUO DE INTENSIDADE MODERADA SOBRE O CONSUMO EXCESSIVO DE OXIGÊNIO PÓS-EXERCICIO (EPOC) EM INDIVIDUOS OBESOS

Pesquisador: Wendell Arthur Lopes

Área Temática:

Versão: 2

CAAE: 91380218.4.0000.0104

Instituição Proponente: CCS - Centro de Ciências da Saúde

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.891.513

Apresentação do Projeto:

Trata-se de projeto de pesquisa proposto por pesquisador vinculado à Universidade Estadual de Maringá.

Objetivo da Pesquisa:

Comparar os efeitos agudos de um protocolo longo HIIT (HIIT-L), um protocolo curto HIIT (HIIT-C) e um protocolo de treinamento contínuo de intensidade moderada em adultos obesos.

Avaliação dos Riscos e Benefícios:

Avalia-se que os possíveis riscos a que estarão submetidos os sujeitos da pesquisa serão suportados pelos benefícios apontados.

Comentários e Considerações sobre a Pesquisa:

O presente estudo caracteriza-se como delineamento experimental, do tipo crossover. A amostra será constituída por 15 mulheres obesas, com idade entre 18 e 35 anos, provenientes da cidade de Maringá e municípios vizinhos. Todos os procedimentos serão realizados no laboratório do Núcleo de Estudos Multiprofissional da Obesidade (NEMO), da Universidade Estadual de Maringá (UEM). Será realizada uma avaliação clínica por meio de anamnese completa realizado por médico cardiologista integrante da equipe, a fim de averiguar possíveis alterações que coloquem em risco o participante ou interfiram na realização dos protocolos de avaliação e sessões experimentais de

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exercício físico. Os participantes que forem liberados para participação da pesquisa receberam um atestado de liberação para a prática de exercícios físicos assinado pelo médico responsável pelas avaliações. Serão adotados como critérios de inclusão: Idade: 18 a 35 anos; IMC: 30 kg/m², classificados como obesos de acordo com a Organização Mundial da Saúde; mulheres com peso corporal estabilizado/estabelecido há pelo menos 12 semanas e que não tenham participado de programas para redução de peso anteriormente; mulheres não portadoras de cardiopatias, diabetes e/ou hipertensão e doenças endócrinas; Indivíduos mulheres não fumantes; mulheres que não estejam fazendo uso de medicamentos que possam alterar sistemas cardiorrespiratório e neuromuscular. Serão adotados como critérios de exclusão: Não participar das avaliações; Não completar os protocolos experimentais. As interessadas em participar da pesquisa serão convidadas para uma reunião para esclarecimentos gerais sobre o projeto de pesquisa e agendamento de avaliação clínica e exame físico com o médico integrante da equipe (Visita I). Na visita II, as aprovadas na avaliação médica, serão submetidas a avaliação antropométrica, composição corporal e teste de esforço em ciclo ergômetro. Nas visitas III a VI, as participantes realizarão os protocolos experimentais (High Intensity Interval Training longo (HIIT-L), High Intensity Interval Training curto (HIIT-C), treinamento contínuo de intensidade moderada (MICT) e condição controle (CONT)), alocados de forma aleatória, respeitando um intervalo de no mínimo 48 horas entre cada protocolo. As participantes serão instruídas a manter suas dietas e atividades diárias habituais e ainda será recomendado que não iniciem nenhum programa de exercícios durante o período do estudo. Além disso, as avaliadas serão instruídas a não ingerirem alimentos num prazo de 2 horas antes do treinamento, a fim de evitar qualquer tipo de desconforto gastrointestinal. Para a condição controle (CONT), as participantes serão orientadas a permanecerem na posição sentada por um período de 35 minutos. Para a condição HIIT-L, o protocolo será constituído de 4 minutos de aquecimento a 15% Wpico, seguidos por 4 estímulos de 4 minutos de exercício em cicloergômetro com intensidade de ~90%Wpico, intercalados por 3 minutos de recuperação ativa na intensidade de ~15% Wpico. A avaliada será instruída a pedalar o mais rápido possível durante o tempo de estímulo e será encorajada verbalmente pelos avaliadores para manter sua cadencia até o final do exercício. Ao final será concedido um tempo de 4 minutos de pedalada a uma intensidade de 15% Wpico para volta à calma. O protocolo terá um tempo total de realização de ~33 minutos. Para a condição HIIT-C o protocolo será constituído de 4 minutos aquecimento a 15% Wpico, seguido por 10 estímulos de 1 minuto de exercício em cicloergômetro com intensidade de ~90%Wpico, intercalados por 1 minuto de recuperação ativa na intensidade de ~15% Wpico. Ao término, será realizado 4 minutos de pedalada a uma intensidade de 15% Wpico para volta à calma em ciclo ergômetro. O protocolo terá um tempo total de realização de ~27 minutos. Para a condição MICT o protocolo será constituído de 4 minutos de aquecimento a 15% Wpico, seguido por 30 minutos de exercício contínuo em cicloergômetro a intensidade de 35% Wpico. A avaliada será encorajada verbalmente pelos avaliadores para manter sua cadencia até o final do protocolo. O protocolo de exercício terá um tempo total de realização de aproximadamente 35 minutos. O pesquisador solicita uma emenda ao protocolo em função da oportunidade de monitorar, além das respostas respiratórias já previstas inicialmente no projeto, as respostas cardiovasculares dos participantes logo após a execução dos protocolos experimentais. Segundo o pesquisador o equipamento é um aparelho oscilométrico da marca Mobil-OGraph® (IEM, Stolberg, Alemanha) que de forma não invasiva avalia a pressão central e a velocidade de onda de pulso. As medidas serão realizadas pelo médico cardiologista responsável pela triagem médica do projeto e que possuem experiência e certificação neste tipo de avaliação.

Considerações sobre os Termos de apresentação obrigatória:

Apresenta a folha de rosto devidamente preenchida e assinada pelo responsável institucional. Apresenta a autorização do Núcleo de Estudos Multiprofissional da Obesidade (NEMO) para a realização do projeto nas suas dependências. Descreve gastos sob a responsabilidade do pesquisador no valor de R$ 239,00. Cronograma de execução prevê o desenvolvimento do projeto durante o período de 25/06/2018 a 31/12/2018. Apresenta TCLE numa linguagem clara e contempla as garantias mínimas de sigilo e confidencialidade.

Conclusões ou Pendências e Lista de Inadequações:

O Comitê Permanente de Ética em Pesquisa Envolvendo Seres Humanos da Universidade Estadual de Maringá é de parecer favorável à aprovação da emenda ao protocolo de pesquisa apresentada.

Considerações Finais a critério do CEP:

Face ao exposto e considerando a normativa ética vigente, este Comitê se manifesta pela aprovação do protocolo de pesquisa em tela.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_1196803_E1.pdf	08/08/2018 17:09:48		Aceito
Projeto Detalhado / Brochura Investigador	PROJETO_Corrigido.pdf	08/08/2018 17:07:12	Wendell Arthur Lopes	Aceito

Outros	Emenda.pdf	08/08/2018 17:06:49	Wendell Arthur Lopes	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_Corrigido.pdf	08/08/2018 17:06:07	Wendell Arthur Lopes	Aceito
Declaração de Pesquisadores	AutorizacaoRogerio.pdf	12/06/2018 18:56:50	Wendell Arthur Lopes	Aceito
Folha de Rosto	FolhaDeRostoAss.pdf	12/06/2018 16:30:02	Wendell Arthur Lopes	Aceito
Declaração de Instituição e Infraestrutura	AutorizacaoNelson.pdf	12/06/2018 16:01:09	Wendell Arthur Lopes	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

MARINGA, 13 de Setembro de 2018

Assinado por:
Ricardo Cesar Gardiolo
(Coordenador)

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UF: PR **Município:** MARINGA
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ANEXO B – PARECER CONSUBSTANCIADO DO CEPE ADENDO II

UNIVERSIDADE ESTADUAL DE MARINGÁ

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITOS DO HIGH-INTENSITY INTERVAL TRAINING (HIIT) SOBRE OS PARÂMETROS METABÓLICOS, INFLAMATÓRIOS, RIGIDEZ ARTERIAL E DEFORMAÇÃO MIOCÁRDICA (STRAIN) EM MULHERES OBESAS: UM ENSAIO CLÍNICO RANDOMIZADO

Pesquisador: Wendell Arthur Lopes

Área Temática:

Versão: 2

CAAE: 08935419.5.0000.0104

Instituição Proponente: CCS - Centro de Ciências da Saúde

Patrocinador Principal: Fundação Araucária

DADOS DO PARECER

Número do Parecer: 3.268.455

Apresentação do Projeto:

Trata-se de projeto de pesquisa proposto por pesquisador vinculado à Universidade Estadual de Maringá.

Objetivo da Pesquisa:

Objetivo Primário: Investigar os efeitos do High-Intensity Interval Training (HIIT) sobre os parâmetros metabólicos, inflamatórios, rigidez arterial e deformação miocárdica (strain) em mulheres obesas. Objetivos Secundários: Caracterizar os parâmetros metabólicos, inflamatórios, rigidez arterial e deformação miocárdica em mulheres obesas; Verificar os efeitos agudos do HIIT sobre os parâmetros de rigidez arterial e deformação miocárdica (strain); Comparar os efeitos agudos do HIIT com o Moderate Intensity Continuous Training (MICT) e grupo controle sobre os parâmetros de rigidez arterial e deformação miocárdica (strain); Verificar os efeitos crônicos do HIIT sobre os parâmetros antropométricos, composição corporal, gordura epicárdica, metabólicos, inflamatórios, rigidez arterial e deformação miocárdica (strain) em mulheres obesas; Comparar os efeitos crônicos do HIIT com o Moderate Intensity Continuous Training (MICT) e grupo controle sobre os parâmetros antropométricos, composição corporal, gordura epicárdica, metabólicos, inflamatórios, rigidez arterial e deformação miocárdica (strain) em mulheres obesas; Correlacionar às mudanças nos parâmetros antropométricos, composição corporal, gordura epicárdica,

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Bairro: Jardim Universitário **CEP:** 87.020-900
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metabólicos, inflamatórios com as mudanças na rigidez arterial e na deformação miocárdica (strain) em mulheres obesas.

Avaliação dos Riscos e Benefícios:

Avalia-se que os possíveis riscos a que estarão submetidos os sujeitos da pesquisa serão suportados pelos benefícios apontados.

Comentários e Considerações sobre a Pesquisa:

Esta pesquisa será composta de duas fases. A FASE I, efeito agudo, tem como objetivo verificar o efeito de uma sessão de exercício (HIIT e MICT) e da condição controle (sentada em repouso), sobre as variáveis cardiovasculares. A FASE II, efeito crônico, irá investigar os efeitos de 16 semanas de intervenção do HIIT e do MICT sobre os parâmetros metabólicos, inflamatórios e cardiovasculares.Protocolos de treinamento Treinamento intervalado de alta intensidade (High Intensity/ Interval Training - HIIT): O protocolo HIIT (GHIIT) consistirá em caminhar/correr numa pista de atletismo num total de 40 minutos de duração. Inicialmente será realizado 10 minutos de aquecimento, sendo 5 minutos na intensidade entre 55 e 65% da FCmáx, seguido de 5 minutos na intensidade entre 65 e 75% da FCmáx. Em seguida, serão realizados 4 estímulos de 4 minutos de exercício na intensidade entre 85 e 95% da FCmáx, alternados por períodos de 3 minutos de recuperação ativa na intensidade entre 65 e 75% da FCmáx. Ao final, será realizado 5 minutos de desaquecimento, sendo 3 minutos na intensidade entre 65 e 75% da FCmáx, seguido de 2 minutos finais na intensidade entre 55 e 65%da FCmáx. A sessão será monitorada durante todo o tempo por um profissional capacitado e a Percepção subjetiva de Esforço e a FC serão obtidas e registradas. A FC será monitorada por meio de monitor cardíaco da marca Polar, modelo H10 e registrada no programa Polar Team instalado em dispositivo IPAD®.Treinamento Contínuo de intensidade moderada (Moderate Intensity Continuous Training- MICT): O protocolo MICT (GMICT) consistirá em caminhar/correr numa pista de atletismo num total de 48 minutos de duração. Inicialmente será realizado 5 minutos de aquecimento na intensidade entre 55 e 65% da FCmáx, seguido de 41 minutos na intensidade entre 65 e 75% da FCmáx. Ao final, será realizado 2 minutos de desaquecimento na intensidade entre 55 e 65% da FCmáx. A sessão será monitorada durante todo o tempo por profissional capacitado e a Percepção subjetiva de Esforço e a FC serão obtidas e registradas. A FC será monitorada por meio de monitor cardíaco da marca Polar, modelo H10 e registrada no programa Polar Team instalado em dispositivo IPAD®.Instrumentos e Procedimentos Avaliação antropométrica e de composição corporal As avaliações serão realizadas por profissionais da Educação Física com experiência neste tipo de avaliação na clínica Biocor. A massa corporal será aferida em balança antropométrica mecânica (Filizola®), com precisão de 0,1

UNIVERSIDADE ESTADUAL DE MARINGÁ

Continuação do Parecer: 3.268.455

kg e capacidade máxima de 150 kg. A estatura será mensurada por meio de um estadiômetro de parede, com precisão de 0,1cm e amplitude de 220 cm. Os indivíduos permanecerão em posição ortostática, descalços, com os braços ao longo do corpo, os calcanhares unidos, as pontas dos pés ligeiramente afastadas, a cabeça voltada para frente e calcanhares, glúteos e ombros adequadamente posicionados, de acordo com o plano de Frankfurt. O índice de massa corporal (IMC) será calculado pela razão entre a massa corporal e o quadrado da estatura e classificado de acordo com os critérios definidos pela Organização Mundial de Saúde para sexo e idade (ONIS et al., 2007). Serão considerados eutróficos os participantes cujo IMC situar-se entre o escore-z -2 e < +1, sobrepeso entre os escores-z +1 e < +2 e obesos aqueles com escore-z +2 da curva de IMC ajustada para idade e sexo.A circunferência de cintura será aferida com fita métrica inelástica (Sanny®), com resolução de 0,1 cm e amplitude de 2m, com a participante em jejum, em posição ortostática, no ponto médio entre a última costela e a crista ilíaca(LOHMAN; ROCHE; MARTORELL, 1988). Para a avaliação de composição corporal, será utilizado o aparelho de bioimpedância da marca BF-900 (Maltron, Reino Unido) seguindo as recomendações de Heyward (2001).

Considerações sobre os Termos de apresentação obrigatória:

Apresenta Informações Básicas do Projeto; Carta resposta acatando todas as pendências; TCLE corrigido; Projeto COPEP; Cronograma; Cartas de autorização da Biocor e de uso da pista de atletismo; Folha de Rosto.

Conclusões ou Pendências e Lista de Inadequações:

O Comitê Permanente de Ética em Pesquisa Envolvendo Seres Humanos da Universidade Estadual de Maringá é de parecer favorável à aprovação do protocolo de pesquisa apresentado.

Considerações Finais a critério do CEP:

Face ao exposto e considerando a normativa ética vigente, este Comitê se manifesta pela aprovação do protocolo de pesquisa em tela.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1305687.pdf	26/03/2019 23:27:04		Aceito
Outros	CARTA_RESPOSTA.pdf	26/03/2019 23:25:09	Wendell Arthur Lopes	Aceito
TCLE / Termos de Assentimento /	TCLE_corrigido.pdf	26/03/2019 23:24:16	Wendell Arthur Lopes	Aceito

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Continuação do Parecer: 3.268.455

Justificativa de Ausência	TCLE_corrigido.pdf	26/03/2019 23:24:16	Wendell Arthur Lopes	Aceito
Projeto Detalhado / Brochura Investigador	PROJETO_COPEP.pdf	27/02/2019 11:52:43	Wendell Arthur Lopes	Aceito
Cronograma	Cronograma.pdf	27/02/2019 11:44:16	Wendell Arthur Lopes	Aceito
Declaração de Instituição e Infraestrutura	Pista_de_Atletismo.pdf	27/02/2019 11:42:32	Wendell Arthur Lopes	Aceito
Declaração de Instituição e Infraestrutura	Biocor.pdf	27/02/2019 11:41:48	Wendell Arthur Lopes	Aceito
Folha de Rosto	Folha_De_Rosto.pdf	27/02/2019 11:26:32	Wendell Arthur Lopes	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

MARINGA, 16 de Abril de 2019

Assinado por:
Ricardo Cesar Gardiolo
(Coordenador(a))

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ANEXO C – QUESTIONÁRIO INTERNACIONAL DE ATIVIDADE FÍSICA (IPAQ – VERSÃO CURTA)

QUESTIONÁRIO INTERNACIONAL DE ATIVIDADE FÍSICA – VERSÃO CURTA -

Nome:____

Data: ______/ _______ / ______ **Idade :** ______ **Sexo: F ( ) M ( )**

Nós estamos interessados em saber que tipos de atividade física as pessoas fazem como parte do seu dia a dia. Este projeto faz parte de um grande estudo que está sendo feito em diferentes países ao redor do mundo. Suas respostas nos ajudarão a entender que tão ativos nós somos em relação à pessoas de outros países. As perguntas estão relacionadas ao tempo que você gasta fazendo atividade física na **ÚLTIMA** semana. As perguntas incluem as atividades que você faz no trabalho, para ir de um lugar a outro, por lazer, por esporte, por exercício ou como parte das suas atividades em casa ou no jardim. Suas respostas são MUITO importantes. Por favor responda cada questão mesmo que considere que não seja ativo. Obrigado pela sua participação !

Para responder as questões lembre que:

- atividades físicas **VIGOROSAS** são aquelas que precisam de um grande esforço físico e que fazem respirar MUITO mais forte que o normal
- atividades físicas **MODERADAS** são aquelas que precisam de algum esforço físico e que fazem respirar UM POUCO mais forte que o normal

Para responder as perguntas pense somente nas atividades que você realiza **por pelo menos 10 minutos contínuos** de cada vez.

1a Em quantos dias da última semana você **CAMINHOU** por pelo menos 10 minutos contínuos em casa ou no trabalho, como forma de transporte para ir de um lugar para outro, por lazer, por prazer ou como forma de exercício?

dias _____ por **SEMANA** ( ) Nenhum

1b Nos dias em que você caminhou por pelo menos 10 minutos contínuos quanto tempo no total você gastou caminhando **por dia**?

horas: ______ Minutos: _____

2a. Em quantos dias da última semana, você realizou atividades **MODERADAS** por pelo menos 10 minutos contínuos, como por exemplo pedalar leve na bicicleta, nadar, dançar, fazer ginástica aeróbica leve, jogar vôlei recreativo, carregar pesos leves, fazer serviços domésticos na casa, no quintal ou no jardim como varrer, aspirar, cuidar do jardim, ou qualquer atividade que fez aumentar

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INFORMAÇÕES ANÁLISE, CLASSIFICAÇÃO E COMPARAÇÃO DE RESULTADOS NO BRASIL
Tel-Fax: – 011-42298980 ou 42299643. E-mail: celafiscs@celafiscs.com.br
Home Page: www.celafiscs.com.br IPAQ Internacional: www.ipaq.ki.se

moderadamente sua respiração ou batimentos do coração **(POR FAVOR NÃO INCLUA CAMINHADA)**

dias _____ por **SEMANA** ( ) Nenhum

2b. Nos dias em que você fez essas atividades moderadas por pelo menos 10 minutos contínuos, quanto tempo no total você gastou fazendo essas atividades **por dia**?

horas: ______ Minutos: _____

3a Em quantos dias da última semana, você realizou atividades **VIGOROSAS** por pelo menos 10 minutos contínuos, como por exemplo correr, fazer ginástica aeróbica, jogar futebol, pedalar rápido na bicicleta, jogar basquete, fazer serviços domésticos pesados em casa, no quintal ou cavoucar no jardim, carregar pesos elevados ou qualquer atividade que fez aumentar **MUITO** sua respiração ou batimentos do coração.

dias _____ por **SEMANA** ( ) Nenhum

3b Nos dias em que você fez essas atividades vigorosas por pelo menos 10 minutos contínuos quanto tempo no total você gastou fazendo essas atividades **por dia**?

horas: ______ Minutos: _____

Estas últimas questões são sobre o tempo que você permanece sentado todo dia, no trabalho, na escola ou faculdade, em casa e durante seu tempo livre. Isto inclui o tempo sentado estudando, sentado enquanto descansa, fazendo lição de casa visitando um amigo, lendo, sentado ou deitado assistindo TV. Não inclua o tempo gasto sentando durante o transporte em ônibus, trem, metrô ou carro.

4a. Quanto tempo no total você gasta sentado durante um **dia de semana**?
______horas ____minutos
4b. Quanto tempo no total você gasta sentado durante em um **dia de final de semana**?
______horas ____minutos

PERGUNTA SOMENTE PARA O ESTADO DE SÃO PAULO

5. Você já ouviu falar do Programa Agita São Paulo? ( ) Sim ( ) Não
6.. Você sabe o objetivo do Programa? ( ) Sim ( ) Não

ANEXO D – PERCEPÇÃO SUBJETIVA DE ESFORÇO (ESCALA DE BORG)

ESCALA DE PERCEPÇÃO DE ESFORÇO

6 7 8	MUITO FÁCIL
9 10	FÁCIL
11 12	RELATIVAMENTE FÁCIL
13 14	RELATIVAMENTE CANSATIVO
15 16	CANSATIVO
17 18	MUITO CANSATIVO
19 20	EXAUSTIVO

ANEXO E – REGISTRO BRASILEIROS DE ENSAIOS CLÍNICOS

EFEITOS DO HIGH-INTENSITY INTERVAL TRAINING (HIIT) SOBRE OS PARÂMETROS METABÓLICOS, INFLAMATÓRIOS, RIGIDEZ ARTERIAL E DEFORMAÇÃO MIOCÁRDICA (STRAIN) EM MULHERES OBESAS: UM ENSAIO CLÍNICO RANDOMIZADO

Tipo do estudo:

Intervenções

Título científico:

PT-BR	EN
EFEITOS DO HIGH-INTENSITY INTERVAL TRAINING (HIIT) SOBRE OS PARÂMETROS METABÓLICOS, INFLAMATÓRIOS, RIGIDEZ ARTERIAL E DEFORMAÇÃO MIOCÁRDICA (STRAIN) EM MULHERES OBESAS: UM ENSAIO CLÍNICO RANDOMIZADO	EFFECTS OF HIGH-INTENSITY INTERVAL (HIIT) TRAINING ON METABOLIC, INFLAMMATORY, BLOOD RIGIDITY AND MYOCARDIAL DEFORMATION (STRAIN) IN OBESE WOMEN: A RANDOMIZED CLINICAL TEST

Identificação do ensaio

Número do UTN: U1111-1231-9753

Título público:

PT-BR	EN
Efeitos do treinamento intervalado de alta intensidade (HIIT) sobre os parâmetros metabólicos, inflamatórios, rigidez arterial e deformação miocárdica em mulheres obesas: um ensaio clínico randomizado	Effects of high intensity interval training (HIIT) on metabolic, inflammatory, arterial stiffness and myocardial deformation in obese women: a randomized clinical trial

Acrônimo científico:

Acrônimo público:

Identificadores secundários:

08935419.5.0000.0104

Órgão emissor: Comitê Permanente de Ética em Pesquisa Envolvendo Seres Humanos da Universidade Estadual de Maringá

Patrocinadores

Patrocinador primário: Caroline Ferraz Simões

Patrocinadores secundários:

Instituição: Wendell Arthur Lopes

Fontes de apoio financeiro ou material:

Instituição: Universidade Estadual de Maringá

Condições de saúde

Condições de saúde ou problemas:

PT-BR	EN
Este estudo será conduzido em mulheres com idade entre 18 e 35 anos, que apresentem um quadro de obesidade de acordo com a classificação proposta pela Organização Mundial da Saúde (IMC: maior ou igual a 30 kg/m²), com peso corporal estabilizado/estabelecido há pelo menos 12 semanas, que não tenham participado de programas para redução de peso anteriormente, não portadores de cardiopatias, diabetes e/ou hipertensão e doenças endócrinas, não fumantes, e que não estejam fazendo uso de medicamentos que possam alterar sistemas cardiorrespiratório e neuromuscular.	This study will be conducted in women aged 18-35 years who presented an obesity profile according to the classification proposed by the World Health Organization (BMI: greater than or equal to 30 kg/m²), with body weight stabilized / established at least 12 weeks, who have not participated in weight reduction programs previously, do not have cardiopathies, diabetes and / or hypertension and endocrine diseases, non-smokers, and who are not taking medications that can alter cardiorespiratory and neuromuscular systems.

Descritores gerais para as condições de saúde:

PT-BR	ES	EN
C23: Condições patológicas, sinais e sintomas	**C23:** Condiciones patológicas, signos y síntomas	**C23:** Pathological conditions, signs and symptoms
C18: Doenças nutricionais e metabólicas	**C18:** Enfermedades nutricionales y metabólicas	**C18:** Nutritional and metabolic diseases

Descritores específicos para as condições de saúde:

PT-BR	ES	EN
C18.654.726.500: Obesidade	**C18.654.726.500:** Obesidad	**C18.654.726.500:** Obesity
C23.888.144.699: Sobrepeso	**C23.888.144.699:** Sobrepeso	**C23.888.144.699:** Overweight

Intervenções

Categorias das intervenções

Other

Intervenções:

PT-BR	EN
Serão formados dois grupos de intervenção: o grupo de treinamento intervalado de alta intensidade (GHIIT) e o de treinamento contínuo de intensidade moderada (GMICT), os quais executaram	Two intervention groups will be formed: the high intensity interval training group (GHIIT) and the moderate intensity continuous training group (GMICT), which performed the following protocols for 16 weeks in the

os seguintes protocolos POR 16 semanas na pista de atletismo da Universidade Estadual de Maringá (UEM): - GHIIT: iniciará com 10 min (minutos) de aquecimento, sendo 5 min a uma intensidade entre 55 e 65% da FCMax, e 5 min entre 65 e 75% da FCmáx, seguidos de 4 estímulos de 4 min de exercício (85-95% FCmáx) alternados por períodos de 3 min de recuperação ativa (65-75% FCmáx) e 5 min de desaquecimento, sendo 3 min entre 65-75% FCmáx e 2 min entre 55-65% FCmáx. - GMICT: consistirá em 5 minutos de aquecimento (55 e 65% da FCMax), seguido de 41 minutos na intensidade entre 65 e 75% da FCmáx, e 2 minutos de desaquecimento (55 e 65% da FCMax).	athletics track of the State University of Maringa (UEM): - GHIIT: will start with 10 min (minutes) of heating, 5 min at an intensity between 55 and 65% of FCMax, and 5 min between 65 and 75% of HRmax, followed by 4 stimuli of 4 min of exercise (85- 95% HRmax) alternated for periods of 3 min of active recovery (65-75% HRmax) and 5 min of quenching, with 3 min between 65-75% HRmax and 2 min between 55-65% HRmax. - GMICT: will consist of 5 minutes of heating (55 and 65% of FCMax), followed by 41 minutes in the intensity between 65 and 75% of HRmax, and 2 minutes of cooling (55 and 65% of FCmax).

Descritores para as intervenções:

PT-BR	ES	EN
G11.427.410.698.277: Exercício	**G11.427.410.698.277:** Ejercicio	**G11.427.410.698.277:** Exercise
I02.233.543: Educação Física e Treinamento	**I02.233.543:** Educación y Entrenamiento Físico	**I02.233.543:** Physical Education and Training
E02.760.169.063.500.387: Terapia por Exercício	**E02.760.169.063.500.387:** Terapia por Ejercicio	**E02.760.169.063.500.387:** Exercise Therapy

Recrutamento

Situação de recrutamento: Not yet recruiting

País de recrutamento

Brazil

Data prevista do primeiro recrutamento: 2020-05-16

Data prevista do último recrutamento: 2020-07-14

Tamanho da amostra alvo:	Gênero para inclusão:	Idade mínima para inclusão:	Idade máxima para inclusão:
64	F	18 Y	35 Y

Critérios de inclusão:

PT-BR	EN
Ser do sexo feminino; ter entre 18 e 35 anos de idade; apresentar quadro de obesidade (IMC: maior ou igual a 30 kg/m²); indivíduos com peso corporal estabilizado por pelo menos 12 semanas; que não participaram de programas de	Be female; be between 18 and 35 years of age; present a picture of obesity (BMI: greater than or equal to 30 kg/m²); individuals with body weight stabilized for at least 12 weeks; who have not participated in weight reduction programs before; not

redução de peso antes; não sofrendo de cardiopatias, diabetes e/ou hipertensão e doenças endócrinas; não fumantes; que não fazem uso de medicamentos que possam alterar os sistemas cardiorrespiratório e neuromuscular; com prontidão para participar de avaliações e intervenções; e assinatura do Termo de Consentimento Livre e Esclarecido (TCLE).

suffering from cardiopathies, diabetes and / or hypertension and endocrine diseases; non smokers; who are not making use of medicines that can alter cardiorespiratory and neuromuscular systems; with readiness to participate in evaluations and interventions; and signing of the Informed Consent Form (TCLE).

Critérios de exclusão:

PT-BR

Voluntárias que apresentem na avaliação clínica e/ou testes laboratoriais qualquer patologia ou outras complicações que possam ser fatores de risco ou adesão à prática regular da atividade física proposta; e qualquer outra condição que possa interferir no teste e/ou intervenção.

EN

Volunteers who present in the clinical evaluation and / or laboratory tests any pathology or other complications that may be risk factors or adhesion to the regular practice of the proposed physical activity; and any other condition that could interfere with the test and /or intervention.

Tipo do estudo

Desenho do estudo:

PT-BR

Ensaio clínico de tratamento, com delineamento paralelo, controlado e randomizado.

EN

Clinical trial of treatment, with a parallel, controlled and randomized design.

Programa de acesso expandido	Enfoque do estudo	Desenho da intervenção	Número de braços	Tipo de mascaramento	Tipo de alocação	Fase do estudo
False	Treatment	Parallel	2	Single-blind	Randomized-controlled	N/A

Desfechos

Desfechos primários:

PT-BR

O desfecho primário 1 previsto para o presente estudo serão parâmetros de rigidez arterial (pressão arterial central, velocidade de onda de pulso carotídeo-femoral e augmentation index). Tais medidas serão avaliadas por um médico cardiologista utilizando o dispositivo SphygmoCor XCEL (EM4C, AtCor Medical, Sydney, Austrália).

EN

The primary outcome 1 predicted for the present study will be parameters of arterial stiffness (central arterial pressure, carotid-femoral pulse wave velocity and augmentation index). Such measurements will be evaluated by a cardiologist using the SphygmoCor XCEL device (EM4C, AtCor Medical, Sydney, Australia).

PT-BR

O desfecho primário 2 previsto para o presente estudo serão parâmetros da função sistólica do ventrículo esquerdo (Fração de ejeção e Strain longitudinal global). Para a avaliação das medidas, serão realizados exames Ecocardiográficos com Doppler, por meio de um aparelho de

EN

The primary outcome 2 predicted for the present study will be parameters of left ventricular systolic function (ejection fraction and overall longitudinal strain). For the evaluation of the measurements, Doppler echocardiographic tests will be performed using an echocardiography /

ecocardiografia/ ultra- som, (modelo Vivid T8, GE Healthcare, Chicago, Illinois, Estados Unidos da América) com transdutor setorial (2,7-8,0 Mhz), conforme as recomendações da Sociedade Americana de Ecocardiografia e da Associação Europeia de Imagem Cardiovascular.

ultrasound device (Vivid T8 model, GE Healthcare, Chicago, Illinois, United States of America) with a transducer (2,7- 8.0 Mhz), as recommended by the American Society of Echocardiography and the European Cardiovascular Imaging Association.

PT-BR

O desfecho primário 3 previsto para o presente estudo serão parâmetros da função diastólica do atrio esquerdo (strain longitudinal). Serão realizados exames Ecocardiográficos com Doppler, por meio de um aparelho de ecocardiografia/ ultra-som, (modelo Vivid T8, GE Healthcare, Chicago, Illinois, Estados Unidos da América) com transdutor setorial (2,7-8,0 Mhz), conforme as recomendações da Sociedade Americana de Ecocardiografia e da Associação Europeia de Imagem Cardiovascular.

EN

The primary outcome 3 predicted for the present study will be parameters of the diastolic function of the left atrium (longitudinal strain). Echocardiographic Doppler examinations will be performed with an echocardiography / ultrasound device (Vivid T8 model, GE Healthcare, Chicago, Illinois, United States of America) with a transducer (2.7-8.0 Mhz), as recommended by the American Society of Echocardiography and the European Cardiovascular Imaging Association.

Desfechos secundários:

PT-BR

O desfecho secundário 1 previsto para o presente estudo serão as alterações metabólicas (hemograma completo, perfil lipídico, glicemia e insulinemia). As amostras sanguíneas serão coletadas após jejum de 12 horas, no período da manhã, por um profissional habilitado, por meio de punção venosa em tubos de sangue com gel, para obtenção de soro e EDTA. Para o cálculo da resistência à insulina será utilizada a Homeostasis Model Assessment (HOMA-IR) descrito por Matthewset al. (1985), enquanto para o cálculo da sensibilidade a insulina será utilizado o Quantitative Insulin Sensitivity Check Index (QUICKI), descrito por Katz et al. (2000).

EN

The secondary outcome 1 predicted for the present study will be the (complete blood count, lipid profile, glycemia and insulinemia). Blood samples will be collected after a fast of 12 hours in the morning by a qualified professional, through venipuncture in blood tubes with gel, to obtain serum and EDTA. For the calculation of insulin resistance, Homeostasis Model Assessment (HOMA-IR) described by Matthewset al. (1985), whereas for the calculation of insulin sensitivity the Quantitative Insulin Sensitivity Check Index (QUICKI), described by Katz et al. (2000).

PT-BR

O desfecho secundário 2 previsto para o presente estudo serão as alterações nos parâmetros inflamatórias (proteína C-reativa ultrassensível (PCR ultrassensível), adiponectina, leptina e óxido nítrico). Para a determinação dos marcadores inflamatórios será utilizado o método ELISA (ensaio imunoenzimático em fase sólida), de acordo com as especificações dos kits de alta sensibilidade (R&D Systems, Minneapolis, USA). Todas as determinações das concentrações de

EN

The secondary outcome 2 planned for the inflammatory parameters changes (ultra-sensitive C-reactive protein, adiponectin and leptin). For the determination of the inflammatory markers, the ELISA (solid phase immunoenzymatic assay) according to the specifications of the high sensitivity kits (R & D Systems, Minneapolis, USA) will be used. All determinations of circulating cytokine and adipokine concentrations will be performed in duplicate. The nitric oxide (NOx) levels in the sample will be prepared

Contatos

Contatos para questões públicas

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Contatos para informação sobre os centros de pesquisa

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Anexos

[Privado]

http://www.ensaiosclinicos.gov.br/static/attachments/parecer-consubstanciado-do-cep-aprovado.pdf (PARECER CONSUBSTANCIADO DO CEP)

OpenTrials v1.2

APÊNDICES

APÊNDICE A - TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE) I

Gostaríamos de convidá-lo a participar da pesquisa intitulada “Efeitos agudos *HIGH INTENSITY INTERVAL TRAINING* (HIIT) versus TREINAMENTO CONTÍNUO DE INTENSIDADE MODERADA sobre o consumo excessivo de oxigênio pós-exercicio (EPOC) em adultos obesos”, que faz parte do curso de Educação Física e é orientada pelo Prof. Dr. Wendell Arthur Lopes, da Universidade Estadual de Maringá. O objetivo da pesquisa é comparar os efeitos agudos de dois protocolos de HIIT versus um protocolo de treinamento contínuo de intensidade moderada sobre o metabolismo pós-exercício em mulheres adultas obesas. Para isto, a sua participação é muito importante e ela se dará da seguinte forma:

(I) Inicialmente, na sua primeira visita (Visita I) ao laboratório, além da sua familiarização com o local você será submetido a uma avaliação médica com cardiologista;
(II) Na visita II, será realizada a avaliação da composição corporal. Você precisa estar vestindo roupas leves. Além disso, no momento da avaliação será solicitado a retirada de todos os objetos de metais presentes no corpo (anel, brincos, piercing, entre outros).
(III) Na visita II ainda também será realizado um teste de esforço físico em bicicleta ergométrica, onde você pedalará em uma determinada velocidade até a exaustão.
(IV) Em 4 ocasiões distintas, respeitando um descanso de no mínimo 48h, será solicitado seu retorno ao laboratório para que você passe pelos 4 protocolos (3 com exercícios e 1 repouso), em dias diferentes, mas sempre no mesmo horário.
(V) Os protocolos de exercício serão constituídos da seguinte forma: HIIT-C: 4 minutos de aquecimento, seguidos por 10 períodos de pedalada em bicicleta ergométrica de 1 minutos á 90%Wpico alternados com 1 minuto de recuperação: HIIT-L: 4 minutos de aquecimento, seguidos por 4 períodos de pedalada em bicicleta ergométrica à 90%Wpico alternados com períodos de recuperação ativa de 3 minutos; MCIT: 4 minutos de aquecimento, seguidos por 30 minutos de pedalada em

intensidade moderada, a 35%Wpico. No protocolo repouso, você será orientado a permanecer em repouso, na posição sentada, por 35 minutos.
(VI) Após a aplicação de cada protocolo você precisará permanecer no laboratório por um prazo de aproximadamente sessenta minutos para as avaliações subsequentes de análise de consumo de oxigênio, gasto calórico e resposta cardiovascular.

Informamos que poderão ocorrer os desconfortos a seguir: I) Um pouco de vergonha durante as realizações das medidas corporais. II) Cansaço extremo, náuseas e tontura e caso isso aconteça, interromperemos os protocolos e será atendido imediatamente por profissional da saúde participante do projeto e encaminhados a ambiente hospitalar, sob a responsabilidade do pesquisador eventuais custos hospitalares. Gostaríamos de esclarecer que sua participação é totalmente voluntária, podendo você: recusar-se a participar, ou mesmo desistir a qualquer momento sem que isto acarrete qualquer ônus ou prejuízo à sua pessoa. Informamos ainda que as informações serão utilizadas somente para os fins desta pesquisa, e serão tratadas com o mais absoluto sigilo e confidencialidade, de modo a preservar a sua identidade. Os benefícios esperados serão: I) receber uma avaliação médica detalhada em relação ao risco de saúde; II) obter informações da composição corporal e do condicionamento cardiorrespiratório atual e III) encontrar o melhor protocolo de treino em relação ao seu estado nutricional, que gere maior gasto energético e menor risco cardiovascular. Caso você tenha mais dúvidas ou necessite maiores esclarecimentos, pode nos contatar nos endereços abaixo ou procurar o Comitê de Ética em Pesquisa da UEM, cujo endereço consta deste documento. Este termo deverá ser preenchido em duas vias de igual teor, sendo uma delas, devidamente preenchida e assinada entregue a você.

Além da assinatura nos campos específicos pelo pesquisador e por você, solicitamos que sejam rubricadas todas as folhas deste documento. Isto deve ser feito por ambos (pelo pesquisador e por você, como sujeito ou responsável pelo sujeito de pesquisa) de tal forma a garantir o acesso ao documento completo.
Eu,……………………………………………..
(nome por extenso do sujeito de pesquisa) declaro que fui devidamente esclarecido

e concordo em participar VOLUNTARIAMENTE da pesquisa coordenada pelo Dr. Wendell Arthur Lopes.

____ Data:……………………..
Assinatura ou impressão datiloscópica

Eu, Karin Hortmann, declaro que forneci todas as informações referentes ao projeto de pesquisa supra-nominado.

____ Data:.............................
Assinatura do pesquisador

Qualquer dúvida com relação à pesquisa poderá ser esclarecida com o pesquisador, conforme o endereço abaixo:

Nome: Karin Hortmann
Endereço: Rua João Luis Dias, nº 746 Telefone: (42)99865-4322
E-mail: karin_hortmann@hotmail.com

Nome: Wendell Arthur Lopes
Endereço: Universidade Estadual de Maringá.
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Qualquer dúvida com relação aos aspectos éticos da pesquisa poderá ser esclarecida com o Comitê Permanente de Ética em Pesquisa (COPEP) envolvendo Seres Humanos da UEM, no endereço abaixo:
COPEP/UEM

Universidade Estadual de Maringá.

Av. Colombo, 5790. UEM-PPG-sala 4.

CEP 87020-900. Maringá-Pr. Tel: (44) 3011-4444

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APÊNDICE B– TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE) II

Gostaríamos de convidá-la a participar da pesquisa intitulada "**Efeitos do treinamento intervalado de alta intensidade (HIIT) sobre os parâmetros metabólicos, inflamatórios, rigidez arterial e deformação miocárdica em mulheres obesas: um ensaio clínico randomizado**", que faz parte do curso de Educação Física e é orientada pelo Prof. Dr. Wendell Arthur Lopes, da Universidade Estadual de Maringá (UEM). O objetivo da pesquisa é investigar os efeitos de diferentes modalidades de exercícios físicos sobre as variáveis morfológicas (como peso, altura, circunferência da cintura e gordura corporal), metabólicas (níveis de glicose, insulina e gordura no sangue), inflamatórias (substâncias inflamatórias no sangue), rigidez arterial (capacidade da arterial em contrair e dilatar para a passagem do sangue, por meio de tonometria de aplanação, através de uma discreta compressão na pele) e deformação cardíaca (capacidade do coração de relaxar e contrair as suas paredes em cada ciclo cardíaco, realizado mediante exame de ultrassom do coração) em mulheres com obesidade.

A FASE I (efeito agudo) tem como objetivo verificar o efeito de uma sessão aguda de três protocolos experimentais (2 com exercícios e 1 repouso) sobre as variáveis de rigidez arterial e deformação miocárdica. A FASE II (efeito crônico) irá verificar o efeito de 16 semanas dos dois protocolos de exercícios físicos sobre os parâmetros cardíacos, vasculares, antropométricos, de composição corporal, aptidão física e nutricional das voluntárias. Para isto, a sua participação é muito importante e ela se dará da seguinte forma: na **FASE I do estudo (efeito agudo)**, serão realizadas seis visitas na clínica Biocor, correspondendo às seguintes atividades:

(I) Será realizada avaliação médica por um cardiologista. Em seguida, serão realizadas avaliações da composição corporal e antropometria, realizadas por profissionais da Educação Física. Para isso, será preciso que nas ultimas 24h antecedentes as avaliações, você não realize exercícios físicos extenuantes e não realize o consumo de bebidas cafeinadas, e nas ultimas 2h, você deverá ficar em jejum (de alimentos e bebidas). Além disso, você deverá estar vestindo roupas leves (apropriadas para a prática de atividade física), e no momento das avaliações, será solicitado a retirada de todos os objetos de metais presentes no corpo (Ex. anel, brincos, *piercing*);

(II) Será realizado um teste de esforço físico em esteira rolante, onde você iniciará caminhando, e a cada estágio de 3 min, será incrementado progressivamente velocidade e inclinação até sua exaustão. O teste será realizado por profissionais da Educação Física com supervisão de um médico cardiologista;

(III, IV e V) Em três ocasiões distintas, respeitando um descanso de no mínimo 48h, será solicitado seu retorno à clínica para que, aleatoriamente, você passe pelos três protocolos experimentais (2 com exercícios e 1 repouso). Todos os protocolos experimentais serão realizados por profissionais de Educação Física e com supervisão de um médico cardiologista. Os protocolos de exercício serão constituídos da seguinte forma: O protocolo de treinamento intervalado de alta intensidade (HIIT) iniciará com 10 min (minutos) de aquecimento, sendo 5 min a uma intensidade entre 55 e 65% da Frequência Cardíaca máxima (FC_{Max}), e 5 min entre 65 e 75% da $FC_{máx}$, seguidos de 4 estímulos de 4 min de exercício (85-95% $FC_{máx}$) alternados por períodos de 3 min de recuperação ativa (65-75% $FC_{máx}$) e 5 min de desaquecimento, sendo 3 min entre 65-75% $FC_{máx}$ e 2 min entre 55-65% $FC_{máx}$. O protocolo de treinamento contínuo de intensidade moderada (MICT) consistirá em 5 minutos de aquecimento (55 e 65% da FC_{Max}), seguido de 41 minutos na intensidade entre 65 e 75% da $FC_{máx}$, e 2 minutos de desaquecimento (55 e 65% da FC_{max}). No protocolo da condição controle, você permanecerá em repouso por 30 minutos na posição sentada. Antes e durante os 60 minutos após os protocolos experimentais, serão realizadas medidas cardiológicas realizadas por médico cardiologista. Informamos que poderão ocorrer cansaço, náuseas e/ou tontura durante e/ou após os protocolos de exercício, mas você sempre estará sendo monitorada pelos profissionais da saúde participantes do projeto, e o médico cardiologista fará o atendimento sempre que necessário;

(VI) Após a conclusão da FASE-I, uma visita no departamento de Educação Física da Universidade Estadual de Maringá (UEM) será agendada a fim da devolutiva dos resultados.

Na **FASE II do estudo (efeito crônico) s**erão formados dois grupos de pesquisa: o grupo de treinamento intervalado de alta intensidade (GHIIT), e o grupo de treinamento contínuo de intensidade moderada MICT (GMICT). As intervenções serão realizadas na pista de atletismo da UEM e terão duração de 16 semanas, sendo realizadas em três dias alternados por semana, com duração média de 1h/sessão. Todos as intervenções serão supervisionadas por profissionais de Educação Física devidamente capacitados. O treino do GHIIT consistirá em aquecimento de 10 minutos (60-70% $FC_{máx}$) seguidos de 4 estímulos de 4 minutos de exercício em uma pista de atletismo (85-95% $FC_{máx}$) alternados por períodos de 3 minutos de recuperação ativa (50-70% $FC_{máx}$) e 5 minutos de volta à calma (60-70% $FC_{máx}$). O protocolo de treinamento do GMICT iniciará com 5 minutos de aquecimento (55 e 65% da $FC_{máx}$), seguido de 41 minutos na intensidade entre 65 e 75% da $FC_{máx}$, e 2 minutos de desaquecimento (55 e 65% da $FC_{máx}$). Informamos que poderão ocorrer cansaço, náuseas e/ou tontura durante e/ou após os treinamentos, mas você sempre estará sendo monitorada pelos profissionais da saúde participantes do projeto, e o médico cardiologista fará o atendimento sempre que necessário. Na semana anterior ao inicio do projeto, e após as semanas 8 e 16, você participará de avaliações cardiovasculares, antropométricas, composição corporal, nível de atividade física, nutricional e exames sanguíneos (a coleta de sangue será realizada em um laboratório comercial da cidade). Após as semanas 4 e 12 do projeto, serão realizadas apenas avaliações cardiovasculares. Após a conclusão da FASE-II, uma visita no departamento de Educação Física da Universidade Estadual de Maringá (UEM) será agendada a fim da devolutiva dos resultados.

Informamos que poderão ocorrer os seguintes desconfortos durante o estudo: a) Um pouco de vergonha durante as realizações das medidas corporais, mas que serão minimizadas pela realização pelo mesmo avaliador e em ambiente reservado; b) Cansaço, náuseas e tontura durante os testes físicos e ou treinamentos, mas que serão sempre monitorados pelos profissionais da saúde participantes do projeto; c) Dor muscular tardia, estiramento muscular ou dor articular, mas que serão reduzidas com a melhora do condicionamento. Caso estes desconfortos persistiram ou algum risco seja detectado, os participantes serão atendidos imediatamente por profissional da saúde participante do projeto e encaminhados a ambiente hospitalar, sob a responsabilidade do pesquisador eventuais custos hospitalares e medicamentosos.

Gostaríamos de esclarecer que sua participação é totalmente voluntária, podendo você recusar-se a participar, ou mesmo desistir a qualquer momento sem que isto acarrete qualquer ônus ou prejuízo à sua pessoa. Comunicamos que não há nenhum tipo de custo relacionado aos exames e intervenções deste projeto. Também não há compensação financeira relacionada à sua participação. Entretanto, você precisará se deslocar até os locais de realização dos exames e dos treinamentos (Clínica Biocor, UEM e laboratório comercial). Caso seja necessário o uso de transporte para os locais onde serão realizados os exames e/ou os treinamentos, os pesquisadores se disponibilizaram em realizar o translado ou o ressarcimento dos custos adicionais com o transporte.

Esclarecemos ainda que as informações serão utilizadas somente para os fins desta pesquisa, e serão tratadas com o mais absoluto sigilo e confidencialidade, de modo a preservar a sua identidade. No final da pesquisa, todo o material utilizado será destruído após análise e uso dos dados.

Os benefícios esperados serão: I) Receber uma avaliação médica completa realizada cardiologista; II) Ter acesso a exames sanguíneos completos que avaliam o risco metabólico geral e estado inflamatório crônico; II) Obter informações da composição corporal e do condicionamento cardiorrespiratório; III) Vivenciar diferentes tipos de treinamento físico sob a supervisão de profissionais de Educação Física.

Caso você tenha mais dúvidas ou necessite maiores esclarecimentos, pode nos contatar nos endereços abaixo ou procurar o Comitê de Ética em Pesquisa da UEM, cujo endereço consta deste documento.

Este termo deverá ser preenchido em duas vias de igual teor, sendo uma delas, devidamente preenchida e assinada entregue a você. Além da assinatura nos campos específicos pelo pesquisador e por você, solicitamos que sejam rubricadas todas as folhas deste documento. Isto deve ser feito por ambos (pelo pesquisador e por você, como sujeito ou responsável pelo sujeito de pesquisa) de tal forma a garantir o acesso ao documento completo.

Eu,……………………………………………..
(nome por extenso do sujeito de pesquisa) declaro que fui devidamente esclarecido e concordo em participar VOLUNTARIAMENTE da pesquisa coordenada pelo Dr. Wendell Arthur Lopes.

____Data:……………………..

Assinatura ou impressão datiloscópica do voluntário

Eu, CAROLINE FERRAZ SIMÕES declaro que forneci todas as informações referentes ao projeto de pesquisa supra-nominado.

____ Data:..............................

Assinatura ou impressão datiloscópica da pesquisadora

Qualquer dúvida com relação à pesquisa poderá ser esclarecida através dos seguintes contatos:

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COORDENADOR DA PESQUISA
Nome: Wendell Arthur Lopes
Endereço: Universidade Estadual de Maringá
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Telefone: (44) 3011-5026
E-mail: warthurlopes@gmail.com

COMITÊ PERMANENTE DE ÉTICA EM PESQUISA ENVOLVENDO SERES HUMANOS DA UEM (COPEP/UEM)

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APÊNDICE C – DECLARAÇÃO DE ACORDO COM A PESQUISA

Comitê de Ética em Pesquisa em Seres Humanos

Maringá, 10 de junho de 2018.

Prezado Coordenador,

Declaro que eu, Prof. Dr. Rogério Toshiro Passos Okawa, médico cardiologista e docente no Departamento de Medicina desta universidade, CRM PR-15265, serei responsável pela avaliação médica e liberação para a prática de exercício físico dos participantes do projeto de pesquisa “Efeito agudo do *high intensity interval training* (HIIT) versus treinamento contínuo de intensidade moderada intensidade sobre o consumo excessivo de oxigênio pós-exercício (EPOC) em adultos obesos” que estará sob a responsabilidade do *Prof. Dr. Wendell Arthur Lopes*.

Estou ciente de que os participantes da pesquisa serão adultos obesos recrutados na cidade de Maringá e municípios vizinhos, bem como de que o presente trabalho deve seguir a Resolução CNS 196/96 e complementares.

Atenciosamente,

____

Dr. Rogério Toshiro Passos Okawa
Médico Cardiologista
HUM/UEM

APÊNDICE D – FICHA DE COLETA DE MEDIDAS CARDIOVASCULARES

GPHARV

Grupo de Pesquisa em Hipertensão Arterial Sistêmica, Rigidez Arterial e Envelhecimento Vascular

Nome: ____ Data Nasc: ____/____/_____
Idade:_____________ Contato: ____
Peso:_____________ Estatura:_______________

	CONTROLE		HIIT		CMIT	
DATA	/ /		/ /		/ /	
AVALIADOR						
Pré	VOP= AIx= ECO=	______h______min	VOP= AIx= ECO=	______h______min	VOP= AIx= ECO=	______h______min
1 min	VOP= AIx=	______h______min	VOP= AIx=	______h______min	VOP= AIx=	______h______min
5 min	ECO=	______h______min	ECO=	______h______min	ECO=	______h______min
30 min	VOP= AIx=	______h______min	VOP= AIx=	______h______min	VOP= AIx=	______h______min
35 min	ECO=	______h______min	ECO=	______h______min	ECO=	______h______min
45 min	VOP= AIx=	______h______min	VOP= AIx=	______h______min	VOP= AIx=	______h______min
60 min	VOP= AIx=	______h______min	VOP= AIx=	______h______min	VOP= AIx=	______h______min
65 min	ECO=	______h______min	ECO=	______h______min	ECO=	______h______min

APÊNDICE E – FICHA DE COLETA DE TREINO HIIT

HIIT:

Nome Completo: ____ Data de nascimento: ___/___/___ Altura: ___________ Peso: ________________

Avaliadores:____ Data: ____/_____/2018 FCmáx (Obt):_____________

5 min 55-65%Fcmax + 5 min 65-75%Fcmax ____h____min	4 min 85-95%Fcmax ____h____min	3 min 65-75%Fcmax ____h____min	4 min 85-95%Fcmax ____h____min	3 min 65-75%Fcmax ____h____min	4 min 85-95%Fcmax ____h____min	3 min 65-75%Fcmax ____h____min	4 min 85-95%Fcmax ____h____min	3 min 65-75%Fcmax + 2min 55-65%Fcmax ____h____min

	AQUECIMENTO	HIIT - 1	RECUP.	HIIT - 2	RECUP.	HIIT - 3	RECUP.	HIIT - 4	DESAQUECIMENTO
Início:____h_____min	(Est) VEL:_______ FC: _______	(Est) VEL:_____ FC: ______	(Est) VEL:_____ FC: ______	(Est) VEL:_____ FC: ______	(Est) VEL:_____ FC: ______	(Est) VEL:_____ FC: ______	(Est) VEL:_____ FC: ______	(Est) VEL:_____ FC: ______	(Est) VEL:_______ FC: _______
Final:____h_____min T= 40 minutos	(Obt) VEL:_____ FC: ______ PSE:______	(Obt) VEL:_____ FC: ______ PSE:____ AF: ______	(Obt) VEL:_____ FC: ______ PSE:_____	(Obt) VEL:_____ FC: ______ PSE:_____ AF: ______	(Obt) VEL:_____ FC: ______ PSE:_____	(Obt) VEL:_____ FC: ______ PSE:_____ AF: ______	(Obt) VEL:_____ FC: ______ PSE:_____	(Obt) VEL:_____ FC: ______ PSE:_____ AF: ______	(Obt) VEL:_______ FC: _______ PSE:_______

Observações:

APÊNDICE F – FICHA DE COLETA DE TREINO MICT

CMIT:

Nome Completo: ________________ **Data de nascimento:** ___/___/___ **Altura:** __________ **Peso:** ______________

Avaliadores:________________________ **Data:** ____/_____/2018 **FCmáx (Obt):**____________

5 min 55-65%$Fc_{Máx}$	41 minutos 65-75%$Fc_{Máx}$					2 min 55-65%$Fc_{Máx}$
AQUECIMENTO (Est) VEL:_______ FC: _______	**MICT (Est)** VEL:_______ FC: _______	**MICT (Est)** VEL:_______ FC: _______	**MICT (Est)** VEL:_______ FC: _______	**MICT (Est)** VEL:_______ FC: _______	**MICT (Est)** VEL:_______ FC: _______	**DESAQUECI. (Est)** VEL:_______ FC: _______
(Obt) VEL:_______ FC: _______ PSE:_______	**(Obt)** VEL:_______ FC: _______ PSE:_______	**(Obt)** VEL:_______ FC: _______ PSE:_______	**(Obt)** VEL:_______ FC: _______ PSE:_______	**(Obt)** VEL:_______ FC: _______ PSE:_______	**(Obt)** VEL:_______ FC: _______ PSE:_______	**(Obt)** VEL:_______ FC: _______ PSE:_______

Início: ____h____min
Final: ____h____min
T= 48 minutos

Observações:

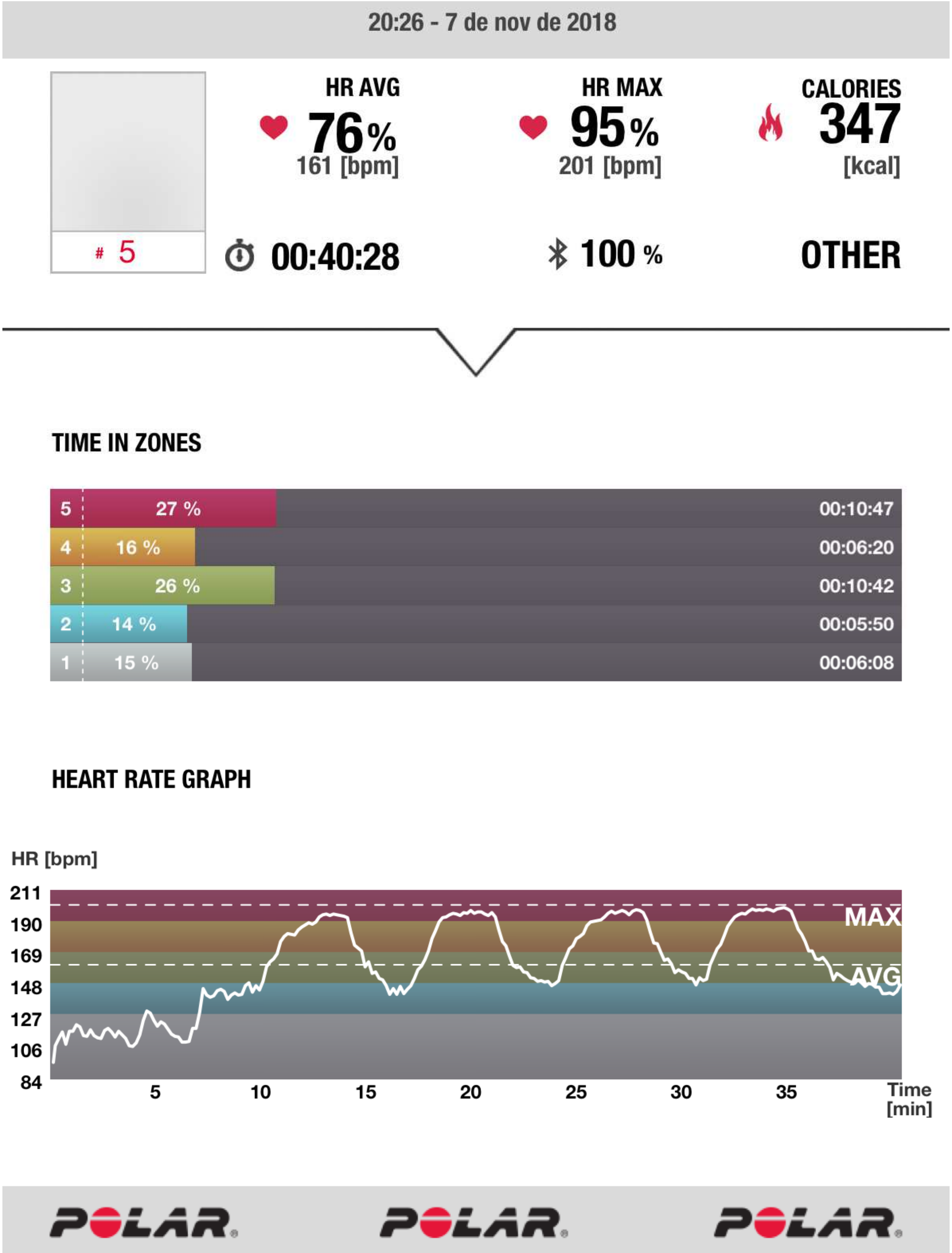
APÊNDICE G – FICHA FAMILIARIZAÇÃO

FAMILIARIZAÇÃO

Avaliadores:____ Data:____/____/2018 FCmáx (Est):____________ FCmáx (Obt):____________

	PRÉ	50%	55%	60%	65%	70%	75%	80%	85%
FC									
VEL									

APÊNDICE H – RESUMO DE UMA SESSÃO DE EXERCÍCIO HIIT



APÊNDICE I - RESUMO DE UMA SESSÃO DE EXERCÍCIO MICT