

**Interindividual Postexercise Hypotension Response in Morbid
Obesity**

NCT05504629

Date: March 17th, 2021

Study documents

Scientific background: Physical inactivity and sedentary behaviour [*i.e.*, Do not adhere to international physical activity guidelines of a minimum of 150 min of physical activity ^{1]} together with other lifestyle conditions (*i.e.*, unhealthy nutrition, or poor sleep time) promote obesity, and cardiometabolic diseases such as type 2 diabetes mellitus (T2DM), and arterial hypertension (HTN) ², two major diseases in the modernity, and of high prevalence in populations with excessive of adiposity such as those with morbid obesity ². Unfortunately, metabolic syndrome (MetS), another more complex cardiometabolic square that implies also obesity, poor glucose control, high blood pressure, dyslipidaemia, and high triglycerides in plasma exacerbates the risk for suffering from cardiovascular disease particularly those with morbid obesity who are candidates for bariatric surgery ³. For example, a relevant meta-analysis of 87 studies with a sample of ($n=951.083$) showed that MetS risk factors were associated with an increased risk for cardiovascular disease (CVD) (Relative Risk, [RR]= 2.35), CVD mortality (RR= 2.40), myocardial infarction (RR= 1.99, stroke (RR= 2.27), and all-cause mortality (RR= 1.58) ⁴. Patients with Morbid obesity are a particular population that suffers from multiple risks for CVD, including MetS, endothelial dysfunction, as well as HTN and T2DM risk factors, all of these related to a better or worse profile to deal with success and better recovery period after bariatric surgery ¹. From the National Health Survey of Chile, there was described that morbid obesity is a worrying concern in women in childbearing ages 20 to 45 y, showing almost no changes from 2003 (2.2%) to 2009-10 Survey (2.1%) ⁵. Thus, among these patients, to acquire the bariatric surgery benefit, these increase their possibilities to lose excess weight near to ~50%, to recover their overall cardiometabolic health ⁶, and this has been strongly related to improvements in their quality of life ⁷.

From here, lifestyle interventions such as exercise training play a key role⁸⁻¹⁰, and relevant international organizations such as the American College of Sports Medicine¹, and the European Association For The Study of Obesity Physical Activity Working Group¹¹ have recently highlighted their benefits before and after bariatric surgery. Exercise training is a known but poorly used strategy for controlling cardiometabolic risk in populations with T2DM, HTN, and MetS^{8,12}. At least in the blood pressure, and vascular context, exercise training decrease chronic, and acute blood pressure levels¹³⁻¹⁶. For example, a single session of endurance training (ET) (also known as moderate-intensity continuous training), decreased the 24 h blood pressure¹⁷, being the magnitude of this effect is superior in subjects with higher blood pressure (systolic [SBP]/diastolic [DBP] $-16.1/-7.5$ mmHg)¹⁷ and to those with HTN controlled and HTN not so controlled^{18,19}, but clearly, less marked in healthy normotensive subjects (SBP/DBP $-5.6/-3.1$ mmHg)²⁰. These effects have been confirmed by relevant meta-analysis where long-term ET has been a recognized strategy to get these goals in pre- and hypertensive populations^{21,22}. On the other hand, RT also decreases blood pressure, where only 45 minutes after an acute resistance training (RT) session in HTN subjects (SBP/DBP $-22.0/-8.0$ mmHg), and this have been also confirmed by other relevant meta-analyses where summarize blood pressure decreases after RT in -4.4 mmHg²³. Recently, and in similar coherence with ET, the RT modality has reported higher magnitude in BP reduction in subjects with elevated (SBP/DBP $-12.0/-4.0$ mmHg), than healthy subjects (SBP/DBP $-4.0/-1.0$ mmHg)²⁴. From here, the postexercise hypotension (PEH) [*i.e.*, defined as a reduction in systolic and/or diastolic arterial blood below control levels after a single but of exercise²⁵] is the first vascular benefits immediately after exercise acquire a meaningful relevance, in terms that the summary of physiological adaptations by each exercise session can promote a renova of the vasculature structure using molecular mechanisms²⁶. Thus, as

after both ET and RT, there are a number of evidence reporting the PEH benefits in different cohorts, but unfortunately there is little evidence reporting this phenomenon after concurrent training (CT), and yet less knowledge in population with MetS risk factors, as those with morbid obesity.

On the other hand, the main PEH studies report data in terms of ‘average data’, and it is well known that there is a wide interindividual variability to exercise training²⁷, being a need for the report of data at an individual level. Thus, considering that there is little knowledge about the role of the order (*i.e.*, starting by ET plus RT or by RT plus ET) in the CT session, taking into account that risk factors for MetS increase the risk for vascular damage and CVD. 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, ACTA N° 080_21). **Design:** A quasi-experimental clinical study. **Methods:** Patients with morbid obesity were invited for participating by a public invitation and directly to the Morbidly Obesity Association of Temuco, City, Chile (OBEMOB). After providing wide information and feedback about the risks/benefits of the intervention, all participants signed informed consent for participating in the study. We recruited diagnosed morbid obesity sedentary/physically inactive subjects (body mass index [BMI] between ≥ 40 kg/m²; aged 30 to 55 years) that were under the OBEMOB institution, who were assigned for convenience in 1:1 allocation to a CT group of endurance [ET] plus resistance training [RT] (ET+RT; $n=17$; BMI 47.8 ± 16.7) or resistance training plus endurance training group (RT+ET; $n=13$; BMI 43.0 ± 8.0). Patients were recruited between 2020 and 2021 year from the above non-governmental mentioned institution. All participants were part of the lifestyle program

previous to the possibility of receiving the bariatric surgery benefit for this disease condition from the Health Ministry of Chile (MINSAL).

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Statistical Analysis Plan (SAP): Data are presented as the mean \pm standard deviation (SD). Normality and homoscedasticity assumptions for all data were checked using the Shapiro-Wilk and Levene tests. Wilcoxon's test was used for non-parametric data. After this, we performed 2-way ANOVA (group x time) to test SBP, DBP, MAP, HR, and PP outcomes in absolute values, where Sidac's *post hoc* was applied to identify

potential differences between ET+RT vs. RT+ET. Additionally, delta changes (Δ) from pre-post were calculated to SBP, DBP, MAP, HR, and PP outcomes to test by the independent Student *t*-test differences between groups, where optionally the non-parametric Wilcoxon test was applied for non-parametric variables. The Cohen *d* effect size was obtained with threshold values at 0.20, 0.60, 1.2, and 2.0 for small, moderate, large, and very large effects, respectively²⁸. These analyses were carried out by the statistical software Graph Pad Prism 8.0 software (Graph Pad Software, San Diego, CA, USA). After this, all results in Δ changes of the sum of SBP $\sum\Delta$ SBP was individualized and presented in quartile to be categorized in those participants ‘nonresponders’ (NRs; Q1 with SBP < -1 mmHg), ‘low’ responders (LRs; Q2 with SBP -1 to -9.9 mmHg), ‘moderate’ responders (MRs; Q3 with SBP -10 to -18 mmHg), and ‘high’ responders (HRs; Q4 with SBP \geq -18 mmHg) according with their blood pressure changes (*i.e.*, particularly decreases) as previously have been reported²⁹. Linear regression was applied in the backward mode for testing those potential body composition, metabolic and physical condition outcomes predictors outcomes of the PEH. The $\sum\Delta$ SBP decreases an average of the session 1 and 2 of both ET+RT and RT+ET groups related to the PEH (*i.e.*, decreases in SBP) was used as ‘dependent’ outcome, while age, height, body mass, BMI, waist circumference, body fat in % and kg, lean mass, skeletal muscle mass, bone mass, total body water, BMR, SBP, DBP, HR at rest, pulse pressure, fasting glucose, total cholesterol, LDL-c, HDL-c cholestetrol, triglycerides, 6Mwt, and handgrip muscle strength (dominan, and non-dominant arm) were used as ‘independent’ predictors. Statistical analyses for these procedures were applied using SPSS software version 28 (SPSSTM Inc., Chicago, Illinois, USA). The alpha level was fixed at ($p < 0.05$) for all tests of statistical significance.