Abstract: Purpose: To determine the effects of 10 wk of resistance or aerobic exercise training on interleukin-6 (IL-6) and C-reactive protein (CRP). Further, to determine pretraining and post training associations between alterations of IL-6 and CRP and alterations of total body fat mass (TB–FM), intra abdominal fat mass (IA-FM), and total body lean mass (TB–LM). Methods: A sample of 102 sedentary subjects were assigned to a resistance group (n = 35), an aerobic group (n = 41), or a control group (n = 26). Before and after intervention, subjects were involved indual-energy x-ray absorptiometry, muscular strength and aerobic fitness, measurements and further provided a resting fasted venous blood sample for measures of IL-6, CRP, cholesterol profile, triglycerides, glucose, insulin, and glycosylated hemoglobin. The resistance and the aerobic groups completed a respective 10-wk supervised and periodized training program, whereas the control group maintained sedentary lifestyle and dietary patterns. Results: Both exercise training programs did not reduce IL-6; however, the resistance and the aerobic groups reduced CRP by 32.8% (P G 0.05) and 16.1% (P = 0.06), respectively. At baseline, CRP was positively correlated with IL-6 (r = 0.35),(TB–FM) (r = 0.36), and IA-FM (r = 0.31) and was inversely correlated with aerobic fitness measures (all r values Q –0.24). Compared with the resistance and the control groups, the aerobic group exhibited significant (P G 0.05) improvements in all aerobic fitness measures and significant reductions in IA-FM (7.4%) and body mass (1.1%). Compared with the aerobic and the control groups, the resistance group significantly (P G 0.05) improved TB–FM (3.7%) and upper (46.3%) and lower (56.6%) body strength. Conclusion: Despite no alteration in baseline IL-6 and significantly smaller reductions in measures of adipose tissue as compared with the aerobic training group, only resistance exercise training resulted in significant attenuation of CRP concentration.

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ABSTRACT

Purpose: To determine the effects of 10-wk resistance or aerobic exercise training on interleukin (IL)-6 and c-reactive protein (CRP). Further, to determine pre- and post-training associations between alterations of IL-6 and CRP, and alterations of total body fat mass (TB-FM), intra-abdominal fat mass (IA-FM), and total body lean mass (TB-LM).

Methods: A sedentary subject sample of 102 were assigned to a resistance group (n =35), an aerobic group (n =41), or control group (n =26). Pre- and post-intervention, subjects were involved in dual-energy x-ray absorptiometry (DEXA), muscular strength and aerobic fitness measurements, and provided a resting fasted venous blood sample for measures of IL-6, CRP, cholesterol profile, triglycerides, glucose, insulin, and glycosylated haemoglobin (HbA1c). The resistance and aerobic groups completed a respective 10-wk supervised and periodised training program, while the control group maintained sedentary lifestyle and dietary patterns.

Results: Both exercise training programs did not reduce IL-6, however, the resistance and aerobic group reduced CRP by 32.8% (P<0.05) and 16.1% (P= 0.06), respectively. At baseline, CRP was positively correlated with IL-6 (r=0.35), TB-FM (r=0.36), and IA-FM (r=0.31); and was inversely correlated with aerobic fitness measures (all $r \geq$ –0.24). Compared to the resistance and control groups, the aerobic group exhibited significant (P<0.05) improvements in all aerobic fitness measures, and significant reductions in IA-FM (7.4%), and body mass (1.1%). Compared to the aerobic and control groups, the resistance group significantly (P<0.05) improved TB-LM (3.7%), and upper (46.3%) and lower (56.6%) body strength.

Conclusion: Despite no alteration in baseline IL-6, and significantly smaller reductions in measures of adipose tissue as compared to the aerobic training group, only resistance exercise training resulted in significant attenuation of CRP concentration.

Keywords: Diabetes; cardiovascular disease (CVD); dual-energy x-ray absorptiometry (DEXA); sedentary; weight training; endurance training.

INTRODUCTION

Paragraph Number 1

Recent evidence highlights the presence of a low-grade chronic systemic inflammatory state with the development and progression of cardiovascular disease (CVD) (12,32) and type 2 diabetes (T2D) (30,37). The importance of conventional risk factors such as hyperlipidemia, hypertension, and smoking for the development of these disease states are well established (17,31). However, it has been reported that more than 50% of myocardial infarctions and strokes occur in patients lacking hyperlipidemia, and 15 to 20% occur in those who do not smoke, or present with hypertension (17,31). Hence, in conjunction with conventional risk factors, novel immunological risk factors are emerging as important screening adjuncts regarding prognostic insight into chronic disease risk (28,31). Two markers of immune system function which have been linked to the development of CVD and T2D include the inflammatory marker c-reactive protein (CRP) and its systemic precursor interleukin (IL)-6.

Paragraph Number 2

Prospective and cross-sectional epidemiological investigations have reported that elevated resting CRP concentrations (high-risk: >3.0 mg·L^{-1}) are associated with increased risk for first-ever CVD event (18,21), ischaemic stroke and transient ischaemic attack (33), the development of hypertension (36), and carotid (34) and peripheral (39) artery disease. Further, elevated baseline concentrations are associated with elevated fasting glucose (24) and fasting insulin (29) concentrations in non-T2D individuals, and the development of T2D in initially T2D-free subjects (30). Recently, guidelines have been endorsed for the utilisation of CRP as a prognostic clinical marker of global cardiovascular and metabolic risk (28). Accordingly, the measurement of CRP has been suggested to offer prospective insight regarding the monitoring of chronic systemic inflammation and chronic disease risk (28).

Paragraph Number 3

Associated with the development of these diseased sates, abdominal obesity has recently been endorsed as an important risk factor for the development of metabolic syndrome and associated chronic diseases (1); this is not surprising given that visceral abdominal adipose tissue secretes two to three times the quantity of IL-6 compared to subcutaneous adipose stores (8,22). Moreover, dual-energy x-ray absorptiometry (DEXA) and within-pair differences in monozygotic twins have demonstrated that intra-abdominal fat mass (IA-FM) is strongly correlated with CRP concentration, independent of genetic influence (9). In addition, a systematic review of 33 weight-loss interventions has revealed a CRP reduction of 0.13 mg·L^{-1} for each 1.0 kg of body mass loss (35); however, regional analysis was not a feature of this study, and thus associations cannot be drawn as to the likely compartmental reductions that may have mediated the reductions in CRP concentration (35).

Paragraph Number 4

Cross-sectional investigations have demonstrated inverse associations between aerobic fitness and chronic systemic inflammation (2,27). As evidence of this, comparison of Bruce protocol treadmill test performance and CRP concentration demonstrated a 0.061 mg·L^{-1} decrease in CRP concentration with each metabolic equivalent gained during the protocol (2). Moreover, another investigation demonstrated inverse associations between weekly exercise patterns and inflammatory markers (27). In comparison to sedentary subjects, and after adjustment for gender, age, smoking habits, body mass index, total cholesterol, glucose, and blood pressure, subjects devoted to high physical activity reported 29% and 32% lower concentrations of CRP and IL-6, respectively (27). Hence, reduced aerobic exercise capacity and sedentariness seem to be associated with increased presence of chronic systemic inflammation, and may provide a rationale for the use of exercise as a therapeutic modality.

Paragraph Number 5

Hepatic stimulation by IL-6 induces the synthesis and systemic release of CRP as part of the acute-phase inflammatory response (9,30). The existing literature presents conflicting and inconsistent findings regarding the effects of exercise training on this response (7). For example, investigations have reported both attenuation (5,19,20,25,38) and no effect (7,11,15,23) of exercise training on CRP. Further, some investigations have reported a reduction in IL-6 with no subsequent effect on CRP (7,23), whilst others have reported the reverse (26,38). Moreover, studies reporting reductions in CRP, and IA-FM, and total body fat mass (TB-FM), have reported no correlation between these reductions (20,25), which is in opposition to the previously demonstrated physiological association between adipose tissue and systemic inflammation (8,9,22). In addition to the large variance in reported subject samples (5,7,19,23,38), much of the published research has included clinically diagnosed subjects, thus reducing the transference of findings to non-diagnosed subject samples (20).

Paragraph Number 6

Therefore, due to the inconsistent findings on the effects of exercise training on systemic inflammatory markers, the purpose of the present study was to determine the respective effects 10-wk of resistance or aerobic exercise training on CRP and IL-6 concentrations in a sedentary adult population matched for baseline CRP and IL-6 concentrations. A further purpose was to investigate whether potential reductions in CRP and IL-6 were associated with the modality of exercise performed, or alterations in body composition, specifically, reductions in IA-FM and TB-FM. Based on previous research, it was hypothesised that both interventions would reduce IL-6 and CRP concentration, and further, that the aerobic intervention would result in a more pronounced reduction in CRP and IL-6 concentration, particularly in response to a hypothesised larger reduction in IA-FM and TB-FM.

METHODS

Subjects

Paragraph Number 7

One-hundred and two sedentary subjects, including both male (n =45) and female (n =57) subjects, volunteered from the local community and were semi-randomly assigned to either a resistance group (male n =16, female n =19, total n =35), an aerobic group (male n =16, female n =25, total n =41, or a control group (male n =13, female n =13, total n =26. Baseline characteristics of the study population are presented in Tables 1 to 3. At baseline, approximately 80% of subjects were randomly assigned to the respective groups; however, approximately 20% were assigned to a group according to a combination of either specific group preference or matching of pre-training IL-6 and CRP concentrations. At baseline, subjects were required to be sedentary, which was defined as no regular pattern of planned or incidental activity longer than 20 min in duration. Further study exclusion criteria included tobacco smoking (<1yr cessation), hormone replacement therapy patients, those suffering from current or recent influenza illness (including flu shot recipients), recent surgical patients, rheumatoid arthritis patients, subjects with known immunological irregularities (such as low white blood cell count), and any other condition associated with a systemic inflammatory response. Subjects with orthopaedic limitations were also advised against becoming involved in the study due to the musculoskeletal demands of both training programs. Subjects attended an information and familiarisation session in which all details of testing and training procedures were explained. All subjects gave verbal and written informed consent prior to engaging in testing procedures and Human Ethics clearance was granted by the Institutional Ethics Committee.

Study Overview

Paragraph Number 8

Prior to and following the 10-wk training intervention, a health screening was performed on all subjects, which involved a consultation with a medical physician. During this session, documentation of past and current health information was provided to ensure the aforementioned exclusion criteria. After this consultation and following an overnight 10–12 h fast, subjects reported to a pathology clinic between 0700 and 0900 h and were seated for 20 min prior to providing a venous blood sample. At baseline, and following exercise training, venous blood samples were obtained after a four day abstinence from exercise or physical activity to ensure that acute fluctuations in IL-6 and CRP concentration would have subsided before collection. In addition, subjects were screened for T2D which was indicated by a fasting glucose measure ≥ 7.0 mmol·L^{-1}, or a glycosylated haemoglobin (HbA1c) measure $\geq 6.5\%$; if T2D was suspected, the subject was excluded from study involvement. Based on previously recommended clinical guidelines, a measure of 10.0 mg·L^{-1} was the cut-off for CRP measures which may have potentially reflected inflammation due to sepsis, and thus may have obscured the identification of resting baseline CRP concentration (28).

Paragraph Number 9

Pre- and post-intervention, subjects attended a testing session at the Institutional Exercise Science Laboratories for assessment of body composition, aerobic fitness and muscular strength. Following pre-intervention testing, the resistance and aerobic subjects completed a 10-wk periodised and progressive exercise training program (Table 4), while subjects in the control group continued their normal sedentary life. Subjects from the three conditions were informed about the importance of maintaining their previous nutritional patterns including food and beverage choice, dietary contribution from carbohydrate, fat, and protein, and the

serving quantity and feeding time. Although required to remain sedentary, subjects in the control group were provided with an exercise and physical activity diary and were required to log the type, duration, and intensity of any physical activity or exercise undertaken during the period. Following the intervention period the authors examined the exercise and physical activity diary of the control subjects to ensure conformity to the study requirements.

Exercise Protocols

Paragraph Number 10

Table 4 presents the 10-wk periodised resistance and aerobic exercise training programs and includes information pertaining to the progression of exercises performed, and the respective intensity, volume, and duration of training. Each training session for both the resistance and aerobic group commenced with a 5 min dynamic stretching warm-up routine, followed by the main respective group session, and concluded with 5 min of stretching exercises. The main session for the resistance group incorporated pulley-weight machine exercises (Panatta Sport, Apiro, Italy) which were performed at pre-intervention 10RM, which is reported to approximate with 75% of a one repetition maximum (1RM) (3). Recovery between sets and exercises was standardised at 120 sec, and an increase in resistance was warranted if two extra repetitions could be performed in the last set on two consecutive occasions, which promoted subjects to train proximally to 'momentary muscle failure' by exercise completion (3). The main session for the aerobic group incorporated cycling exercise on Monark stationary cycle ergometers (Monark 828E, Monark Exercise AB, Varburg, Sweden) which incorporated the monitoring (Vantage NV, Polar, Finland) and adjustment of heart rate through manual adjustment of pedalling resistance. Resistance and aerobic exercise training was performed within the Institutional Exercise Science Laboratories under full supervision by exercise physiologist research assistants whom monitored all workout sessions.

Additionally, each session was monitored for heart rate, pedalling resistance, rating of perceived exertion (RPE), and cycling duration in the aerobic group, and session exercises, resistance levels, and completion rates (exercises, sets and repetitions) in the resistance group.

Measures

Paragraph Number 11

All pre-intervention and post-intervention measures were conducted in a climate-controlled exercise physiology laboratory, by the same research team and with time of day standardised. Anthropometric measures included height (stadiometer: Custom CSU, Australia), body mass (HW 150 K, A & D, Australia), waist and hip girths (steel tape, EC P3 metric graduation, Australia), and a supine whole body dual-energy x-ray absorptiometry (DEXA) scan for body composition (XR800, Norland, Cooper Surgical Company, USA). Scanning resolution was set at 6.5 x 13.0 mm, and scanning speed was set at 260 mm/sec. Subject scanning position was standardised for pre- and post-testing analysis. The whole body scan was analysed (Illuminatus DXA, ver. 4.2.0, USA), and total body lean mass (TB-LM), TB-FM, and IA-FM quantities were quantified in kg. The analysis of IA-FM was performed with the creation of a region of interest (ROI) according to previously reported procedures (14). Muscular strength was measured with a ten repetition maximum (10RM) test procedure which incorporated chest press and leg press for identification of upper-body and lower-body strength, respectively. Multiple RM testing was utilised firstly, to assist the identification of an initial training load (10RM), and secondly, to minimise muscular soreness of the subjects due to their sedentary condition. Subjects were instructed in the appropriate operation of the pulley weight machines, and were familiarised with the strength test procedures. During strength assessment, subjects were required to attempt ten repetitions of ascending resistances in

which each attempt was separated by 3–5 min recovery. The determination of 10RM for each the upper- and lower-body exercise usually required 2 to 3 attempts (2 to 3 sets). Aerobic fitness measures were obtained with the utilisation of the aerobic power index (API) component of the tri-level fitness profile, which has been demonstrated as a highly reliable sub-maximal exercise protocol in sedentary subjects (40). The API protocol was performed on an electronically-braked cycle ergometer (LODE Excalibur Sport, LODE BV, Groningen, The Netherlands). The API protocol is an incremental step protocol which commences at 25W, and increases in increments of 25W each minute. Heart rate was recorded each minute throughout the protocol (Vantage NV, Polar, Finland), and was combined with the subjects' mass and interpolated power output to calculate an aerobic power (fitness) index (API) (40).

Blood Analysis

Paragraph Number 12

Blood samples were collected into evacuated lithium heparin tubes for the analysis of CRP, IL-6, insulin, cholesterol, and triglycerides; additionally, fluoride oxalate tubes and EDTA tubes were used for the analysis of glucose and glycosylated haemoglobin (HbA1c), respectively. All biochemistry variables were analysed according to manufacturer's instructions provided in the respective assay kits (Dade Behring Dimension Xpand, Siemens Healthcare Diagnostics, Sydney, Australia). Total cholesterol was assayed using an enzymatic method and polychromatic endpoint technique measurement. High-density lipoprotein (HDL) cholesterol was measured using accelerator selective detergent methodology. Triglycerides were assayed using an enzymatic method and bi-chromatic endpoint technique measurement. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedwald Equation, which incorporates total cholesterol, HDL cholesterol and triglyceride measures. Glucose was assayed using an enzymatic method and bi-chromatic

endpoint technique measurement. Insulin was measured using a solid-phase, two-site chemiluminescent immunometric assay. CRP was manually diluted according to manufacturer's instructions and analysed with the particle enhanced turbidimetric immunoassay technique (PETIA). IL-6 was analysed with a solid-phase, enzyme-labelled, chemiluminescent sequential immunometric assay. HbA1c was measured using automated high-performance liquid chromatography (HPLC) methodology (Bio-Rad Variant, Sydney, Australia). Intra- and inter-assay coefficients of variation were less than 5.0% for all biochemistry variables.

Statistical Analysis

Paragraph Number 13

All data are reported as mean ±standard deviation (SD). A repeated measures (condition x time) ANOVA was used to determine significant differences between the respective groups (resistance, aerobic, control). Where a significant main effect and/or interaction was observed, one-way ANOVA of pre to post differences (absolute values) with Tukey's HSD post-hoc tests were applied to determine the source of significance, which was set at $P \leq 0.05$. Paired sample t-tests with Bonferroni adjustment were conducted on all measured variables to determine within-group significance. Finally, Pearson Product Moment correlations were calculated to identify any significant associations between CRP baseline, CRP change, and baselines and change in other measured variables. All statistical procedures were performed using SPSS™ for MS-Windows version 16.0 (Statistical Package for the Social Sciences, Chicago, Il, USA).

RESULTS

Muscular strength and aerobic fitness

Paragraph Number 14

Table 1 presents pre- and post-intervention within-group and between-group results for muscular strength and aerobic fitness variables. Pre-intervention comparisons between conditions revealed significant differences ($P<0.05$) in baseline strength, with a higher 10RM lower-body strength in the control compared to aerobic and resistance groups, while 10RM upper-body strength was also higher compared to the aerobic group. However, following the intervention period there was no improvement in strength or aerobic fitness measures for the control group. The training session completion rate of both the resistance and aerobic groups was 27 of the 30 organised sessions (91%). The resistance group increased 10RM upper-body strength by 46.5±21.9%, and 10RM lower-body strength by 56.6±23.3% (Table 1; $P<0.05$) which was a significantly larger improvement than the aerobic and control groups, respectively ($P<0.05$). The resistance training group also improved time to THR in the aerobic fitness test by 7.4±12.6% ($P<0.05$); however, no improvements were reported for final stage of test and calculated API ($P>0.05$). Following training, the aerobic group significantly improved time to THR by 20.9±8.6%, final stage of test by 16.8±12.3%, and calculated API by 22.5±11.1% (Table 1; $P<0.05$). The improvements in time to THR, final stage of test, and calculated API were significantly greater than improvements of the resistance and control groups, respectively ($P<0.05$). Additionally, the aerobic group also demonstrated a significant 25.8±24.6% increase in 10RM lower-body strength ($P<0.05$).

Anthropometry and DEXA

Paragraph Number 15

Table 2 presents pre- and post-intervention within-group and between-group data for the measured anthropometric and DEXA variables. Pre-intervention comparisons revealed no significant differences between groups ($P>0.05$) for any body composition variable. The

control group experienced an increase in hip girth and TB-LM (kg) following the 10-wk period ($P<0.05$). The resistance training group experienced a $1.0\pm1.9\%$ increase in body mass, which comprised a $3.7\pm5.0\%$ increase in TB-LM (kg), and a $3.4\pm6.6\%$ decrease in TB-FM (%) (Table 2; $P<0.05$). The increase in TB-LM was significantly larger than the increase in the aerobic group ($P<0.05$). The resistance group also experienced a $3.5\pm7.2\%$ decrease in IA-FM, and a $1.5\pm2.7\%$ decrease in waist girth ($P<0.05$). Additionally, the decrease in waist girth, hip girth, and IA-FM were significantly larger than the changes in the control group ($P<0.05$). Moreover, the aerobic group also demonstrated reductions (Table 2; $P<0.05$) in variables relating to body composition, including a $1.0\pm2.3\%$ decrease in body mass, a $0.9\pm2.2\%$ decrease in BMI, a $2.4\pm3.0\%$ decrease in waist girth, a $2.0\pm2.2\%$ decrease in hip girth, a $7.7\pm7.8\%$ decrease in IA-FM, and a $3.7\pm4.9\%$ and $3.4\pm4.2\%$ decrease in TB-FM (kg) and TB-FM (%), respectively. The aerobic training group also exhibited a $1.5\pm3.5\%$ increase in TB-LM ($P<0.05$). The decreases in body mass, BMI and IA-FM were significantly larger than the resistance and control groups (Table 2; $P<0.05$). Further, the decrease in waist and hip girth was also significantly larger than those demonstrated by the control group ($P<0.05$).

Biochemistry

Paragraph Number 16

Pre- and post-intervention within-group and between-group biochemistry variables are presented in Table 3. Prior to the intervention, there were no significant differences ($P>0.05$) between conditions for any variable. For the control condition, the only biochemistry variable that was significantly changed following the intervention was an increase in fasting glucose ($P<0.05$). Both the 10-wk resistance and aerobic exercise programs had no effect on baseline IL-6 concentration ($P>0.05$), however, the resistance group experienced a significant $32.7\pm27.2\%$ decrease in CRP concentration (Table 3; $P<0.05$). Post-hoc analyses

demonstrated a trend for a difference in CRP to the post-intervention control group ($P= 0.08$), and aerobic group ($P= 0.11$). The aerobic exercise group did not significantly reduce CRP concentration in response to the exercise program; however, a trend for a reduction was evident (16.1%; $P= 0.06$). The resistance group also experienced a 1.1±8.7% increase in total cholesterol which was significantly different ($P<0.05$) to the reduction exhibited by the aerobic group ($P<0.05$). The resistance group also experienced a 4.9±11.3% and a 5.4±5.1% increase in fasting glucose concentration and HbA1c concentration, respectively ($P<0.05$). Similar to the resistance group, the aerobic group also featured a 5.1±4.7% increase in HbA1c concentration ($P<0.05$). The increase reported for HbA1c for the resistance and aerobic groups was different compared to the small decrease experienced by the control ($P<0.05$); however, these increases were minor and did not alter T2D risk classification.

Correlations between CRP and other variables at baseline

Paragraph Number 17

Table 5 presents Pearson correlation coefficients and associated significance levels between baseline CRP and other pre-intervention variable values. At baseline, BMI, hip girth, IA-FM, TB-FM (kg), and TB-FM (%), were all moderately positively correlated with baseline CRP concentration (all $r \geq 0.25$; $P<0.05$). Baseline TB-LM (kg) and TB-LM (%) were weakly ($r= -0.23$; $P<0.05$) and moderately ($r= -0.36$; $P<0.05$) inversely correlated with baseline CRP concentration, respectively. At baseline, IL-6 was moderately positively correlated with CRP ($r= 0.35$; $P<0.05$); however, no other biochemistry variables demonstrated significant correlations with baseline CRP (all $r \leq 0.16$; $P>0.05$). Pre- to post-intervention change in CRP concentration demonstrated a correlation with baseline CRP concentration ($r= 0.23$; $P<0.05$). At baseline, final stage of test and API demonstrated moderate inverse correlation

with pre-intervention CRP concentration (all r ≥0.26; P <0.05), and time to THR featured a weak inverse correlation (r= –0.24; P<0.05).

Correlations between CRP change and other variable change

Paragraph Number 18

Table 6 presents Pearson correlation coefficients and associated significance levels between pre to post intervention change in CRP concentration and changes in other variables. Change in body mass and waist to hip ratio were weakly positively correlated with the change in CRP concentration (all r ≥0.21; P <0.05). The change in total/HDL-C ratio and HbA1c demonstrated weak inverse correlations with change in CRP concentration (all r ≤ –0.22; P<0.05). Change in 10RM lower-body strength produced a moderate inverse correlation with change in CRP concentration (r= –0.25; P<0.05), whilst change in 10RM upper-body strength demonstrated a moderate inverse correlation with change in CRP concentration (r= –0.22; P<0.05). No correlations were evident between change in CRP concentration and change in the measures of aerobic fitness (all r ≤ 0.04; P>0.05).

DISCUSSION

Paragraph Number 19

The purpose of the present study was to evaluate the effects of resistance or aerobic exercise training respectively to attenuate elevated IL-6 and CRP concentrations in a sedentary and disease free population. The baseline CRP concentrations reported in this study were classified as "high-risk" according to recently published guidelines (28), and similar (30) or elevated (18,21) compared to previous investigations which demonstrated prospective disease association. Moreover, baseline IL-6 concentration was similar (18,30) or elevated (21) in comparison to that reported in these same investigations. At study baseline, and according to

the prospective association between elevated chronic systemic inflammation and chronic disease risk, the finding that blood lipid and glycaemic control measures were in the normal range, whilst IL-6 and CRP were elevated, provides prospective context to the findings that approximately half of all MI and stroke patients present with 'normal' lipid levels (17,31). Similar to other investigations, subjects in the present study were sedentary at baseline and demonstrated an inverse association between aerobic fitness and inflammatory marker concentration (2,27). Hence, it is likely the subject population in the current study presented with increased atherosclerotic and metabolic risk, despite conventional risk screening markers not necessarily resulting in a classification of 'at risk'.

Paragraph Number 20

Following the 10-wk exercise training period, the IL-6 concentration of both exercise groups and the control group remained unchanged; however, a significant reduction in CRP concentration was experienced by the resistance training group. At baseline, CRP was moderately correlated with IL-6, highlighting the proposed relationship between systemic IL-6 release and systemic CRP concentration (9). Following exercise training, IL-6 remained unaltered, which given the reduction in CRP by the resistance group, is similar to findings reported by previous studies (26,38). Recent evidence following one year of moderate resistance training (26) also reported a reduction in CRP with no change in IL-6. Moreover, this recent study additionally reported no change in blood lipids, fasting glucose, fasting insulin, body mass or fat mass, and a significant increase in TB-LM, which corroborate findings for the resistance group in the present study.

Paragraph Number 21

The improvement in 10RM upper- and lower-body strength in the resistance group was accompanied by an improvement in TB-LM that was significantly greater than the aerobic group. This increase in TB-LM implies that the resistance group exhibited more protein synthesis and/or protein degradation and subsequently experienced greater skeletal muscle hypertrophy (6). At baseline, TB-LM (kg) was weakly correlated to CRP concentration ($r = 0.23$), however, when TB-LM was correlated as a percentage of body mass, the strength of the association increased markedly ($r = 0.36$). Despite the baseline correlation between TB-LM and CRP concentration, 10RM upper- and lower-body strength was not correlated to baseline CRP concentration. However, following exercise training, reductions in CRP concentration were correlated to 10RM lower- and upper-body strength improvements. Similar to previous investigations (5,26), the present study supports resistance exercise training in the reduction of elevated CRP concentrations.

Paragraph Number 22

Following exercise training, significant aerobic fitness improvements in time to THR, final stage of test, and calculated API measures were reported for the aerobic group compared to the resistance and control groups. The improvement in these measures suggests that aerobic adaptations accompanied the 10-wk training program, including an improved subject heart rate response to the API test protocol, indicative of stroke volume and blood volume adaptations to aerobic exercise training (4). At baseline, all aerobic fitness measures were moderately and inversely correlated with CRP concentration ($r > -0.24$); however, despite correlations between baseline CRP concentration and aerobic fitness measures, post-training aerobic fitness improvements were not correlated to reductions in CRP concentration ($r > -0.04$). Similar to the present study, two other investigations also reported moderate inverse correlations between CRP and aerobic fitness at baseline (20,25). Additionally, these

investigations also demonstrated no association between improvement in aerobic fitness measures and reduction in CRP concentration (20,25).

Paragraph Number 23

Regarding body composition, all pre-training adipose tissue measures were moderately correlated to CRP concentration ($r > 0.31$), which is in support of findings from previous investigations (20,25). Post-training, the aerobic group demonstrated a reduction in measures of adiposity to a larger extent than the resistance training group. Further, the aerobic group also demonstrated significant improvements in all but one of the measured anthropometric variables, with the decreases in body mass, BMI, and IA-FM all significantly larger than the resistance group. Moreover, of the post-training body composition measures, only body mass correlated to the reduction in CRP concentration, which was likely due to the comparatively larger increase in body mass exhibited by the resistance group; while concomitantly reporting the most notable CRP reduction. Moreover, reduction in CRP concentration was not correlated with improvement in TB-LM measures. Together, the post-training IA-FM, TB-FM, and TB-LM DEXA results from the present 10-wk study reinforce a lack of association between reduction in CRP and alteration of body composition. Regarding resistance exercise training, these results suggest that attenuation of low-grade systemic inflammation need not necessarily occur in the presence of clinically meaningful alterations of body composition.

Paragraph Number 24

In elucidating the mechanisms potentially responsible for the attenuation of CRP, a study of the effects of blood mononuclear cell and associated cytokine activity reported a 35% decrease in CRP concentration following six moths of aerobic exercise (16). In comparison to a pre-exercise training blood sample, a post-exercise training blood sample demonstrated

suppressive effects over the pro-atherogenic cytokines IL-1α and tumor necrosis factor (TNF)-α, and an augmented effect towards the anti-inflammatory cytokines IL-4, IL-10, and transforming growth factor (TGF)-β (16). In another investigation, 12 weeks of resistance exercise performed 3 times per week, similar to the protocol in the present study, reported a significant reduction in TNF-α messenger RNA activity and TNF-α protein expression (10). Moreover, at study baseline, a strong inverse relationship between muscle protein synthesis rate and muscle TNF-α protein content was also reported (10). Accordingly, in the present study the resistance group experienced a significant increase in TB-LM which is indicative of an enhanced protein synthesis rate due to the resistance exercise stimulus. As such, it may be the suppression of pro-inflammatory responses related to the enhanced protein synthesis rate that results in a more pronounced reduction in CRP concentration (10,16). A limitation of the present study is that TNF-α was not measured, however, while speculative, it is possible that the resistance group may have suppressed TNF-α and other cytokine activity associated with blood mononuclear cells as has been previously reported following exercise (10,16). Hence, future exercise studies should further investigate myofibrillar protein signalling pathways which may involve mechanisms that repress pro-inflammatory signalling pathways, and thus the potential for increases in pro-inflammatory markers associated with chronic systemic inflammation.

Paragraph Number 25

In conclusion, 10-wk of resistance or aerobic exercise training in sedentary disease-free subjects did not affect elevated baseline IL-6 concentration; however, resistance training attenuated elevated baseline CRP concentration from 'high-risk' (3.57 mg·L^{-1}) to 'moderate-risk' (2.40 mg·L^{-1}) status, and aerobic exercise training demonstrated a trend for reduction. Additionally, the reduction in CRP concentration in the resistance group presented despite

markedly less reduction in intra-abdominal and total body adipose tissue measures than the aerobic group. The findings of the present study have implications for sedentary populations, and suggest that resistance exercise training may attenuate elevated chronic systemic inflammation prior to clinically meaningful reductions in adipose tissue. It is recommended that future studies should investigate muscle protein synthesis adaptations to resistance exercise training and the effect on pro- and anti-inflammatory cytokines.

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