Dissertation title:

Comparing the Effect of Low-frequency High-intensity Interval Training (HIIT) with Moderate-intensity continuous Training (MICT) on Visceral Fat Reduction in Centrally Obese Adults

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Comparing the Effect of Low-frequency High-intensity Interval Training (HIIT) with Moderate-intensity continuous Training (MICT) on Visceral Fat Reduction in Centrally Obese Adults

Abstract

Background: Obesity is a disease affecting people worldwide with prevalence surging especially in recent few decades. Central obesity is the type of obesity with accumulation of visceral fat at the abdominal region and is highly associated with heightened risk of comorbidities. Exercise to increase physical activity is well-established as a major lifestyle modification component to treat obesity. Moderate-intensity continuous training (MICT) and high-intensity interval training (HIIT) are two forms of aerobic exercises practiced at different intensities but with at least comparable benefits in reducing visceral fat. Preliminary evidence has even suggested superiority of HIIT in reducing adiposity despite requiring less time commitment. Contradicting to most findings that suggested HIIT delivered at a frequency of 3 times weekly to be the minimal requirement for reducing body fat, our research team recently demonstrated the effectiveness of once-weekly HIIT over MICT in improving body composition. Purpose: Therefore, to validate the contradicting evidence on the minimal amount of HIIT required, this study compared the effect of low-frequency HIIT and MICT on reducing visceral fat in centrally obese adults. Methods: Twenty-three adults with central obesity (BMI≥25; with waist circumference ≥90 cm for men and ≥80 cm for women) aged 18-60 were randomized into the control group (n=7), HIIT group (HIIT x1/week; n=8) or MICT group (MICT x1/week; n=8) for 3 months. Visceral fat (VAT) and subcutaneous fat (SAT) volumes were measured at baseline and after 3-months intervention using Magnetic Resonance Imaging (MRI). Results: VAT volume reduction was the greatest in the HIIT group, while
SAT volume reduction was the greatest in the MICT group. Intervention effects on the reduction in VAT and SAT volumes, as well as differences between groups however were not statistically significant. **Conclusion:** Results showed that both low-frequency HIIT and MICT were not effective in reducing abdominal visceral fat, and the difference between the effects of HIIT and MICT on eliminating visceral adiposity was minimal. Thus, studies with greater sample sizes and longer durations are required to detect true differences. Future research should also aim at finding the minimal amount of HIIT required for effectively reducing abdominal visceral adiposity in centrally obese adults to facilitate application in clinical settings.

**Keywords:** Central Obesity, Visceral Fat, Magnetic Resonance Imaging, High-intensity Interval Training, Moderate-intensity Continuous Training

**Abbreviations:**

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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<td>GEE</td>
<td>Generalized Estimated Equation</td>
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<td>HIIT</td>
<td>High-Intensity Interval Training</td>
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<td>HRmax</td>
<td>Maximal Heart Rate</td>
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<td>MET</td>
<td>Metabolic Equivalent</td>
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<td>MICT</td>
<td>Moderate-Intensity Interval Training</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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Introduction

Prevalence of obesity and its disease burden

Overweight and obesity is a global pandemic that is affecting billions of people around the world. It is reported by the World Health Organization (WHO) that by 2016, nearly 40% of adults are overweight, while 11% and 15% of men and women are obese respectively (1). More worryingly, data collected from the National Health and Nutrition Examination Survey (NHANES) has reflected a significant increase in obesity prevalence across almost all ethnicities over the past 20 years (2). Indeed, obesity prevalence has experienced a two-fold increase in 70 countries since the 1980s (3), while countries in the Middle East and China even had tripled obesity rates (4), showing that there had been a shift in prevalence from more developed countries to developing countries with lower socioeconomic levels (5).

Overweight and obesity do not only affect one’s body image, but are also associated with increased risks of most non-communicable chronic diseases (6). In fact, high body mass index (BMI) was already found to be greatly associated with heightened risk of hypertension, stroke and coronary heart disease which are cardiovascular-related diseases, metabolic disorders such as type 2 diabetes and dyslipidaemia, bone diseases including osteoarthritis, as well as various cancers (7, 8). Although obesity itself may not be the direct cause of mortality, cardiometabolic diseases that it imposes have contributed to nearly half of the mortality cases among people with high BMI (3). Given with the high prevalence of comorbidities related to obesity including cardiovascular diseases and type 2 diabetes, healthcare burden has experienced a sharp rise in recent decades (9). While obesity-related medical expenses was increased by 68.5 billion from 1998 to 2008 in solely the United States (US) (10), increase in healthcare cost is even more significant in developing countries like China, reaching a double of the US (11). In fact, in the
case of China, 25.5% of the direct health cost for the four major non-communicable diseases, including coronary heart disease, hypertension, stroke and diabetes, was found to be obesity-related by 2003 (12), and the overall obesity-associated healthcare cost is expected to continually rise, reaching $112 billion in 2025 (13).

Central obesity better predicts health risk

BMI has been one of the most common standards that is used globally to infer one’s weight status and obesity-related health condition. While it is adopted widely due to its ease of measurement, cut-offs issued by the World Health Organization (WHO) may not be universally representative of obesity status across all ethnicities (14). To be specific, higher fat percentages were found at lower BMI in Asian populations when compared to Westerners (14). Therefore, while a BMI ≥30 defines obesity in Western populations, Asians with BMI ≥25 are already classified as obese (8). This also shows that BMI measurement alone may not accurately infer obesity, and solely high BMI may not be sufficient in predicting risks of complications associated with obese conditions.

To further illustrate the reason why high BMI may not be inferential to detrimental health outcomes, it is important to understand that while having a greater weight is generally indicative of having a larger amount of fat, the location of fat deposition has even more significant implications on the impact on health. In fact, obesity can be further divided into two main categories according to the site where fat is deposited, including visceral fat obesity and subcutaneous fat obesity (15). While subcutaneous fat obesity refers to fat accumulation beneath the skin, visceral fat obesity has fat accumulation around internal organs as apparent in the abdominal cavity, and thus is also commonly referred as central obesity (15). Studies found that obese people with higher visceral fat area have heightened risks of complications
when compared to those with subcutaneous fat obesity. For instance, they are more prone to developing comorbidities ranging from metabolic diseases related to glucose and lipid metabolism like diabetes and dyslipidaemia (15, 16), as well as cardiovascular diseases like hypertension (16), in which strong correlation between central obesity and type 2 diabetes has been profound among South Asian populations (17). As such, central obesity is already acknowledged by the International Diabetes Federation as one of the most significant and shared risk factors to a variety of metabolic diseases (18). Together, these shows that abdominal visceral fat accumulation is more indicative of heightened obesity-associated health risks than high BMI alone, and the significance of identifying people with central obesity in addition to high BMI is highlighted. In fact, a study in 2013 on Chinese populations found an increasing trend of central obesity development among populations with normal BMI (19). Therefore, to better predict health risk associated with visceral fat deposition, it is suggested that waist circumference that measures obesity around the trunk may be preferred over using BMI alone due to its applicability over all ethnicities to predict central obesity (20). By taking waist into consideration, obese participants with heightened risks of more severe disease burden and complications can be better identified, and treatment for these patients may also consider targeting visceral fat reduction in addition to reducing body weight alone.

Physical activity as one of the most modifiable risk factor of obesity

Overweight and obesity are mainly caused by a prolonged “imbalance” of energy intake and output, in which intake constantly outweights output, causing a gain in weight (21). Other than increasing intake of energy-dense food (21), decreasing physical activity is also identified as a major attributable factor of increasing obesity and obesity-related disease prevalence in developing countries (22), which may be explained by a more sedentary lifestyle promoted by rising living standards (21). Thus, one of the most well-known and plausible ways to promote
weight loss and reduce body fat mass is by increasing energy expenditure with a higher physical activity level (23). Moreover, in addition to low level of physical activity, reduction in the ability of one’s body to oxidize fat is also believed to be a possible cause of weight gain (24), which can also be improved by exercise. Particularly for aerobic exercise, it can increase the amount and ability of mitochondria to carry out fat oxidation, thereby reversing the compromised fat-oxidizing ability in obese individuals (25).

At present, lifestyle changes, pharmacotherapy and bariatric surgery are the three common ways to treat overweight or obesity patients (26). While pharmacotherapy and bariatric surgery are only used to treat patients with more severe obesity, modification in lifestyle is recognised as the most preferrable and effective option to be delivered alone or in combination with the latter two treatments (26). Given that low physical activity is the major cause to increment of weight and body fat (22), performing exercise contributes to the most significant part of lifestyle modification in order to reduce weight. Thus, increasing physical activity is already proven to be the best way to treat obesity and prevent obesity-related complications like coronary heart diseases in South Asians (17).

Although the exact mechanism for exercise to result in weight loss is complex, and the underlying causal relationships are still under investigation, the capability of exercise to reduce weight and body fat is already strongly proven and agreed among the scientific community. When comparing the effect of the two major forms of exercises: aerobic exercise and resistance exercise on visceral fat reduction, a review concluded significant effect of aerobic exercise to achieve reduction in visceral fat but not for resistance exercise (27). Therefore, aerobic exercise is the commonly adopted form of exercise that makes up the major component of lifestyle modification to increase physical activity among obese individuals, and is also suggested to be
incorporated in all programs that are aiming for weight maintenance (28). Given that the ability of exercise in reducing abdominal visceral fat is valid even without an apparent weight decrease (29), its application to treat centrally obese patients to achieve visceral adiposity reduction is especially meaningful, so as to lower their risks to a variety of cardiometabolic diseases.

**Different exercise intensities on health outcomes**

Aerobic exercise can be further classified by its intensity. One of the most traditionally practiced form of aerobic exercise is moderate-intensity continuous training (MICT), also known as endurance training, where exercise is sustained at a moderate-intensity for a prolonged period of time (30). Endurance training has been established with recognizable effect in reducing adipose tissue at the abdominal region, with its effect extending to reducing visceral adiposity (31). While MICT is generally recommended for obese individuals to reduce fat, complains associated with boredom due to the monotonous nature of it, as well as a great time consumption have largely contributed to low motivation and adherence to MICT exercise programs (32). Moreover, while studies done in earlier years suggested that only the total exercise volume (in other words total energy expenditure) mattered for an exercise to be effective in reducing body fat (33, 34), increasing evidence has demonstrated the importance of also taking into the account of exercise intensity to maximize exercise’s benefit on reducing body adiposity. Therefore recently, high-intensity interval training (HIIT) that is also aerobic in nature has emerged with novelty, which can be performed in a more timely-efficient manner with 40% less time commitment when compared to MICT (35). HIIT refers to intervals of vigorous intensity exercise that “elicits $\geq 80\%$ of maximal heart rate (HRmax)”, and is interspersed with rests between each bout of submaximal efforts (36, 37). The shorter time commitment required in HIIT is especially encouraging, as despite recognised effectiveness of
exercise to reduce obesity, inadequate time has been identified as a significant hindering factor for people with weight issues to participate in any forms of physical activity (38).

In fact, the at least comparable effect of HIIT and MICT on reducing body adiposity is already recognized, and the interchangeability of moderate and high intensity aerobic exercises with matched volume (intensity x duration x frequency) to produce comparable health benefits has been suggested in the Physical Activity Guidelines issued by the WHO (39). In particular, the guideline issued in 2020 stated that a weekly involvement in either 150 minutes of moderate intensity exercise or 75 minutes of vigorous intensity exercise, or the mixture of both that makes up a similar exercise volume can all result in similar health benefits (39). Three reviews on studies that investigated the effect of HIIT (delivered 3 times a week) and MICT on improving body composition also found comparable effects of both in reducing body fat (35, 40, 41), and waist circumference (35). It is important to note that studies which found exercise interventions of HIIT or MICT effective in reducing fat significantly also delivered trainings for longer periods of time (eg. 10 weeks (35) & 12 weeks (42)), in which short-term HIIT or MICT were both not sufficient in reducing body fat (40). This shows that a continual effort to perform exercise, and more preferably a habitual change, is fundamental for both HIIT and MICT to accumulate their effects to produce significant adiposity reducing results.

Even more, some previous studies that compared the effectiveness of MICT and HIIT on other health parameters (especially cardiorespiratory fitness) have suggested that they may not give health benefits to an exact same extent or at the same rate. When comparing to MICT, a study has demonstrated superior effect of HIIT over MICT in improving cardiorespiratory fitness in both healthy individuals and patients suffering from cardiometabolic diseases (43). A more recent study in 2021 also demonstrated comparable efficacy of HIIT and MICT in lowering fat
mass and risks of cardiovascular diseases, while HIIT was even found to be superior over MICT to improve cardiorespiratory fitness (42). Indeed, other than HIIT being more effective in improving fitness (42, 43), a greater effect of higher intensity exercises in modifying body fat content has been suggested (44), and several other studies have also shown that despite a matched energy expenditure, higher intensity exercises were associated with larger reductions in subcutaneous fat (45, 46), as well as visceral fat (47). Particularly to achieve visceral adiposity reduction, MICT was concluded to be less effective than higher intensity exercises in a study that compared the effect of sprint interval training (similar to HIIT except all-out effort is required during high-intensity intervals) with MICT (48). Taken these together, preliminary evidence has inferred a possible superiority of HIIT in lowering abdominal fat when compared to MICT that is practiced at a lower intensity. However, a common limitation among most studies was that little of them used “multicomponent methods” including magnetic resonance imaging (MRI) or computed tomography (CT) as their measurement tools to track visceral fat changes (49). Multicomponent measurement is recognized to be the “gold standard” method to infer body composition among obese patients due to their ability to accurately access the location of fat deposition (50, 51), which is particularly useful for giving clinical implications due to a higher accuracy in distinguishing between visceral and subcutaneous fat. Given that most studies that found superior effects of higher intensity exercises in reducing fat mass used less optimal measurement tools such as the bioelectrical impedance analyser (42), and dual-energy X-ray absorptiometry (48), whether HIIT truly exerts a greater effect on reducing visceral adipose tissue when compared to MICT practiced at a lower intensity has to be further validated using more accurate multicomponent measurement tools.

**HIIT may be a better alternative of MICT for treating obese patients**
Despite possible differential efficacies of HIIT and MICT on visceral fat reduction, there are still several reasons why HIIT can be an alternative to traditional MICT. First, the feasibility and safety of applying different kinds of exercises in overweight and obese individuals are often of major concerns due to their higher susceptibility to cardiovascular diseases (52). Despite the fact that HIIT requires exercising in short bouts of higher intensities, it is found to be safely applied in populations with weight issues and no major adverse events were reported in trials that involved obese patients (53).

Second, apart from HIIT that can be safely prescribed to obese patients, the ability of it to promote greater adherence due to a lower perceived physical demand and higher enjoyment during exercise is another advantage of HIIT over MICT to be adopted as a treatment. As low cardiorespiratory fitness is common among overweight and obese individuals (54), perception of tiredness and a feeling of incapability to complete exercise training can also hinder them from exercising. Given the interval nature of high intensity bouts involved in HIIT, less physical demand may be placed on individuals when compared to MICT which prolong continual efforts are needed (55). Shorter bouts of intense efforts is also believed to increase confidence for physically unfit individuals to complete the exercise protocol (56). Progressively, the ability to complete training may further give a sense of achievement that can motivate them to adhere to the training (57). The ability to make exercise enjoyable is especially important for promoting long term lifestyle changes, in which having the habit of exercise that can be carried on towards their later years of life is essential for sustained fat reduction and weight maintenance (58). Therefore, HIIT may be a preferrable exercise alternative to MICT that can be safely applied and adhered more strongly by obese individuals, thereby increasing the likelihood of incorporating exercise into their daily life for maintaining good body composition and gaining long term health benefits.
Possibility of low-volume HIIT

Recently, increasing interests are raised on the possibility of delivering low-volume HIIT to further reduce time commitment required to generate benefits from exercises such as improving fitness and body composition. Low-volume HIIT generally refers to HIIT practiced less frequently or at lower intensities, which most studies delivered low-volume exercises in a way that the total training volume is less than 500 metabolic equivalent minutes weekly (MET-min/week) (49). It was concluded in a review that while low-volume HIIT could better boost cardiorespiratory fitness when compared to equivalent volume of MICT (49), both exercise protocols were not effective in improving body composition (49). Similar results were observed in a study on overweight or obese males, in which both low-volume HIIT and MICT could improve fitness to a similar extend, but were not effective in reducing body fat (59). Contradicting to these results, our research team has recently conducted a study on overweight or obese men that demonstrated the effectiveness of low-frequency HIIT in reducing total body fat mass (60). In this study, subjects in all HIIT intervention groups (delivered once/ twice/ three times weekly) had experienced improved aerobic fitness, body composition and lowered blood pressure after 8 weeks even faster than those that practiced MICT 3 times weekly. Thus, it is hypothesised that study which found low-volume exercise protocols ineffective in reducing body fat was due to a relatively short study duration (6 weeks) and used cycling as the exercise modality (59), which might have less effect on eliminating body fat mass when compared to running (35). However, given that our previous study also did not use MRI or CT scan as its measurement tool to specifically look at visceral fat changes, the superior effect of low-frequency HIIT over MICT in reducing visceral adiposity in obese individuals remains to be investigated.
As high-quality evidence that compared the effectiveness of HIIT and MICT on visceral fat reduction is lacking, and inconclusive findings on the minimal amount of HIIT required to reduce abdominal visceral adiposity is present, the aim of this study is to compare the effectiveness of low-frequency HIIT (practiced once weekly) with MICT on visceral fat reduction in centrally obese adults. Given with the fact that the amount of visceral fat accumulated at the abdominal region is more indicative of risks for obesity-related complications (15, 16), waist circumference along with BMI was used to identify participants with central obesity. To enhance the validity of results, MRI, which is a “gold standard” multicomponent measurement tool, was also used to accurately track changes in the volume of visceral fat accumulated at the abdominal region before and after exercise intervention (61). It is hypothesised that low-frequency HIIT would be able to reduce abdominal visceral fat in centrally obese adults to a greater extent when compared to MICT practiced at the same frequency.
Methodology

Subjects
Twenty-three adults aged 18-60 years old were recruited to participate in this randomized control trial. Participants of both sexes were included.

Inclusion criteria
1. Adults aged 18-60
2. Centrally obese (BMI ≥ 25 with waist circumference ≥ 90 cm or ≥ 80 cm for men and women respectively)
   A BMI of 25 or over is classified as central obesity according to the definition adopted by the Hong Kong Government, while waist circumference greater than or equal to 90 cm or 80 cm for men and women accordingly are defined as abdominal obesity under the criteria issued by the International Diabetes Federation for Chinese population.

Exclusion criteria
1. With physical activity level that met the WHO physical activity guidelines for adults (≥ 150 min moderate-intensity or ≥ 75 min vigorous-intensity exercises, or the mixture of both that makes up equivalent exercise volume (62))
2. Had participation in regular exercise training (HIIT or MICT) more than once a week over the past 6 months period
3. With clinical depositions or somatic conditions that may limit exercise options (Presently or once being diagnosed of cardiovascular disease, heart failure, chronic kidney or pulmonary disease, cancer, etc. or having physical constraints such as loss of limbs)
4. With compromised mobility due to chronic diseases such as osteoarthritis and musculoskeletal diseases
5. Had a daily habit of smoking or drinking
6. Had undergone treatment for weight loss or reducing obesity (surgery such as gastric bypass or gastric band; therapies such as dietary programs prescribed by a dietitian; or medication) in the past 6 months

_Selection of eligible participants & informed consent_

Interested subjects were invited to the lab to attend a screening session to see whether they were eligible for this study. Informed consents with verbal explanation were then delivered to selected subjects. All subjects signed an informed consent form before any baseline measurements were conducted.

**Intervention & control groups**

Twenty-three adult participants were randomly allocated to one of the three groups: the health education group (control) (n=7), the HIIT group (n=8), or the MICT group (n=8). The intervention period lasted for 3 months after baseline measurements were conducted.

**Health education (usual care control group)**

Subjects participated in a health education program of 70 minutes per lesson delivered twice a month (6 lessons in total). The program included delivering of information related to obesity and health, giving advice on weight loss (eg. dietary restrictions on calories), counselling on lifestyle modifications and stretching. This health education group also acted as the usual care control group for the study.
HIIT group

The HIIT program was delivered in small groups on a weekly basis by qualified trainers. Subjects performed HIIT on treadmill, reaching 85%-95% HRmax, for 4 minutes repeated for 4 bouts, interspersed with active rest periods of recovery walking at 50%-70% HRmax. 5-minute warm-up and cool-down periods were included in each training session before and after the main program, making up a total duration of 35 minutes for each session. The OH1 optical heart rate sensor on Polar M300 watch was used to keep track of each participant’s heart rate during performance of exercise, this was to make sure that their target heart rate could be met during training.

MICT group

The MICT program was delivered in small groups on a weekly basis by qualified trainers. Subjects performed MICT on treadmill, reaching 65%-75% HRmax. Each training session lasted for a longer duration when compared to the HIIT group so that the exercise volumes of both groups were matched. The OH1 optical heart rate sensor on Polar M300 watch was also used to keep track of each participant’s heart rate during performance of exercise.

Randomization & blinding

Randomized allocation with a parallel assignment intervention model was used to assign subjects to different intervention groups. The study was carried out in a single-blinded manner, in which the outcome accessor was masked from the groups by which the participants were allocated to. The subjects were also asked not to give hints on their intervention groups during assessment of outcomes.

Adverse events
Trainers of the exercise programs were asked to pay attention to each subject in their class to see if any unusual events occurred during class time. Subjects were also told to report any kind of discomforts felt during physical activity or throughout the intervention period. Other than great discomforts such as cardiac abnormality, subjects were also asked to report mild discomforts including headaches, dizziness, prolonged muscle pain or fatigue, without consideration of whether discomforts felt were due to the interventions or not. Discomforts reported were to be immediately followed-up to determine further actions. In case of adverse events, they were to be reported with reference to the consolidated standards of reporting trials (CONSORT) guidelines.

**Outcome measurements**

Outcomes were measured before the start of intervention (0-month baseline measurement (PRE)) and after 3 months of intervention (post-intervention measurement (POST)).

*Primary outcome*

Visceral fat (VAT)

The volume of visceral fat (VAT) in the abdominal region was measured using the 1.5-Teala whole-body scanner. The abdominal region was defined as the region between the lower border of the thoracic diaphragm and the upper border of the first sacral vertebra. Before the MRI scan, a breath-hold localizer scan was performed. Fast spoiled gradient-echo sequences were used to collect T1-weighted in-phase images at end-expiration suspension. After images were collected, manual marking of the VAT region was performed on every transverse image found within the abdominal region, which were later used to compute the total abdominal VAT volume using the software *sliceOmatic* by TomoVision.
Secondary outcome

Subcutaneous fat volume (SAT)

The volume of subcutaneous fat (SAT) in the abdominal region was measured using the 1.5-Teala whole-body scanner. The abdominal region was defined as the region between the lower border of the thoracic diaphragm and the upper border of the first sacral vertebra. Before the MRI scan, a breath-hold localizer scan was performed. Fast spoiled gradient-echo sequences were used to collect T1-weighted in-phase images at end-expiration suspension. After images were collected, manual marking of the SAT region was performed on every transverse image found within the abdominal region, which were later used to compute the total abdominal SAT volume using the software sliceOmatic by TomoVision.

Statistical analysis

Data collected from measurements were kept confidential. The Statistical Analysis Software (SAS) was used in performing statistical analysis on the data. Generalized estimated equation (GEE) model was used to analyse intervention effects on the respective outcomes (VAT volume & SAT volume) and the covariate was taken from the baseline value. R programming was used in conducting the GEE analysis, using the package “geeM”. Multiple pairwise comparisons were done to compare differences between each intervention group using the Tukey’s multiple comparison test. P values were used to assess the significance of differences, and the level of acceptable significance was set at p-value < 0.05. For pairwise comparisons, the Benjamin & Hochberg (BH) method was used to adjust the p-values so as to control for multiplicity and reduce the chance of type I errors (63). Mean ± Standard Deviation (SD) was used to present the data.
Results

**Visceral fat (VAT) volume**

The visceral fat (VAT) volume (cm$^3$) at baseline (PRE) and after completing the 3 months of intervention (POST) are presented in Table 1 and Figure 1. After 3 months of the intervention period, all the 3 groups experienced reductions in VAT volume. GEE analysis showed that there were no statistically significant group-by-time interactions in VAT volume (interaction effect: p=0.4804). The largest reduction in VAT volume was experienced in the HIIT group (-405.49 ± 468.31 cm$^3$), followed by the control group (-193.01 ± 785.04 cm$^3$), and the MICT group (-111.5 ± 233.85 cm$^3$). Pairwise comparisons showed that there were no significant differences in VAT volumes between all intervention groups after adjustment for baseline values (HIIT vs CON: p=0.456; MICT vs CON: p=0.6247; HIIT vs MICT: p=0.2028). The BH-adjusted p-values were HIIT vs CON: p=0.754, MICT vs CON: p=0.754, and HIIT vs MICT: p=0.588 respectively.

**Subcutaneous fat (SAT) volume**

The subcutaneous fat (SAT) volume (cm$^3$) at baseline (PRE) and after completing the 3 months of intervention (POST) are presented in Table 1 and Figure 1. After 3 months of the intervention period, all the 3 groups experienced reductions in SAT volume. GEE analysis showed that there were no statistically significant group-by-time interactions in SAT volume (interaction effect: p=0.9454). The largest reduction in SAT volume was experienced in the MICT group (-728.63 ± 717.85 cm$^3$), followed by the control group (-360.54 ± 764.56 cm$^3$), and the HIIT group (-356.25 ± 473.12 cm$^3$). Pairwise comparison showed that there were no significant differences in SAT volumes between all intervention groups after adjustment for baseline values (HIIT vs CON: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT: p=0.99846; MICT vs CON: p=0.13561; HIIT vs MICT:
p=0.11458). The BH-adjusted p-values were HIIT vs CON: p=0.9985, MICT vs CON: p=0.2312, and HIIT vs MICT: p=0.2312 respectively.

**Adverse events**

No subjects withdrew from the study due to any adverse events that were attributable to the exercise interventions. None of them reported any major or mild discomforts throughout the intervention period.

**TABLE 1**

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<th>CON</th>
<th>HIIT x1/week</th>
<th>MICT x1/week</th>
<th>Interaction effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PRE</td>
<td>POST</td>
<td>PRE</td>
<td>POST</td>
</tr>
<tr>
<td><strong>VAT volume (cm³)</strong></td>
<td>2921.47</td>
<td>2728.46</td>
<td>3546.45</td>
<td>3140.96</td>
</tr>
<tr>
<td></td>
<td>± 914.63</td>
<td>± 878.22</td>
<td>± 1663.93</td>
<td>± 1352.14</td>
</tr>
<tr>
<td><strong>SAT volume (cm³)</strong></td>
<td>4921.14</td>
<td>4560.60</td>
<td>5481.38</td>
<td>5125.13</td>
</tr>
<tr>
<td></td>
<td>± 1064.97</td>
<td>± 985.05</td>
<td>± 1254.39</td>
<td>± 1287.42</td>
</tr>
</tbody>
</table>

Values were presented as mean ± SD.

NS: the interaction effect (group x time) is statistically insignificant (P>0.05)

**Figure 1** - Visceral fat (VAT) volume (A), and subcutaneous fat (SAT) volume (B) of subjects in the usual care control group (CON), the HIIT group (HIIT) and the MICT group (MICT) respectively measured at baseline (PRE) and after the 3-month intervention period (POST). Values are presented as means, and the error bar represents the standard deviation within each group.
Discussion

Extending on studies that found comparable effects of HIIT and MICT in reducing body fat (35, 40, 41), this study was conducted to find and compare the effects of low-frequency HIIT and MICT on reducing visceral and subcutaneous fat respectively in centrally obese adults. Although our results found a small trend of differences in visceral fat reduction that suggested low-frequency HIIT to be relatively more effective over MICT and no intervention in reducing abdominal visceral fat, it should be brought to attention that the extent of reductions following both MICT and HIIT, as well as the differences between groups were not statistically significant, inferring a possible inefficacy of both low-frequency HIIT and MICT in achieving visceral adiposity reduction to a significant extent. Indeed, the importance of an aerobic exercise program to reach certain volume before exerting its ability in producing significant visceral fat reduction was acknowledged by a number of studies. While some has suggested 10 MET hours ($METs\cdot hr\cdot wk^{-1}$) of energy expenditure for a week to be the minimum volume of aerobic exercise required for obese patients without metabolic diseases to reduce visceral adiposity (64), another study also suggested that meeting the Physical Activity Guidelines with a weekly performance of 150-250 minutes of moderate intensity exercise might be the prerequisite for achieving at least 3% weight loss in adults (65), in which 2-3% weight reduction was regarded as the minimal amount of fat reduction effective in lowering obesity-associated chronic disease risks (66, 67). In particular for MICT, its effect on visceral adiposity reduction seemed to be dose-dependent for individuals with obesity as suggested by two other studies that also found MICT practiced at low volume insufficient in reducing visceral fat (64, 68). Whereas for HIIT, Keating et al. (2017) suggested that there might be a requirement for HIIT to elicit enough energy expenditure to effectively reduce body fat (40), and Sultana et al. (2019) also found low-volume HIIT not effective in reducing total body fat (49). As people
with habitual physical activity levels meeting the WHO recommended guidelines were excluded from our study, it is reasonably assumed that most of our subjects were rather physically inactive in their daily life during the intervention period. Thus, only by attending either one HIIT or MICT exercise session per week might not be sufficient in helping participants to increase their energy expenditure up to the requirement needed for visceral fat reduction.

Contrasting to these findings, Zhang et al. (2017) suggested that while the effect of MICT on visceral fat loss was dependent on exercise volume, the same mechanism might not apply to HIIT, and training volume might not be detrimental for a HIIT program to effectively eliminate excess visceral fat in obese individuals (68). However, most studies (38 out of 39) that found HIIT effective in significantly reducing abdominal visceral fat also delivered HIIT at least 3 times a week (69), and it should be noted that Zhang’s (2017) study also delivered HIIT 3 sessions weekly, instead of using as low as one session per week that was adopted in our study. This implies that although it may be possible that HIIT practiced more than three sessions per week might not result in additional reductions in visceral fat, more trials are needed to confirm whether there may still be a minimal volume of HIIT required to effectively lower abdominal visceral adiposity. Given that most studies that demonstrated a greater ability of HIIT over lower intensity continuous exercises to cause reduction in abdominal visceral fat delivered HIIT at least three times weekly (69-72), and there is presently not much evidence on the effectiveness of low-frequency HIIT, it might well be too early to draw conclusions on the effectiveness of it on modulating visceral adiposity, despite its established ability in improving cardiorespiratory fitness even when practiced at low frequency (49).
Indeed, not only that visceral fat reduction in all exercise groups did not reach statistical significance, but the same condition appeared for subcutaneous fat, which may also be attributable to insufficient exercise volume. Particularly for HIIT, it was also suggested in a study which found high intensity exercise more effective in reducing abdominal fat that an approximate of 1600 calories expended per week might be necessary to achieve meaningful fat loss (47). Although this study’s findings seemed to have deviated from our previous trial that found low-frequency HIIT effective in significantly reducing total body fat mass (60), it might be explained by the differences in measurement tool used to quantify body fat, in which while the previous trial measured total body fat (without distinguishing between visceral and subcutaneous adipose tissue) using bioelectrical impedance analyser, this study adopted MRI to separately quantify reductions for the two types of fat focusing only at the abdominal region. Thus, back to our results that found statistical insignificance in both abdominal visceral and subcutaneous fat reductions, it seemed to support the claim that although intensity is also a crucial factor in affecting the effectiveness of an exercise program to reduce abdominal adiposity (46, 47), the importance of exercise to reach an appropriate volume cannot be neglected for effective fat loss to occur. While considering our study that only delivered both HIIT and MICT once a week, which made up to only either 35 minutes of vigorous-intensity or 47 minutes of moderate-intensity exercises weekly, the exercise volume remained to be much lower than what was suggested in either the Physical Activity Guidelines or previous studies that found exercises (no matter HIIT or MICT) effective in significantly reducing abdominal fat mass. Therefore, while we could not make arbitrary inference from the latest WHO Physical Activity Guidelines that recommends at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic exercise, or the equivalent mixture of both, to be the minimal amount of exercise needed to bring benefits to adults’ health (39), there is a necessity in finding the minimum volume and optimal mode of exercise for specifically
reducing abdominal fat targeting centrally obese patients. It will also be meaningful to extend on our findings by conducting studies with greater sample sizes and longer durations to investigate whether low-frequency HIIT can also exert significant effects in reducing abdominal visceral fat, so as to effectively reduce obesity-associated risks of comorbidities (15, 16).

To further understand possible differences between the effect of HIIT and MICT, several physiological pathways have also been suggested to explain why they may have differential abilities in modulating body adiposity. First for substrate utilization, it is known that increasing exercise intensity causes a change in major energy source from predominantly fat to carbohydrates (73). As HIIT requires exercising at a higher intensity when compared to MICT, instead of relying on lipolysis to provide energy like prolonged MICT does, muscles used during HIIT may have a greater reliance on carbohydrates as their substrate to provide energy required at higher intensities (73). While only by taking into consideration this physiological adaptation may imply that HIIT can have a relatively weaker ability in modifying adipose tissue due to its lower dependence on fat stored in body as energy source, a study that found comparable effects of HIIT and MICT in reducing abdominal visceral fat argued for a compensatory effect provided by the differences in metabolic rate after exercise cessation (68).

In fact, higher intensity exercise is generally associated with a higher metabolic rate that can be elevated for a longer time after exercise performance when compared to exercises at lower intensities (74, 75). Thus, this may serve to explain why despite HIIT that mobilizes less body fat storage during the exercise session, its ability to maintain a higher post exercise metabolic rate when compared to MICT may contribute to a comparable reduction in fat at the end (74). While by combining factors related to substrate utilization and post exercise metabolic rate suggests an at-least comparable effect of HIIT and MICT on reducing abdominal visceral fat,
a possibly greater ability of HIIT to achieve fat loss when compared to MICT can also be reasoned when considering other physiological responses to exercise stimulus. To further elaborate on this, it is found that fat breakdown in the adipose tissue occurs at a larger degree after performing HIIT when compared to lower intensity exercises (76), and Nrg4 was hypothesised to be a possible mediator to this observation (77). Particularly, a study found that HIIT increased Nrg4 to a much greater extend when compared to MICT, while performance of HIIT was also associated with a greater amount of fat loss (77). As a plausible mechanism to explain why Nrg4 elevation may lead to more fat reduction, Nrg4 is an adipokine released from adipocytes, which has established importance in maintaining energy balance (78). In fact, Nrg4 plays a significant role in maintaining metabolic homeostasis (79), which not only contributes to resist the build-up of fat but also promotes lipolysis (78). Therefore, given that HIIT can cause more release of Nrg4 from adipocytes, higher Nrp4 level following the performance of HIIT may be a possible mediator for the greater ability of HIIT to promote fat loss when compared to MICT. Moreover, apart from Nrp4 elevation, some studies also suggested that a greater need for muscle glycogen resynthesis after higher intensity exercises as more glycogen is depleted, could also serve as a possible explanation to enhanced lipolysis after HIIT (80). Enhanced fat oxidation (lipolysis) might be promoted by increase in growth hormone and epinephrine, which were both found to be elevated to a higher level after performing higher intensities exercises (81), thus also explaining why there might be a higher post-exercise oxygen consumption following HIIT when compared to MICT (75). However, despite efforts to establish the many possible metabolic pathways that underlie the adaptations of body fat to exercise stimulus of different intensities, there are still many uncertainties in the field that are opened for investigation. Thus, much more research on the related physiological responses is required to deepen understanding and consolidate evidence for explaining the relative ability of HIIT and MICT in modulating fat content.
Although the ability of low-frequency HIIT in reducing abdominal fat needs further investigation before appropriate conclusions can be drawn, our study still demonstrated that each session of HIIT was associated with 25% less time commitment when compared to MICT (HIIT session: 35 min VS MICT session: 47 min). HIIT could also be safely performed by obese individuals as apparent from the fact that were no reported discomforts or adverse events. This is also supported by other studies that concluded HIIT to be a time-efficient and safe exercise option for people with weight issues (53). Together these suggested a higher potential of HIIT to be incorporated into the daily life of busy modern obese citizens which inadequate time was found to be a major barrier for them to exercise (38). Besides, time efficiency was also found to a plausible factor leading to higher preferability and enjoyment of HIIT over traditional exercises that consumes more time (55). Although we did not specifically look into the enjoyment experienced by participants when performing their assigned exercise interventions, some studies have suggested HIIT to be associated with higher exercise enjoyment (56, 82), especially in previously sedentary adults (82). Apart from time efficiency being a possible explanation for higher exercise enjoyment, factors such as the perception of being less physically demanding due to the interval nature of HIIT (56), and its ability to provide varying stimulus that makes it less monotonous when compared to traditional MICT which requires prolonged constant effort (55), also serve to explain why HIIT is generally a more preferrable exercise option. Given that the perception of exercise being unenjoyable was not only recognized as a common barrier for regular exercise participation (83, 84), but was also found to be a major cause of low adherence (85), the ability of HIIT to arouse greater perceived enjoyment may also be a benefit of it over conventional MICT. Thus, especially for obese individuals that generally have lower baseline fitness levels and exercise capabilities, HIIT seems to be a better option to be considered for practice to increase their energy
expenditure for achieving fat loss. The higher enjoyability of HIIT is also important in terms of promoting long-term behavioural changes, so that HIIT can be continually practiced even after intervention cessation to further improve the body compositions of centrally obese individuals (85).

One of the strengths of this study was the utilization of MRI in measuring visceral and subcutaneous fat volumes, which MRI is considered as a “gold standard” imaging technique with high resolution to quantitatively track changes in adiposities at different locations (visceral VS subcutaneous) (40, 61). A meta-analysis on 39 studies that investigated HIIT’s effect on fat reduction also found that significant visceral adipose tissue changes were only observed when MRI or CT scan were adopted (69). Apart from measurement technique, using running as the exercise modality instead of cycling is another strength of this study to maximize the potential benefit of exercise interventions on fat reduction (86). As it was believed that running which recruits more muscles may lead to greater fat oxidation, it might contribute to a more significant fat reduction when compared to cycling even when both were practiced at the same intensity (86).

However, a rather small sample size might be one of the limitations in this study, which might have contributed to a lower power to detect differences between groups. Thus, larger trials in the future may be essential to find out the true differences in the effects of HIIT and MICT on reducing visceral fat. In addition, another limitation of this present study might be the incompetency in controlling for two possible confounders, which were habitual physical activity and diet. According to objectively measured actigraphy data, it was observed that a subject in the control group had significantly higher habitual physical activity level during the intervention period, and this same subject was also found to experience substantial reduction
in both VAT and SAT volumes after 3 months that might not be attributable to the effect of the intervention it was assigned to. Thus, inability to completely control physical activity in daily life might also serve to explain part of the insignificant differences in fat volume reduction found between the control and exercise intervention groups. Apart from physical activity being a possible confounding variable that can mask intervention effects, as it is known that diet can also exert a significant influence on energy balance, differences in dietary intake between subjects during the intervention period might have also affected the results. As such, future studies should also take into the consideration of these potential confounders by controlling for both the daily physical activity levels and diet of participants, so as to minimize their possible interferences on finding the true effects of different exercise interventions.

Regardless, while this study focused on looking into the effects of HIIT on reducing abdominal visceral and subcutaneous adiposity, benefits of HIIT for individuals who are overweight or obese is not limited to fat loss. In fact, HIIT has great potential to be adopted as an alternative exercise choice to more commonly-practiced MICT with greater ability in improving cardiorespiratory fitness (43), even when practiced at low frequency (49). These benefits also extend beyond adiposity reduction and better fitness to improving mental health such as reducing depression (87), as well as reducing metabolic risk factors related to obesity such as promoting glycaemic homeostasis (88), and lowering blood pressure (89), showing that HIIT has its wide-range significance to be practiced among adults with central obesity. Moreover, HIIT intervention when used in combination with dietary control to restrict caloric intake is also believed to enhance the effect in promoting extra weight loss, as both exercising to maximize energy expenditure and controlling diet to minimize energy intake were acknowledged to be important to achieve significant reduction in visceral adiposity (65).
To conclude, visceral fat reduction is crucial for adults with central obesity, as excess visceral fat at the abdominal region is highly associated with heightened risks of cardiometabolic diseases (15, 16). This study showed that both low-frequency HIIT and MICT were not effective in reducing abdominal visceral fat, and the difference between the effects of HIIT and MICT on eliminating visceral adiposity was insignificant. Therefore, while increasing the sample size, and controlling for habitual physical activity level and diet may be essential to increase the power for detecting the true difference between the effects of HIIT and MICT on reducing visceral fat, future studies are also warranted to confirm whether there may be an actual minimum volume of HIIT required to achieve clinically significant reduction in abdominal visceral adiposity among centrally obese adults.

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Trial registration

ClinicalTrials.gov Identifier (NCT number): NCT04545320
References
