The effects of two different orders of concurrent training on the interindividual variability of health markers of metabolic syndrome and fitness in severe/morbidly obesity women. A randomized control trial

ID: RP08042020

Date: April1 10th, 2019

Study documents

Scientific background: Morbid obesity, defined as a body mass index (BMI) of ≥40 kg/m^2 (class III obesity), is a chronic disease with life-threatening cardiometabolic consequences such as elevated blood pressure (systolic [SBP] or diastolic BP [DBP]), fasting plasma glucose (FPG), triglycerides (Tg), and low high-density lipoprotein cholesterol (HDL-c), all summarised as metabolic syndrome (MetS) (Baffi, Wood et al. 2016), increasing substantially the rates of total mortality, with most of the excess deaths due to heart disease, cancer, diabetes, and important life expectancy reductions in compared with normal weight (Kitahara, Flint et al. 2014). Moreover, morbid obesity has been associated with impairments of cardiorespiratory fitness and muscle strength, limiting the capacity to perform activities of daily living (Pazzianotto-Forti, Moreno et al. 2020) Additionally, this fact increases the economic costs associated with healthcare in this population (Espallardo, Busutil et al. 2017).

Due to the multi-factorial aetiology of morbid obesity, such as the genetic load (e.g. the *FTO* gen), and other environmental factors, including mainly lifestyle determinants such as physical activity/exercise training participation, and diet as main modulators, the application of lifestyle strategies have been proposed prior to alternative surgical intervention in these populations (Bächler, Papamargaritis et al. 2013, Espallardo, Busutil et al. 2017). In this sense, exercise training as the resistance training (RT), defined as any exercise that causes voluntary skeletal muscle contraction by using external weights including dumbbells and metal bars (Schoenfeld, Grgic et al. 2017), is a known non-pharmacotherapy strategy for improving muscle strength and functional capacity in obese patients undergoing bariatric surgery (Huck 2015). Similarly, high intensity interval training (HIIT), defined as several and brief bouts of high-intensity effort usually by cycling/running, interspersed by recovery periods (Gibala, Little et al. 2012, Delgado-Floody, Izquierdo et al. 2020), has produced strong evidence for the improvement of cardiometabolic risk factors for type 2 diabetes mellitus, arterial hypertension, central arterial stiffness, vascular function, and cardiorespiratory fitness (Ramírez-Vélez, Hernández-Quiñones et al. 2019). Thus, HIIT might have protective effects against the development of cardiometabolic diseases including populations with poor glucose control and high blood pressure in comparison to moderate-intensity continuous training (MICT) (Campbell, Kraus et al. 2019). Thus, following RT or HIIT alone, there have been described unique physiological adaptations for improving for example muscle strength, the endurance performance by walking test, as well as beneficial metabolic improvements at MetS markers including fasting glucose reductions, increases at HDL-c, and decreases in Tg in populations with higher adiposity.

Thus, in individuals with morbid obesity for example, exercise training has proven to be effective for inducing clinically significant weight loss (5–10%) (Gerber, Anderin et al. 2015), and for the reduction of cardiovascular risk (Delgado-Floody, Alvarez et al. 2019), in accordance with the standard recommendations for these cohorts prior to bariatric surgical. Additionally, there are also other benefits such as the increase of skeletal muscle mass, the reduction of body fat, and better glucose control by the lowering of fasting plasma glucose (FPG), and lipids regulation (i.e., increases of HDL-c, and decreases of Tg) (Han and Lean 2016). Briefly, 12 weeks of concurrent training (CT), defined as a combination of both MICT / plus RT, decreased body weight (by ~7.3

kg), blood pressure, and FPG in this cohort (Marc-Hernández, Ruiz-Tovar et al. 2019). In addition, part of our preliminary findings have shown that 20 weeks of RT decreases MetS risk factors in morbidly obese patients, showing a low inter-individual variability those patients with greater adiposity, revealing that with more adiposity alteration, the benefits of RT are also more visible (Delgado-Floody, Alvarez et al. 2019). However, some inconsistences have been described after CT, that are directly related with the 'order' (i.e. starting the CT session with MICT followed by RT, or vice versa) of the CT session. For example, some literature reports that by starting the exercise session with RT, participants can get more benefits and improve their physical fitness markers (i.e. increases of upper body strength and neuromuscular markers) (Murlasits, Kneffel et al. 2018). However, in contrast, other studies have reported that starting CT with MICT/or HIIT does not alter physiological adaptations in similar outcomes (Wilhelm, Rech et al. 2014). Other evidence shows that starting CT with firstly RT exercises clearly promotes greater lower-body strength gains and neuromuscular economy (Cadore, Izquierdo et al. 2013). By contrast, other reports claim no more benefits by starting with MICT/HIIT or RT to physical fitness markers in populations of athletes (Eddens, van Someren et al. 2018), and additionally, no additional benefits for decreasing body fat using one or another exercise modality when starting the CT session (Cadore, Izquierdo et al. 2012). However, little is known about the interindividual variability of exercise training (IVET) in relation to different order session of CT in morbidly obese populations, and in health-related outcomes, such as MetS markers. Briefly, IVET means that some subjects achieve benefits after training, and are termed responders (Rs), while others exhibit a worsened or unchanged response, that are commonly known as nonresponders (NRs) (Bouchard, Blair et al. 2012). With regard to the causes of IVET, genetic (Stephens, Xie et al. 2015), and environmental factors including the mode of exercise training (Alvarez, Ramirez-

Campillo et al. 2017), have been described. In addition, considering the health-related benefits of CT including MICT/or HIIT plus RT in terms of physical fitness, and the metabolic markers in different populations, as well as taking into account the previous discrepancies of the order session in relevant literature, it is necessary to investigate the exercise modalities interaction as a precision medicine for improving MetS markers. This study will follow the CONSORT guidelines for randomised trials, will be developed in accordance with the Declaration of Helsinki (2013), and has been approved by the Ethical Committee of the Universidad de La Frontera, Temuco, Chile (DI18-0043 Project). **Design:** An experimental, and randomized control clinical study. **Methods:** This study is a parallel-group randomised controlled trial in which 43 women with morbid obesity that will be randomly allocated to one of the two similar CT exercise programmes. The exercises will be applied in different session order by the two groups (HIIT+RT, *n*=17), and resistance training plus high-intensity interval training (RT+HIIT, *n*=17). All volunteers will read and signed an informed consent. The inclusion criteria will be; (*i*) being a candidate for bariatric surgery, (*ii*) aged between 18 and 60 years, (*iii*) being medically authorised, and (*iii*) with a body mass index (BMI) ≥40 kg/m^2 or ≥35 kg/m^2 with additional comorbidities (i.e. diabetes, hypertension, insulin resistance) controlled by pharmacotherapy according to the Chilean requirements for morbidly obese patients in order to be a candidate for bariatric surgery. The exclusion criteria will be; (*i*) having physical limitations preventing the performance of exercise (e.g. restricting injuries of the musculoskeletal system), (*ii*) having exercise-related dyspnoea or respiratory alterations, (*iii*) having chronic heart disease with any worsening in the last month, and (*iv*) adhering to less than 80% of the total interventions (these results were excluded from the statistical analyses).

REFERENCES

Alvarez, C., et al. (2017). "Prevalence of Non-responders for Glucose Control Markers after 10 Weeks of High-Intensity Interval Training in Adult Women with Higher and Lower Insulin Resistance." Front Physiol **8**(479): 479.

Bächler, T., et al. (2013). "Treatment of Morbid Obesity: Intensive Lifestyle Intervention vs. Bariatric Surgery." Surgery Curr Res **3**(147): 2161-1076.1000147.

Baffi, C. W., et al. (2016). "Metabolic Syndrome and the Lung." Chest **149**(6): 1525-1534.

Bouchard, C., et al. (2012). "Adverse metabolic response to regular exercise: is it a rare or common occurrence?" PloS one **7**(5): e37887.

Cadore, E. L., et al. (2012). "Strength prior to endurance intra-session exercise sequence optimizes neuromuscular and cardiovascular gains in elderly men." Experimental gerontology **47**(2): 164-169.

Cadore, E. L., et al. (2013). "Neuromuscular adaptations to concurrent training in the elderly: effects of intrasession exercise sequence." Age **35**(3): 891-903.

Campbell, W. W., et al. (2019). "High-intensity interval training for cardiometabolic disease prevention." Medicine and science in sports and exercise **51**(6): 1220.

Delgado-Floody, P., et al. (2019). "Preventing metabolic syndrome in morbid obesity with resistance training: Reporting interindividual variability." Nutr Metab Cardiovasc Dis **29**(12): 1368-1381.

Delgado-Floody, P., et al. (2020). "Effect of High-Intensity Interval Training on Body Composition, Cardiorespiratory Fitness, Blood Pressure, and Substrate Utilization During Exercise Among Prehypertensive and Hypertensive Patients With Excessive Adiposity." Front Physiol **11**(1171): 558910.

Eddens, L., et al. (2018). "The role of intra-session exercise sequence in the interference effect: a systematic review with meta-analysis." Sports Medicine **48**(1): 177-188.

Espallardo, O., et al. (2017). "The Impact of Severe Obesity on Healthcare Resource Utilisation in Spain." Obes Surg **27**(8): 2058-2066.

Gerber, P., et al. (2015). "Weight loss prior to bariatric surgery: an updated review of the literature." Scandinavian Journal of Surgery **104**(1): 33-39.

Gibala, M. J., et al. (2012). "Physiological adaptations to low-volume, high-intensity interval training in health and disease." The Journal of Physiology **590**(5): 1077-1084.

Han, T. S. and M. E. Lean (2016). "A clinical perspective of obesity, metabolic syndrome and cardiovascular disease." JRSM cardiovascular disease **5**: 2048004016633371.

Hopkins, W. G., et al. (2009). "Progressive statistics for studies in sports medicine and exercise science." Medicine and science in sports and exercise **41**(1): 3-13.

Huck, C. J. (2015). "Effects of supervised resistance training on fitness and functional strength in patients succeeding bariatric surgery." J Strength Cond Res **29**(3): 589-595.

Kitahara, C., et al. (2014). "Association between class III obesity (BMI of 40–59 kg/m 2) and mortality: a pooled analysis of 20 prospective studies." PLoS Med **11**(7): e1001673.

Marc-Hernández, A., et al. (2019). "Impact of exercise on body composition and cardiometabolic risk factors in patients awaiting bariatric surgery." Obesity surgery **29**(12): 3891-3900.

Murlasits, Z., et al. (2018). "The physiological effects of concurrent strength and endurance training sequence: A systematic review and meta-analysis." Journal of sports sciences **36**(11): 1212-1219.

Pazzianotto-Forti, E. M., et al. (2020). "Impact of Physical Training Programs on Physical Fitness in People With Class II and III Obesity: A Systematic Review and Meta-Analysis." Phys Ther **100**(6): 963-978.

Ramírez-Vélez, R., et al. (2019). "Effectiveness of HIIT compared to moderate continuous training in improving vascular parameters in inactive adults." Lipids in health and disease **18**(1): 42.

Schoenfeld, B., et al. (2017). "Strength and hypertrophy adaptations between low-vs. high-load resistance training: a systematic review and meta-analysis." The Journal of Strength & Conditioning Research **31**(12): 3508-3523.

Stephens, N. A., et al. (2015). "A transcriptional signature of “exercise resistance” in skeletal muscle of individuals with type 2 diabetes mellitus." Metabolism **64**(9): 999-1004.

Wilhelm, E. N., et al. (2014). "Concurrent strength and endurance training exercise sequence does not affect neuromuscular adaptations in older men." Experimental gerontology **60**: 207-214.

Statistical Analysis Plan (SAP): We will apply 2 main forms of statistical analyses a) to report the pre-post changes in mean terms, and b) to report the results according with the inter-individual responses based on the technical error criteria, where according with the error calculated in the three previous measurements registered by the sample that was voluntary. Graph pad Prisma statistical software 8.0 (San Diego, CA, USA) will be used. The normal distribution of all the variables were tested using the Shapiro-Wilk test. Data will be presented as the mean and (95%CI) in tables, as mean with (±) standard error in Figures 1, 2, and 3, and as individual delta in Figure 4 for identification of Rs and NRs. Normality and homoscedasticity assumptions for all data were analysed using the Shapiro–Wilk and Levene's test, respectively. In the HIIT+RT group, the Tg outcome, as well as in the RT+HIIT group, LDL-c, and lean mass outcomes were analysed by the *Wilcoxon* non-parametric test. For training-induced changes, the student's t test was used to identify differences at baseline, while a repeated measure two-way ANOVA was applied to assess the occurrence of an actual training effect; namely, $p < 0.05$ for the interaction (time x group) on the main MetS (WC, SBP, DBP, FPG, HDL, and Tg, as well as to the secondary outcomes). A Sidack's post hoc test was used for multiple comparisons. Additionally, the Eta partial squared for interaction (Time x Group) was assessed by η^2 obtained from the ANCOVA with small (η^2=0.01), medium (η^2=0.06), and large (η^2=0.14) effects defined according to (Lakens, 2013). The prevalence of NRs was described using the comparisons by percentage between both experimental groups using a Chi square test X^2. All statistical analyses were performed with SPSS statistical software version 23.0 (SPSS™ Inc., Chicago, IL). The alpha level was set at $p < 0.05$ for statistical significance.