

## The effect of aerobic and concurrent training on cardiovascular and metabolic control in middle-aged type II diabetics

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### Abstract

The present study investigated the effect of concurrent or aerobic training on middle-aged patients with T2DM. For this, 36 participants (24 women, 54.6±6.9 yrs.) completed a 12-week intervention program in the following groups: control (CON; n=12), concurrent training (CROS; n=12), and aerobic training (AER; n=12). Body mass, glycosylated hemoglobin (HbA1c), total cholesterol and fractions, rate-pressure product, walking speed test and cardiovascular risk were measured before and after the intervention. The main results indicated that after 12 weeks, the trained groups presented lower rate-pressure product in comparison to the pre-intervention means ( $\Delta=-544.0$  for CROS and  $\Delta=-998.0$  mmHg.bpm for AER,  $p\leq 0.043$ ). The CROS presented a lower mean for HbA1c (6.8±1.7, 5.2±1.3, 7.8±1.6%, for CON, CROS and AER, respectively;  $p\leq 0.049$ ) and total cholesterol (171.8±43.3, 155.2±30.7 and 272.8±24.0 mg/dL, for CON, CROS and AER, respectively;  $p=0.001$ ) compared to the other groups at the post-intervention moment. The CROS showed a significant difference for low density lipoprotein (LDL) at the post-intervention compared to the pre-intervention moment ( $\Delta=-20.3$  mg/dL,  $p=0.001$ ). The AER showed a higher mean for the Walking speed test compared to the other groups (420.2±37.5, 502.4±28.5 and 626.7±39.9 meters, for CON, CROS and AER, respectively;  $p\leq 0.001$ ) at the post-intervention moment. In conclusion, the present evidence allows us to conclude that the AER and CROS interventions provide metabolic and cardiovascular improvements after 12 weeks in middle-aged T2DM for both genders. The AER group showed a better response in the rate-pressure product and walking-speed test, whereas the CROS presented a better response to HbA1c, total cholesterol and LDL.

**Keywords:** Glycosylated hemoglobin; Cholesterol; Diabetic Cardiomyopathies; Rehabilitation Exercises.

### Introduction

Increased risk for cardiovascular disease is due to a complex clustering of risk factors associated with type 2 diabetes (T2DM), including insulin resistance, hyperglycemia, dyslipidemia, hypertension, hyperinsulinemia, and systemic inflammation (Asfaw & Dagne, 2022; Jorsal, Wiggers, & McMurray, 2018). Changes in adipose tissue mass and metabolism may be related to insulin resistance and visceral obesity commonly associated with T2DM (Geiss, Bullard, Brinks, Hoyer, & Gregg, 2018; Jorsal et al., 2018).

The number of T2DM cases has increased in recent years, and according to standards of medical care in diabetes, it is defined as non-insulin dependent diabetes, with a progressive loss of insulin secretion and peripheral insulin resistance (Geiss et al., 2018). Lifestyle modifications including physical activity are the bases to reduce T2DM comorbidities (Umpierre et al., 2011). In this sense, aerobic exercise training is the main prescription that promotes beneficial effects on the clinical and glycemic profile, with a decreased HbA1c level, increased maximum oxygen consumption and improved insulin sensitivity (Grace, Chan, Giallauria, Graham, & Smart, 2017; Way, Hackett, Baker, & Johnson, 2016). However, concurrent training is an exercise option for people with diabetes, as this type of training is performed in combination and is not the same as exercise sessions of aerobic and resistance training (Cadore et al., 2018). Both resistance and aerobic exercise are indicated for

metabolic control (Asfaw & Dagne, 2022), however, concurrent exercise has a more potent effect than resistance and aerobic exercises performed alone (Sigal et al., 2007). To the best of our knowledge, concurrent training is still poorly investigated in T2DM.

Chile has had a cardiovascular health program since 2002, which has changed the focus of isolated pathologies such as hypertension, T2DM, and dyslipidemia to one where it integrates all these pathologies, resulting in an overall risk of cardiovascular disease (Núñez et al., 2009). Interestingly, there is no scientific evidence available in Chile on the clinical prescription of exercise in people with T2DM. The benefits of concurrent or aerobic training and its effects are undervalued by medical teams, demonstrating a lack of knowledge and consolidation on incorporating exercise in the treatment of diabetic patients. Therefore, the aim of this study is to verify the response of T2DM patients to aerobic and concurrent training, quantifying their effect on metabolic control and cardiovascular risk. We hypothesize that concurrent exercise also composed by resistance exercises will provide more benefits when compared to the aerobic training and the control group.

## **Material & Methods**

### ***Research design***

This is a longitudinal study with pre-test and post-test measures. To do so, a group of T2DM were divided into 3 groups and followed up by a multi-professional team during 12 weeks of an intervention program. All data for this study were obtained between August and December 2018. The study was performed in San Vicente de Tagua Tagua commune and the Jose Dionisio Astaburuaga Family Health Center (Chile). A set of measures were carried out in order to achieve the aims of the present study. The levels of total cholesterol and fractions, HbA1c and body mass were measured as metabolic activity indicators. The rate-pressure product walking speed test was conducted and analyzed by the United Kingdom Prospective Diabetes Study (UKPDS) Risk Engine v.2.0 software program in order to estimate cardiovascular risk.

### ***Participants***

A meeting was held prior to data collection with the health department director, the mayor of the commune and supervisor of the health center, where the problem, the aims and methods of the study were presented. Once written authorization from the health department was obtained, the clinical records of the patients were reviewed. The participants were composed of 36 (24 women) patients with T2DM (54.6±6.9yrs; 45-69 yrs.) randomly selected according to the following inclusion criteria: a) adults of both genders > 35 years old with a diagnosis of T2DM > 6 months; b) having an evaluation and medical authorization to participate in the study; c) received a positive evaluation of their feet from a podiatrist for performing physical exercise; d) having stable pharmacological treatment and no insulin dependence; d) not having participated in exercise programs during the last six months; e) presenting a cardiovascular risk of mild or moderate level, according to the values obtained in the evaluation from the Chilean recommendation and Risk Engine Software; f) participating in at least 75% of the interventions in the CROS and AER groups. The exclusion criteria were: a) those who did not complete the entire protocol or wished to withdraw from the study; b) not maintaining updated pharmacological medication; c) presenting uncontrolled complications derived from diabetes such as coronary disease, peripheral vascular disease, retinopathy, nephropathy, peripheral neuropathy, or autonomic cardiac neuropathy; d) maintaining insulin dependence; e) severe heart disease; f) having been operated on for some type of severe heart disease or heart attack; g) presenting some type of skeletal muscle alteration which affects performance of aerobic or resistance exercise.

This study was approved by the Ethics Committee of the University where the study was conducted (CAAE: 44399515.1.0000.5147; Ethic Committee Protocol: 1.089.162), and signed informed consent was obtained from all participants before enrolment in the present study. All participants were randomly divided into 3 groups: 1) Control – CON (57.3±5.8 yrs.); 2) Concurrent training – CROS (48.9±6.8 yrs.); or; 3) Aerobic training – AER (57.6±4.4 yrs.).

### ***Procedures***

The interventions were performed three times a week (≈60-min/session) for 12 weeks in: 1) CON: 60-min sitting; 2) CROS: 20-min of aerobic training (50-80% HR<sub>res</sub> – Heart rate monitor Polar FS1, Kempele, Finland), 15-min of resistance training, 8-16 repetitions of a continuous chest, back, abdomen and leg-press (3-min interval between sets), and 15-min of aerobic training with (40-60% HR<sub>res</sub>) and 10-min cool down (walking); 3) AER: 15-min warm-up, 35-min of continuous exercise (50-80% HR<sub>res</sub>) and 10-min cool down (walking). Otherwise, if the patient did not have an updated exercise test, a submaximal test such as the 6-minute gait test was used to obtain their maximum heart rate and to estimate the working heart rate. In the latter case, the 6-minute walk test was performed for patients who did not do the stress test in the first work session (Annex). Each patient's heart rate and blood pressure were measured at the beginning and end of each session. In addition, heart rate was measured at some point in the training session.

### ***Anthropometry***

Anthropometry was performed with calibrated material by a trained ISAK level I anthropometrist who collected weight and height measurements, with weight measured on a scale with maximum capacity of 200-kg

and an accuracy of 100-g (SAGE®, Madrid, Spain), while height was measured using a stadiometer (Harpender®, British Ind., London, England).

**Rate-pressure product** The rate-pressure product was calculated by multiplying the heart rate – HR (Polar FS1, Kempele, Finland) by systolic blood pressure – SBP (OMRON 905 IT, Omron Dualtec Electronics, Lake Forest, IL, USA).

**Walking speed test (WST)** All the participants performed the WST with no warm-up and no encouragement. The WST was conducted according to a standardized protocol (Lee, 2018). It was performed on a seldom-used, flat, straight track (40-m long, marked every 1 m with cones to indicate turnaround points) with a hard surface. This test was performed between 6 p.m. and 8 p.m. in order to minimize intraday variability, temperature effects, and biological rhythms with a stable ambient temperature of 20-24°C. The participants were instructed to avoid intense exercise in the last 48 hours prior to testing, to wear appropriate walking shoes and clothes, and to take their medication normally (Lee, 2018). The participants sat in a chair located near the starting position for at least 10 minutes before the test started. The recommended reasons for immediately stopping the WST included the following: chest pain, intolerable dyspnea, leg cramps, staggering, diaphoresis, and pale or ashen appearance (Lee, 2018).

**Coronary heart disease risk estimates** The United Kingdom Prospective Diabetes Study (UKPDS) Risk Engine v.2.0 software program was used to estimate coronary heart disease and stroke risk according to the methodology described by Stevens, Kothari, Adler, Stratton, and Holman (2002).

**Biochemical measures** Blood samples were collected after overnight fasting. Venipuncture was performed in the cubital vein. A tourniquet was used, but was released just before sampling to avoid artificial increase in the concentration of serum lipids. The blood was centrifuged at 5,000 rpm for 10-min. Serum was separated within 2-hours of collection to prevent artificial changes in the total cholesterol, Low-density Lipoprotein (LDL) and High-density Lipoprotein (HDL) concentrations. The HbA1c was determined using routine laboratory methods in the local clinic by an auto-analyzer (Roche Modular P-800, Holliston MA, USA).

#### Statistical analysis

Descriptive data are presented as mean and standard deviation (SD). Normal Gaussian distribution was verified by the Shapiro-Wilk test. ANCOVA [Group x (Pre- x Post-intervention)] and the Bonferroni post hoc test was performed when significant differences were identified, confidence interval (95%CI) and partial eta squared ( $\eta^2$ ) was calculated as effect size (ES). This analysis considers ES-score as small ( $ES \geq 0.10$ ), medium ( $ES \geq 0.30$ ) or large effect size ( $ES \geq 0.50$ ) (Cohen, 1992). We applied the Mauchly sphericity test for validating repeated measurements, and the Greenhouse-Geisser correction was used when necessary. Statistical significance was set at  $p \leq 0.05$ , and all analyses were performed with the Statistical Package for the Social Sciences (20.0, Chicago, IL, USA).

## Results

Table 1 presents the results for body mass, systolic blood pressure, HbA1c, total cholesterol and fractions, and cardiovascular risk indicators for CON, CROS and AER groups pre- and post-intervention.

**Table 1.** Descriptive and inferential analysis of pre and post intervention for body mass, systolic blood pressure, HbA1c, total cholesterol, and fractions, cardiovascular risk indicators for CON, CROS and AER and cardiovascular risk.

| Groups | Pre                      | Post                       | Difference (95%CI)                    | Pre                             | Post                       | Difference (95%CI)   |
|--------|--------------------------|----------------------------|---------------------------------------|---------------------------------|----------------------------|----------------------|
|        | <b>Body mass</b>         |                            |                                       | <b>Low-density lipoprotein</b>  |                            |                      |
| CON    | 85.2±8.0                 | 85.6±8.4                   | 0.4 (-0.7; 14.0)                      | 113.4±30.0                      | 118.1±34.1                 | 4.7 (-4.0; 13.4)     |
| CROS   | 72.3±7.0                 | 72.2±6.6                   | -0.1 (-0.3; 9.1)                      |                                 |                            | -20.3 (-29.0; -11.6) |
| AER    | 80.4±7.1                 | 80.1±7.5                   | -0.3 (-0.3; 10.2)                     | 146.7±39.8                      | 126.3±39.4 <sup>a</sup>    | -8.5 (-17.2; 0.2)    |
|        | <b>Double product</b>    |                            |                                       | <b>High-density lipoprotein</b> |                            |                      |
| CON    | 12365.7±743.8            | 12546.8±835.4              | -181.2 (-345.7; 708.0)                | 44.7±8.3                        | 44.8±7.6                   | 0.2 (-1.7; 2.0)      |
| CROS   | 13181.2±2031.3           | 12637.2±1778.6             | -544.0 (-1070.8; -17.1) <sup>a</sup>  | 34.1±2.9                        | 40.8±4.9 <sup>a</sup>      | 6.7 (4.9; 8.5)       |
| AER    | 13525.3±995.2            | 12527.3±776.1              | -998.0 (-1524.8; -471.2) <sup>a</sup> | 46.9±9.5                        | 48.3±8.3 <sup>a</sup>      | 1.3 (-0.5; 3.2)      |
|        | <b>HbA1c</b>             |                            |                                       | <b>Cardiovascular risk</b>      |                            |                      |
| CON    | 6.6±1.7                  | 6.8±1.7                    | 0.2 (-0.4; 0.1)                       | 12.0±4.3                        | 11.3±3.8 <sup>a</sup>      | -0.7 (-2.7; 1.4)     |
| CROS   | 6.4±1.7                  | 5.2±1.3 <sup>***a</sup>    | -1.2 (-1.4; -1.0)                     | 13.7±7.9                        | 7.2±3.5 <sup>***a</sup>    | -6.5 (-8.5; -4.5)    |
| AER    | 8.1±1.7                  | 7.8±1.6                    | -0.2 (-2.9; 0.5)                      | 21.4±7.5                        | 17.7±5.0 <sup>***a</sup>   | -3.7 (-5.7; -1.7)    |
|        | <b>Total cholesterol</b> |                            |                                       | <b>Walking speed test</b>       |                            |                      |
| CON    | 168.7±45.9               | 171.8±43.3                 | 3.2 (-3.0; 9.3)                       | 421.3±35.3                      | 420.2±37.5                 | -1.1 (-11.6; 13.8)   |
| CROS   | 194.4±38.7               | 155.2±30.7 <sup>***a</sup> | -39.3 (-45.4; -33.1)                  | 444.0±21.9                      | 502.4±28.5 <sup>***a</sup> | 58.4 (45.7; 71.1)    |
| AER    | 281.7±19.9               | 272.8±24.0 <sup>***a</sup> | -8.9 (-15.0; -2.8)                    | 580.0±35.1                      | 626.7±39.9 <sup>***a</sup> | 30.8 (18.1; 43.6)    |

Note: CON – Control, CROS – concurrent training, AER – aerobic training. <sup>a</sup>  $p \leq 0.05$  vs. Pre-intervention; #  $p \leq 0.05$  vs. AER; \*  $p \leq 0.05$  vs. CON.

No effect was observed for body mass ( $F_{2,33}=0.077$ ;  $p=0.78$ ;  $\eta^2=0.004$ ). A significant interaction effect was observed for rate-pressure product ( $F_{2,33}=5.275$ ;  $p=0.01$ ;  $\eta^2=0.242$ ), where CROS ( $p=0.043$ ) and AER ( $p=0.001$ ) showed lower means at post vs. pre-intervention moment. A significant interaction effect was observed for HbA1c ( $F_{2,33}=34.078$ ;  $p\leq 0.001$ ;  $\eta^2=0.674$ ), where CROS ( $p\leq 0.001$ ) showed a significantly lower mean at post-intervention in comparison to pre-intervention moment, while CROS showed a lower mean in comparison to AER  $[-2.6 (-4.2; -1.0)$ ;  $p=0.001$ ] and CON  $[-1.6 (-3.2; -0.01)$ ;  $p=0.049$ ] groups at the post-intervention. A significant interaction effect was observed for total cholesterol ( $F_{2,33}=52.812$ ;  $p\leq 0.001$ ;  $\eta^2=0.762$ ), where the AER ( $p=0.006$ ) and CROS ( $p\leq 0.001$ ) showed a significantly lower mean at post- vs. pre-intervention moment, while AER showed a significant difference from the CROS  $[-117.6 (82.8; 152.4)$ ;  $p=0.001$ ] and CON  $[100.9 (66.1; 135.8)$ ;  $p=0.001$ ] groups at the post-intervention moment.

A significant interaction effect was observed for LDL ( $F_{2,33}=8.547$ ;  $p=0.001$ ;  $\eta^2=0.341$ ), where the CROS group showed a significantly lower mean ( $p\leq 0.001$ ) when comparing the post- vs. pre-intervention moment. A significant interaction effect was also observed for HDL ( $F_{2,33}=15.097$ ;  $p\leq 0.001$ ;  $\eta^2=0.478$ ), where CROS showed a significantly higher mean when comparing post vs pre-intervention ( $p\leq 0.001$ ); while the AER group showed a higher mean in comparison to the CROS group  $[7.5 (0.2; 14.8)$ ;  $p=0.042$ ] at post-intervention. A significant interaction effect was observed for cardiovascular risk ( $F_{2,33}=8.708$ ;  $p=0.001$ ;  $\eta^2=0.345$ ) in comparing the pre-CROS group ( $p\leq 0.001$ ), and AER ( $p=0.001$ ) showed a lower mean at post-intervention moment, while AER showed a higher mean in comparison to CROS  $[10.5 (6.2; 14.7)$ ;  $p\leq 0.001$ ] and CON  $[6.4 (2.1; 10.6)$ ;  $p=0.002$ ] groups at post-intervention. A significant interaction effect was observed for the WST ( $F_{2,33}=22.697$ ;  $p\leq 0.001$ ;  $\eta^2=0.579$ ) compared to pre-CROS, and AER ( $p\leq 0.001$ ; for all comparisons) showed a higher mean at post-intervention, while AER also showed a higher mean when comparing CROS  $[124.3 (87.6; 160.9)$ ;  $p\leq 0.001$ ] and CON  $[206.5 (169.8; 243.2)$ ;  $p\leq 0.001$ ] groups at the post-intervention, and CROS showed a higher mean vs. CON  $[82.3 (45.6; 118.9)$ ;  $p\leq 0.001$ ].

## Discussion

Preceding reports in Chile have indicated that higher levels of self-reported sitting time are associated with higher risk of type 2 diabetes, independent of physical activity (Díaz-Martínez et al., 2017). In fact, T2DM middle-aged subjects tend to present progressive muscle mass loss and increased body fat, and these changes in body composition impair glycemic control, increase the risk for falls and chronic inflammation, however a physical exercise intervention prevents complications associated with evolution and disease complications (Annibalini et al., 2017). Our main results indicate that specific benefits can be achieved by different exercise programs, as the AER group showed a better response in two cardiovascular measures (rate-pressure product and walking-speed test), whereas the CROS group presented better metabolic response (HbA1c, total cholesterol and LDL). The main factors determining the impact of exercise on disease control are associated with the volume, intensity and type (Balducci et al., 2010). Sigal et al. (2007) observed that aerobic and resistance training contribute to glycemic control (Asfaw & Dagne, 2022), however, concurrent training is more potent when compared to programs which use either method alone.

Much evidence has shown that aerobic and concurrent training sessions have essential independent effects on inflammation markers, non-insulin mediated glucose transport, insulin resistance, lipid profile, blood pressure, fitness, and reducing fat mass (Annibalini et al., 2017). These effects are more observed in research using multi component interventions (Annibalini et al., 2017; Church et al., 2010; Sigal et al., 2007). Although this is interesting, few studies have compared aerobic exercise and concurrent exercise (Sigal et al., 2007). To the authors' best knowledge, this is the first study with a Chilean population that has compared the chronic effects of an aerobic training program versus a combined aerobic and resistance training program. This finding may be important compared to methodological shortcomings in exercise-only interventions which demonstrated limitations such as insufficient exercise volume, low adherence and/or length of intervention (Marcus et al., 2006).

Despite the more intense effect of chronic adaptation to aerobic exercise, our results also demonstrated a beneficial effect of concurrent training. Despite the rate-pressure product's ability to predict main adverse cardiovascular events (Xu et al., 2017), we do not know of any studies that investigated the training effect on the rate-pressure product in T2DM. In addition to the rate-pressure product, we also measured the walking speed test, which is a short-term, easy-to-apply test with higher predictive power for cardiovascular events in older people (Newman, Simonsick, Naydeck, & et al., 2006), and is also valid for measuring cardiorespiratory fitness in T2DM (Lee, 2018). Finally, the cardiovascular risk estimated by the UKPDS risk engine (2.0), which analyzed HbA1c, SBP, total cholesterol and HDL together, showed a protective effect in the AER and CROS protocols, but there was a lower risk after the concurrent training. The variables analyzed by this software can be modified by physical exercise and are indicators of metabolic and cardiovascular control in T2DM (Clarke et al., 2004; Ho et al., 2023).

HbA1c is one of the main indicators of a patient's metabolic control and health status (Church et al., 2010). According to the American Diabetes Association (Association, 2018),  $\geq 6.5\%$  is an indicator of increased

cardiovascular risk and diabetic retinopathy. Only the AER group in our study were above the cut-off point for risk, and this intervention was not efficient for promoting control of this indicator. On the other hand, the CROS group showed a significant decrease in HbA1c levels. Our results partially agree with the findings of Sigal et al. (2007), who also observed higher efficiency of concurrent training, but the decrease was higher in patients who showed higher baseline mean. Regarding HbA1c differences, a preceding study reported that progressive high-intensity resistance training demonstrated improvement in HbA1c levels, however these results were not observed in the low-intensity aerobic exercise group (Mavros et al., 2013). Unlike our results, a study with concurrent training (Dobrosielski et al., 2012) also showed more modest results in subjects with well-controlled HbA1c ( $\Delta$ -0.2% after 6 months).

Concurrent training is more cost-effective when comparing isolated aerobic and resistance exercise prescription, so this may be a better option to be offered in physical activity programs for T2DM treatment (Coyle et al., 2012). Roberts, Craig, Adler, McPherson, and Greenhalgh (2018) observed that even with the low-cost and efficiency of the British treatment program to improve glycemic control and HbA1c, only a small portion of the people are treated. Therefore, there is a need to propose new strategies focused on wider care being provided. Among the limitations in our study, the results were obtained from mixed gender groups, and more specific results can be obtained by groups separated by gender.

## Conclusion

The present longitudinal study allows us to conclude that the AER and CROS interventions provide metabolic and cardiovascular improvements in middle-aged T2DM of both genders after 12 weeks. The AER group showed a better response in the rate-pressure product and walking-speed test, whereas the CROS presented a better response to HbA1c, total cholesterol and LDL.

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