Supplementary Appendix

Fitness, strength and body composition during weight loss in women with clinically severe obesity: a randomised clinical trial

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The supplementary material below contains additional detail on specific methods and supporting results.

Methods

Recruitment

Participants volunteering for the study were recruited through Deakin University, Monash Medical, and Baker IDI Heart and Diabetes Institute internal email networks. Advertisements were placed in one large locally subscribed weekend newspaper and other local area newspapers. Study details and contact details were listed on the Baker IDI Heart and Diabetes volunteer webpage, promoted on social media (Facebook and Twitter). One page information flyers were given to medical practices in the local area after meeting with practice nurses and dietitians, and flyers placed in medical practice waiting rooms. Interested volunteers self-initiated contact with the research team via email or phone. Interested volunteers were screened against the inclusion criteria prior to being given the participant information and consent form, and medical clearance form.

Randomisation

Participants were randomised individually by a researcher external to the project and had no contact with the participants prior to or during the trial. This researcher had no intellectual or personal investment into the study design or outcomes. The women were randomised into either (ER) or

(EXER) groups via the use of sealed opaque envelopes in blocks of six. The envelopes were stored in a locked cabinet within the independent researchers' office. Each envelope contained a single sheet of paper identifying the group allocation. The sheet of paper was folded twice to reduce chance of transparency. One envelop was chosen at random from the stack of six envelopes containing 3 of each group allocation (EX and EXER). Once reduced to a single envelope, it was combined with the next group of six envelopes to reduce the chance of predictability. The independent researcher was provided with a participant identification number and completed randomisation once the prospective participant provided the study investigators (CM, TR, DV or JD) with a medical clearance from their own general practitioner, preliminary participant screening, and completed all of the baseline measures to ensure safety and suitability for study participation. Participants, and researchers involved in delivering participant interventions were not blinded to group allocation. Some of these researchers (CM, DV, TR) were also be involved in study co-ordination and data collection.

Study Interventions

Exercise training

EXER follow a standardised progressive exercise program led by Accredited Exercise Physiologists or student Exercise Physiologist supervised by an Accredited Exercise Physiologist. The exercise intervention consists of a supervised exercise program that was complemented by a home-based exercise routine. The supervised exercise training commenced the same week as the VLED and consisted of the following:

3 x 1 hour supervised exercise sessions per week (weeks 1-6)
2 x 1 hour supervised exercise session per week (weeks 7-12)
1 x 1 hour supervised exercise session per week (weeks 13-26)
2 x 1 hour supervised exercise sessions per month (weeks 27-52)

The exercise training consisted of a progressive moderate intensity aerobic conditioning, and resistance training program using a variety of machines and free weights. Each training session lasted 60 minutes and comprised of a 5 minutes warm up, 45-50 minutes conditioning, and 5 minutes of cool down and stretching. The conditioning component consisted of approximately 20-30 minutes of aerobic training (12-16 on Borg's RPE scale, 60-80% HRR) followed by 20-30 minutes of

resistance exercise (1-3 sets of 8-10 repetitions). The resistance exercise involved 6-10 different, predominantly multi-joint exercises for the upper and lower extremities at an intensity of two repetitions below volitional fatigue, with a 2 sec concentric and eccentric contraction speed. Exercise prescription followed clinical judgement and ACSM's guidelines [1] to ensure fitness improvement and program compliance. Once participants completed three sets of ten repetitions with correct technique, for two consecutive training sessions the resistance was increased. The cardiorespiratory fitness training was progressed from 40-60% HRR in the first five weeks to 60-80% HRR for the remainder of the program. The mode of aerobic exercise varied depending on participant's choice, however weight bearing exercise such as walking was encouraged as one of the principle exercise modes.

The exercise physiologists follow a structured resistance training program with eight core exercises that included: leg press, squats, bench press, seated row, lateral pull down, shoulder press, biceps curl and triceps kickbacks.

The exercise physiologist's kept a record of attendance, exercises undertaken and progress achieved by participants. It was required that any adverse events or adverse signs and symptoms were documented including feelings of general fatigue, soft tissue soreness, light-headedness, colds and flu and injury or illness. The reason for non-attendance was also be included on the exercise program card. Make up sessions were made available where possible during the same training week or the following week.

The participants were assisted in the development of a home-based exercise program that gradually replaced the supervised exercise sessions. This was designed to transfer to a self-management model. The program consisted predominantly of cardiorespiratory exercise devised around each individual's access to facilities and equipment. Participants were also encouraged to increase incidental physical activity. Participants progressively increased their weekly training hours and frequency of home based exercise during the period of the study so that all participants aimed to be exercising most if not all days of the week. The participants were to set a goal of exercising at a moderate intensity for 200 minutes per week in week one, progressing to 300 minutes by week six and sustain this level of exercise participation for the remainder of the 12 month intervention to assist with developing a regular exercise habit conducive for weight maintenance [2-4]. The purpose of the exercise physiologist was to provide advice, guidance and support for the prescription of exercise, but at no time provide dietary advice to the participants. Exercise physiologists referred participants back to the study dietitian for assistance with diet.

Participants randomised to the energy restriction only group were encouraged to exercise at study commencement and during the dietary consultations along with general lifestyle advice, but were not provided with any specific guidance or follow up support. These participants were not discouraged from changing their exercise habits.

Outcome measures

Aerobic power

VO_{2peak} was assessed using a sign and symptom-limited incremental treadmill test. Participants warmed up at a comfortable walking pace at 0% gradient and speed was then adjusted gradually until Ratings of Perceived Exertion (6-20 Borg point scale; RPE) (28) reached 7-8 / 20. The speed then remained constant and the gradient was increased by 2% per minute until the participant reached RPE 17 / 20 (very hard) (29). Expired respiratory gases were collected and analysed using a breath-by-breath pneumotach system (Innocor Innovision version 6.15, Glamsbjerg, Denmark) and this was calibrated according to the manufacturer guidelines. $HbO_{2sat\%}$ using pulse oximetry was recorded at the end of each minute during the test and recovery.

Muscular Strength

Maximal muscular strength was determined using a 3 repetition maximum (3RM) [1] for bench press, supine leg press, and seated row using standard resistance training equipment. The participants were shown, explained and practiced correct lifting and breathing technique for each exercise prior to the test and complete ten repetitions of the exercise at a low to moderate load. This also served as a specific warm up to the exercise test. Participants were asked to self-select an estimated starting weight which was then increased gradually until only three repetitions are possible. The progressive increase in load ranged from 1-10kg for bench press, 2-10kg for leg press and 1-9kg for seated row. The rest period between attempts was set to 90-120 sec or until fully recovered. The bench press was performed using a smith machine (BodySolid, Powerline PSM144X, Forest park, IL, USA). The seated row was completed using a Dual pulley (Nautilus tower pulley system, F3ATFS, Independence, VA, USA) with a with a V-pulldown/row bar. The pulley height was set in line with the zyphoid process and feet placed on a step to ensure full arm length from the pulley. The back and shoulders rested on the back of the upright bench to avoid the use of momentum. The leg press (Synergy Omni leg press S-31-OPD, QLD, AUS) was performed in supine

with the seat lowered until the knee reached 90 degrees. For all strength tests, the machine settings in relation to anatomy were recorded and replicated in subsequent tests.

Blood Sampling and Analysis

Fasting Blood Collection and Analysis

Venous blood samples was collected prior to the oral glucose tolerance test (OGTT) by a trained phlebotomist. 40ml of blood was extracted into vacutainer tubes, and 2 tubes were sent to a commercial pathology laboratory for analysis of fasting glucose, insulin, blood lipids, haemoglobin A1c, and C reactive protein. The remaining was centrifuged and stored in a -80°C freezer. Each participant was advised to maintain their normal diet and exercise patterns for the three days prior to the testing. After a 12 hour overnight fast, participants attended the BakerIDI Heart and Diabetes institute. BakerIDI Heart and Diabetes institute research colleagues performed the oral glucose tolerance test. An intravenous catheter was placed in an antecubital vein for blood sampling. Volunteers ingested 75 g of glucose over 2 min (Glucotol™, Orion Laboratories, Welshport, WA, Australia). Blood samples were drawn at –15, 0, 30, 60, 90 and 120 min for determination of plasma glucose and insulin concentrations. The remaining blood was centrifuged and plasma stored in a -80°C freezer at the BakerIDI Heart and Diabetes Institute.

Anthropometry

Three compartment body composition and bone mineral density using a Dual energy x-ray absorptiometry (DXA) scanner (GE Lunar Prodigy Pro, Madison, WI 53718) with software version 12.1 for total body fat mass, lean body mass, and total body bone mineral content and density. For instances where portions of the trunk remained outside of the scan area, half body scans (28) were completed on the right side and multiplied by two. Body weight was measured with participants wearing hospital gown without shoes. Waist circumference (NHANES III procedure) (29) and hip circumference (widest part of hips) (30) were measured using a steel tape measure.

Results

Adverse events

Energy restriction only

One participant reported a temporary knee pain not likely related to study participation. One participant reported deep vein thrombosis following a long haul plane flight that is not likely related to study participation. Minor adverse events likely related to study participation: bloating (n=1), flatulence (n=1), headache (n=5), constipation (n=2), diarrhoea (n=2), dry skin (n=1), postural hypotension and dizziness (n=2), hair loss (n=3), heart palpitations (n=1), sensitivity to cold (n=2), back pain (n=2), skin infection (n=1) .

Energy restriction plus exercise training

One participant reported a meniscal injury to the knee as a result of running down a set of stairs suffered during self-administered exercise. The injury is likely related to participation in the study. This incident was not part of the exercise training program and the participant had a history of meniscal injury. A second participant experienced a minor lumbar strain during a leg press exercise which is likely related to participation in the study as it was sustained during the regular supervised training session. Adverse events likely related to study participation: headache (n=1), constipation (n=3), dry skin (n=3), postural hypotension and dizziness (n=5), hair loss (n=6), sensitivity to cold (n=5), polycthaemia (n=1), Itchiness (n=1), vision disturbance (n=1), falls when intoxicated (n=2), skin rash (n=1), nausea (n=1), increased sense of smell (n=1).

Attendance to dietary consultations

Attendance to dietary consultations were similar between groups. 12 ± 5 (M ± SD) dietary consultations in ER, and 14 ± 4 (M ± SD) in EXER, (Mean diff ± SEM; 1.9±1.2; p=0.139). Attendance to the supervised exercise training decreased over time with attendance highest in the first three months (Mean± SD, 73± 26%), reducing to 64± 36% (Mean± SD) between three and six months, and to 42± 39% (Mean± SD) between six and twelve months. Overall attendance to supervised training sessions was 63± 27% (Mean± SD). These values are inclusive of all participants that withdrew from the study and were lost to follow-up.

Seven-day exercise recall

Participants reported the previous seven days of moderate intensity exercise which consisted of ten minutes or more. Participants increased exercise in EXER more than ER at all three, six and twelve months, however both groups increased weekly exercise minutes at all timepoints. ER increased exercise minutes at three months (72 ± 21.8 min, $p<0.05$), six months (66.3 ± 20.8 min, $p<0.05$), 12

months (60.9 ± 22.7 min, $p<0.05$). EXER increased exercise minutes at three months (178 ± 20.9 min, $p<0.05$), six months (157.5 ± 20.4 min, $p<0.05$), 12 months (170.9 ± 20.3 min, $p<0.05$).

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