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Exercise-Induced Weight Loss Is More Effective Than Dieting for Improving Adipokine Profile, Insulin Resistance, and Inflammation in Obese Men

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The adipokines chemerin and adiponectin are reciprocally related in the pathogenesis of insulin resistance and inflammation in obesity. Weight loss increases adiponectin and reduces chemerin, insulin resistance, and inflammation, but the effects of caloric restriction and physical activity are difficult to separate in combined lifestyle modification. We compared effects of diet- or exercise-induced weight loss on chemerin, adiponectin, insulin resistance, and inflammation in obese men. Eighty abdominally obese Asian men (body mass index [BMI] ≥ 30 kg/m^2, waist circumference [WC] ≥ 90 cm, mean age 42.6 years) were randomized to reduce daily intake by ~500 kilocalories (n = 40) or perform moderate-intensity aerobic and resistance exercise (200–300 min/week) (n = 40) to increase energy expenditure by a similar amount for 24 weeks. The diet and exercise groups had similar decreases in energy deficit (–456 ± 338 vs. –455 ± 315 kcal/day), weight (–3.6 ± 3.4 vs. –3.3 ± 4.6 kg), and WC (–3.4 ± 4.4 vs. –3.6 ± 3.2 cm). The exercise group demonstrated greater reductions in fat mass (–3.9 ± 3.5 vs. –2.7 ± 5.3 kg), serum chemerin (–9.7 ± 11.1 vs. –4.3 ± 12.4 ng/ml), the inflammatory marker high-sensitivity C-reactive protein (–2.11 ± 3.13 vs. –1.49 ± 3.08 mg/L), and insulin resistance as measured by homeostatic model assessment (–2.45 ± 1.88 vs. –1.38 ± 3.77). Serum adiponectin increased only in the exercise group. Exercise-induced fat mass loss was more effective than dieting for improving adipokine profile, insulin resistance, and systemic inflammation in obese men, underscoring metabolic benefits of increased physical activity.

Keywords: metabolism, nutrition, exercise

Obesity, particularly abdominal obesity that is associated with pathological accumulation of visceral fat, results in aberrant production of adipokines associated with insulin resistance and chronic inflammation that underlie obesity-related comorbidities (Klimcakova et al., 2010). Chemerin, a protein produced in adipose tissues, is found in higher concentrations in obese individuals (Rourke et al., 2013) and increases insulin resistance by inhibiting insulin-mediated glucose uptake in skeletal muscle and impairing insulin receptor signaling at the levels of insulin receptor substrate 1, Akt and glycogen synthase kinase 3 phosphorylation (Sell et al., 2009). Chemerin also promotes inflammation through binding to chemokine-like receptor 1 (CMKLR1, ChemR23) and chemoattraction of macrophages (Lehrke et al., 2009). Adiponectin, an adipocyte-derived protein with anti-inflammatory and insulin-sensitizing effects, is decreased in obesity (Klimcakova et al., 2010). Overweight and obese adults with high chemerin and low adiponectin levels have a sixfold higher risk of metabolic syndrome compared with those with low chemerin and high adiponectin (Chu et al., 2012), suggesting that reciprocal alterations in the proportions of these adipokines contribute to the derangements seen in obesity. Chemerin and adiponectin are promising novel early biomarkers of adipose tissue dysfunction and adverse metabolic outcomes.

Bariatric surgery (Chakaroun et al., 2012; Sell et al., 2010), caloric restriction (Blüher et al., 2012), and combined diet and exercise (Kim et al., 2014; Lee et al., 2013) reduced adiposity and circulating chemerin, as did exercise alone (Chakaroun et al., 2012; Saremi et al., 2010; Stefanov et al., 2014; Venojärvi et al., 2013). However, none of the exercise-only interventions induced significant weight loss nor directly compared effects with isocaloric dietary restriction, so the effects of exercise-induced weight and fat mass loss in obese individuals remain to be clarified. Adiponectin concentration increases in association with improved insulin

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sensitivity after weight loss (Madsen et al., 2008) and exercise-induced reduction in body fat (Malin et al., 2014). However, few randomized trials of weight loss that included aerobic exercise have controlled for caloric restriction, and they are inconclusive regarding the effects of chronic exercise on adiponectin (Ryan et al., 2003; Simpson & Singh, 2008; Auerbach et al., 2013).

The relative contributions of caloric restriction and increased physical activity to weight-loss-induced changes in chemerin and adiponectin production remain unknown. It is difficult to compare results between diet and exercise because of the heterogeneity of weight-loss interventions, the difficulty of separating effects of caloric restriction from physical activity in combined lifestyle interventions, and the paucity of exercise studies utilizing comparable energy deficit to diet interventions. A meta-analysis of weight-loss trials (Franz et al., 2007) included six exercise studies and 51 diet trials, and a recent review found only seven studies between 1990–2013 that compared diet- and exercise-induced weight loss (Washburn et al., 2014). Moreover, adipokine levels were not evaluated in these studies. We therefore aimed to compare the effects of weight and fat mass losses induced by regular moderate-intensity exercise with an equivalent energy deficit from dieting, and we hypothesized that exercise would reduce chemerin and increase adiponectin by a larger degree, with greater improvements in body composition, insulin resistance, and inflammation.

Participants and Methods

Eighty abdominally obese Asian (body mass index [BMI] ≥ 30 kg/m^2, waist circumference [WC] ≥ 90 cm as defined by the World Health Organization [WHO] recommendations for Asian men; WHO Expert Consultation, 2004), previously sedentary (exercise < 30 min/day), community-dwelling men between 30 and 65 years of age were recruited by advertisements to participate in a 6-month weight-loss study and were randomized to either dietary modification or exercise training in Singapore between December 2010 and March 2013. Participants with vascular disease, inability to perform regular moderate-intensity aerobic exercise, or recreational drug and alcohol abuse were excluded. Eleven participants had hypertension which was well-controlled with calcium channel blockers and/or beta blockers, and 10 participants were on statins. The proportion of subjects with hypertension and/or dyslipidemia was similar in both groups (~25%). There were no changes in medications. The study was approved by a formally constituted ethics review board. Informed consent was obtained in writing. Sample size was calculated at 36 to detect 5% of weight loss from baseline (mean = 95 kg, *SD* = 7.5 kg) in the same population of Asian men as in a previous study of lifestyle modification (Khoo et al., 2013), with 80% power at 5% significance, but 40 participants were recruited in each group to account for drop-outs. Participants were randomized by a dietitian who was not part of the study, using sealed envelopes.

Diet Modification

Men in the diet group were provided with written plans designed to reduce daily energy intake by 500 kcal/day, with 50–55% of total calorie intake as carbohydrate, 20% protein, and 25–30% fat. Daily energy requirement was estimated using basal metabolic rate (BMR; calculated with the Mifflin–St. Jeor equation [Mifflin et al., 1990]) multiplied by activity factor. Participants were instructed to consume ~1.5 L of fluids daily. Dietitians demonstrated how to fill in the diaries using standardized food models and examples of household measures and serving size, and they reviewed food diaries at 4-week intervals.

Exercise Training

Men in the exercise group were prescribed a moderate-intensity (60–80% of predicted maximum heart rate) aerobic exercise program (e.g., stationary cycling, treadmill, elliptical cross-training), starting at 90 min/week in three divided sessions. Participants were helped to measure and maintain appropriate heart rates using a monitor that was worn or attached to gym equipment (HR-100CN, Omron, Kyoto, Japan). Exercise was gradually increased in duration (by 10–15 min/session/week) and frequency (starting at two sessions and increasing by one per week) until the target exercise volume of 200–300 min/week (five to seven sessions of 45–60 min including resistance training, ~1,400–2,100 MET-min as recommended by the American College of Sports Medicine for weight loss [Donnelly et al., 2009]) was achieved at 4 weeks to target 3,500 kcal/week. Participants exercised in the research center gym under supervision at 2-week intervals in the first 4 weeks and then 4- to 6-week intervals, with the rest of the exercise (similar in intensity and type to the gym sessions) performed outside the research center.

Energy Intake and Expenditure Analysis

Nutrient intakes at baseline and the end of the study were calculated using the Dietplan6 Software (Forestfield Software Ltd., Horsham, West Sussex, UK) from 3-day (2 weekdays and 1 weekend) consecutive food diaries at baseline and 24 weeks. Total energy expenditures (TEE) on the same days were calculated as the sum of the daily activity thermogenesis (DAT), where DAT = the sum of (energy equivalent of each of the activities recorded in the participant's diary × time spent in each activity), and averaged for a mean daily TEE. Energy equivalents were derived from tables of values of approximate caloric expenditure for various activities (Ainsworth et al., 2011). The net energy balance was the difference between caloric intake and TEE.

Outcome Measures

Weight and WC (mean of three measurements midway between the lower costal border and the top of the iliac crest) were measured by the same investigator for each participant, who was blinded to group assignment. Fat

mass, fat-free mass, and body fat percentage were measured by bioimpedance electrical analysis using a body composition analyzer (BC-118E, Tanita, Tokyo, Japan). Maximal oxygen uptake ($\dot{V}O_{2max}$) tests were conducted using a graded direct cycling ergometer (Aerobike 75XL-II, Combi Wellness Co. Ltd., Tokyo, Japan) under the supervision of a physical trainer with an initial workload of 100 W starting after 5 min of warm-up, increasing at 20 W/min on a continuous ramped protocol. Participants cycled between 70 and 120 revolutions per minute (rpm) with termination when they were unable to maintain a cadence of 20 rpm below the preferred cycling rate with a plateau in the VO_2 for 15 s, and with maximal heart rate and respiratory exchange ratio > 1.15. $\dot{V}O_{2max}$ (L/min) was determined as the highest recorded 15 s-averaged $\dot{V}O_{2max}$ as measured with indirect calorimetry.

Venous blood was collected at 8 a.m. after overnight fast of at least 10 hr and stored at –70 °C for subsequent assays. All participants had been instructed not to exercise or excessively restrict caloric intake for 3 days before the blood tests were taken, so as to minimize the potential effects of exercise and diet on insulin, glucose, and adipokines, as the effects of a 50-min bout of exercise at 75% VO_{2max} in reducing fasting insulin and glucose levels were observed to disappear 72 hr after exercise (Boulé et al., 2005) while fasting for 72 hr has been shown to reduce chemerin and leptin (Chamberland et al., 2013). The UniCel DxC 800 analyzer (Beckman Coulter, Brea, CA) was used to measure serum glucose (lower limit of detection LLD 0.3 mmol/L, intra-assay and interassay coefficients of variation [CVs] 2.0% and 3.0%) and high-sensitivity C-reactive protein (CRP) (CV_{intra} 2.1%, CV_{inter} 3.4%). Serum insulin was measured using sandwich electrochemiluminescence immunoassay (Cobas e601, Roche Diagnostics, Indianapolis, IN, CV_{intra} 4.0%, CV_{inter} 6.0%). Insulin resistance was calculated using homeostasis model assessment (HOMA-IR) = glucose in mmol/L × insulin in μmol/L/22.5. Serum leptin (CV_{intra} 5.9%, CV_{inter} 8.7%; DRG Instruments GmBH, Marburg, Germany), adiponectin ($CV_{intra} \leq 10\%$, $CV_{inter} \leq 12\%$ %; DRG Instruments GmBH, Marburg, Germany) and chemerin (CV_{intra} 4.3%, CV_{inter} 7.6%; Kamiya Biomedical, Seattle, WA) concentrations were measured by enzyme-linked immuno-sorbant assay.

Statistical Analysis

Statistical analysis was performed using SPSS v.16.0 (Chicago, IL). Differences in baseline measurements and changes between the groups were evaluated with maximum likelihood repeated measures mixed models analysis of variance in an intention-to-treat analysis. The relationships between changes in outcomes after 24 weeks were determined using Pearson's correlations. A p value < .05 was considered significant.

Results

Baseline characteristics were similar between the diet and exercise groups (Table 1). Three participants in the diet group and 2 in the exercise group dropped out at 4–8 weeks, citing difficulties in complying with the diet or exercise regimen due to personal and/or occupational reasons. Their mean age and BMI were similar to the study completers. No adverse events or injuries were observed.

Energy Deficit and Anthropometry

At 24 weeks, there was similar negative daily energy balance of ~450 kcal in both diet and exercise groups (Table 1). Although the diet group lost significantly (p < .01) more weight in the first 8 weeks (–5.1 ± 2.4 kg) compared with the exercise group (–1.1 ± 2.0 kg), they subsequently regained weight before stabilizing (Figure 1). In contrast, weight steadily decreased in the exercise group after 4 weeks. Weight did not change significantly in the last 4 weeks (0.1 ± 0.7 kg in the diet group and 0.3 ± 1.0 kg in the exercise group), such that at 24 weeks both groups had lost ~4% from baseline weight and WC (Table 2). Total body fat mass and percentage of fat decreased to a greater extent in the exercise group (Table 2).

Insulin Resistance, Inflammation, and Adipokines

Serum glucose and leptin decreased comparably in both groups (Table 2). In the exercise group, insulin, HOMA-IR, CRP, and chemerin (Figure 2) decreased significantly more than in the diet group. At baseline, chemerin concentration was significantly associated with fat mass (r = .32, p = .01), CRP (r = .33, p < .01), and HOMA-IR (r = .22, p = .04). The decrease in chemerin was significantly associated with reductions in fat mass, HOMA-IR, and CRP (Table 3). The reductions in chemerin and HOMA-IR remained significantly associated with each other (r = .25, p = .04) in a multivariate analysis with baseline chemerin and HOMA-IR, and changes in weight and fat mass as the covariates.

Baseline adiponectin concentration was inversely associated with HOMA-IR (r = –.26, p = .02) while increase in adiponectin, which only occurred in the exercise group (Figure 3), was associated with reduction in fat mass (r = –.21, p = .04) but not in weight, WC, or chemerin. Baseline leptin concentration was significantly (p < .01) associated with WC (r = .44) and fat mass (r = .48). The decrease in leptin was significantly associated with reduction in fat mass (Table 3), but not with changes in HOMA-IR, CRP, chemerin, or adiponectin.

Discussion

We found that compared with calorie restriction, increased exercise was associated with greater reductions in serum chemerin, fat mass, insulin resistance and CRP, and with increased serum adiponectin, despite similar weight loss. Our findings concur with previous studies wherein hypocaloric diets (Blüher et al., 2012; Chakaroun et al., 2012), combined diet and exercise (Kim et al., 2014; Lee et al., 2013), and exercise alone (Chakaroun et al., 2012; Saremi et al., 2010; Stefanov et al., 2014;

Table 1 Baseline Intake, Energy Expenditure, Anthropometry, Physical Capacity, Glucose, Insulin, CRP, and Adipokines in Obese Men

Baseline Parameters	Diet Group (*n* = 40)	Exercise Group (*n* = 40)	*p*
Age (years)	41.8 ± 7.2	43.3 ± 9.0	.41
Intake (kcal/day)	2,167 ± 371	2,442 ± 293	.08
TEE (kcal/day)	2,632 ± 185	2,540 ± 241	.74
NetE (kcal/day)	–465 ± 349	–398 ± 336	.20
VO2max (L/min)	2.85 ± 0.34	2.88 ± 0.38	.89
BMI (kg/m2)	32.1 ± 3.0	32.1 ± 2.6	.49
Weight (kg)	95.7 ± 9.4	96.2 ± 10.9	.84
WC (cm)	106.1 ± 7.2	106.0 ± 8.5	.87
FFM (kg)	61.7 ± 6.7	63.3 ± 5.5	.53
FM (kg)	33.2 ± 5.6	32.1 ± 7.6	.74
% body fat	35.3 ± 4.7	34.7 ± 5.5	.35
Glucose (mmol/L)	6.19 ± 0.90	6.48 ± 0.98	.12
Insulin (μU/ml)	22.75 ± 13.26	20.19 ± 8.30	.44
HOMA-IR	6.62 ± 4.83	5.62 ± 2.51	.49
CRP (mg/L)	4.49 ± 4.78	3.94 ± 3.56	.51
Leptin (nmol/L)	15.89 ± 9.80	16.02 ± 14.75	.97
Adiponectin (μg/ml)	5.42 ± 0.63	5.22 ± 0.61	.09
Chemerin (ng/ml)	121.4 ± 12.6	122.2 ± 9.4	.78

Note. All values are given as mean ± *SD*. CRP = serum high-sensitivity C-reactive protein; TEE = total energy expenditure; NetE = energy balance = TEE minus intake; VO_{2max} = maximal oxygen uptake; BMI = body mass index; WC = waist circumference; FFM = total fat-free mass; FM = total fat mass; HOMA-IR = homeostasis model assessment of insulin resistance. Intake, TEE, and NetE values are averages of daily caloric intake, total energy expenditure, and net energy deficit, derived from 3-day food and physical activity diaries kept by all participants.

Table 2 Intake, Energy Expenditure, Anthropometry, Physical Capacity, Glucose, Insulin, CRP, and Adipokines in Obese Men After 24 Weeks of Diet or Exercise

Changes in Parameters	Diet Group (*n* = 40)	Exercise Group (*n* = 40)	*p*
Intake (kcal/day)	–423 ± 392*	9 ± 319	< .01
TEE (kcal/day)	33 ± 209	464 ± 221*	< .01
NetE (kcal/day)	–456 ± 338*	–455 ± 315*	.80
VO_{2max} (L/min)	0.07 ± 0.06	0.45 ± 0.06*	< .01
BMI (kg/m^2)	–1.2 ± 1.9*	–1.3 ± 1.2*	.86
Weight (kg)	–3.3 ± 4.6*	–3.6 ± 3.4*	.83
WC (cm)	–3.4 ± 4.4*	–3.6 ± 3.2*	.81
FFM (kg)	–0.7 ± 3.2	0.4 ± 2.8*	.04
FM (kg)	–2.7 ± 5.3*	–3.9 ± 3.6*	.02
% body fat	–2.1 ± 4.4*	–3.7 ± 3.4*	.04
Glucose (mmol/L)	–0.25 ± 0.59*	–0.29 ± 0.75*	.26
Insulin (μU/ml)	–3.56 ± 10.92*	–6.91 ± 5.12*	.02
HOMA-IR	–1.38 ± 3.77*	–2.45 ± 1.88*	.03
CRP (mg/L)	–1.49 ± 3.08*	–2.11 ± 3.13*	.03
Leptin (nmol/L)	–4.92 ± 5.73*	–4.36 ± 7.38*	.71
Adiponectin (μg/ml)	–0.10 ± 0.45	0.41 ± 0.48*	.01
Chemerin (ng/ml)	–4.3 ± 12.4*	–9.7 ± 11.1*	.04

Note. The values are given as mean ± *SD* An asterisk indicates a significant difference from baseline. The level of significance is set at $p < .05$. CRP = serum high-sensitivity C-reactive protein; TEE = total energy expenditure; NetE = energy balance = TEE minus intake; VO_{2max} = maximal oxygen uptake; BMI = body mass index; WC = waist circumference; FFM = total fat-free mass; FM = total fat mass; HOMA-IR = homeostasis model assessment of insulin resistance. Intake, TEE, and NetE values are averages of daily caloric intake, total energy expenditure, and net energy deficit, derived from 3-day food and physical activity diaries kept by all participants.

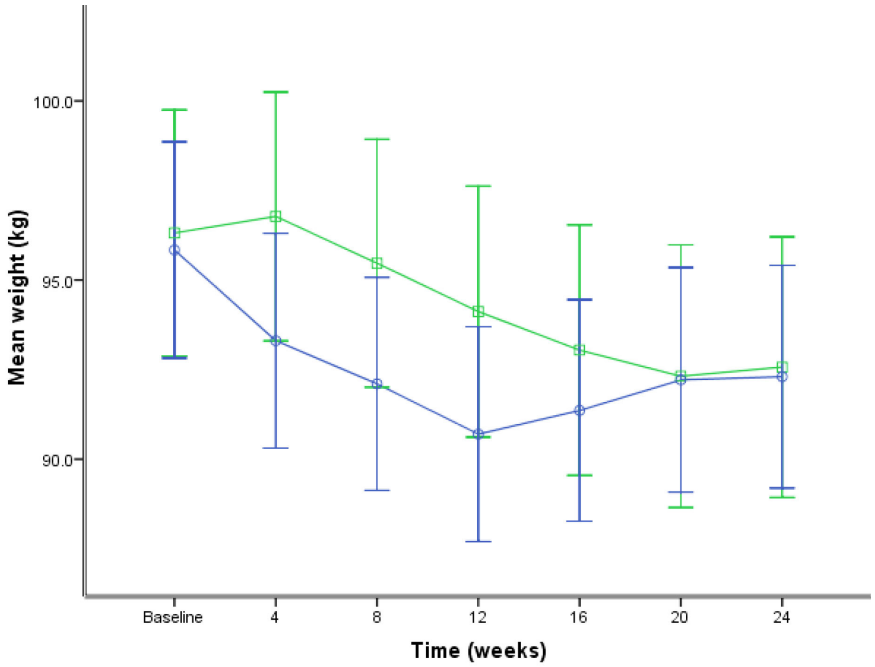

Figure 1 — Changes in weight over 24 weeks of dieting (circles) or exercise (squares) in obese men.

Table 3 Significant Correlations (Given as *r* Values) Between Changes (Δ) in Body Fat Mass, Insulin Resistance (HOMA-IR), Serum CRP, Leptin, and Chemerin Levels, After 24 Weeks of Lifestyle Modification

Variable	ΔFM	ΔHOMA-IR	ΔCRP	ΔLeptin	ΔChemerin
ΔFM	—	.35*	.15	.48**	.34*
ΔHOMA-IR	.35*	—	.16	.22	.32*
ΔCRP	.15	.16	—	.13	.33*
ΔLeptin	.48**	.22	.13	—	.20
ΔChemerin	.34*	.32*	.33*	.20	—

Note. CRP = high-sensitivity C-reactive protein; FM = total body fat mass; HOMA-IR = homeostasis model assessment of insulin resistance.
*$p < .05$. **$p < .01$.

Venojärvi et al., 2013) decreased chemerin. However, none of these studies directly compared isocaloric diet and exercise interventions or found greater improvement in adipokine profile and metabolic outcomes with the same degree of exercise-induced weight and fat mass loss. Our study therefore provides evidence for the greater benefits of exercise compared with diet-induced fat mass loss on adipokines such as chemerin and adiponectin that are increasingly recognized as novel biomarkers for metabolic outcomes.

Exercise was associated with improvement in body composition independent of weight loss (Chakaroun et al., 2012; Oh et al., 2013), so the greater reduction in fat mass is likely to contribute to the larger improvements in adipokine profile and insulin resistance in the exercise group. The associations between postintervention

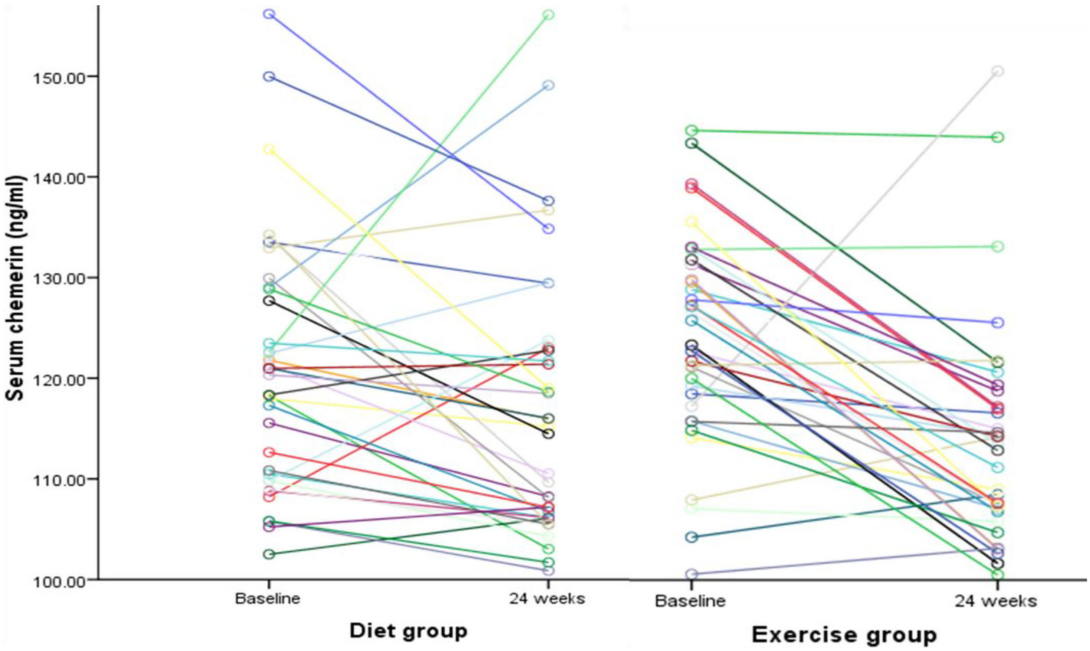

Figure 2 — Changes in serum chemerin after 24 weeks of diet- or exercise-induced weight loss in obese men.

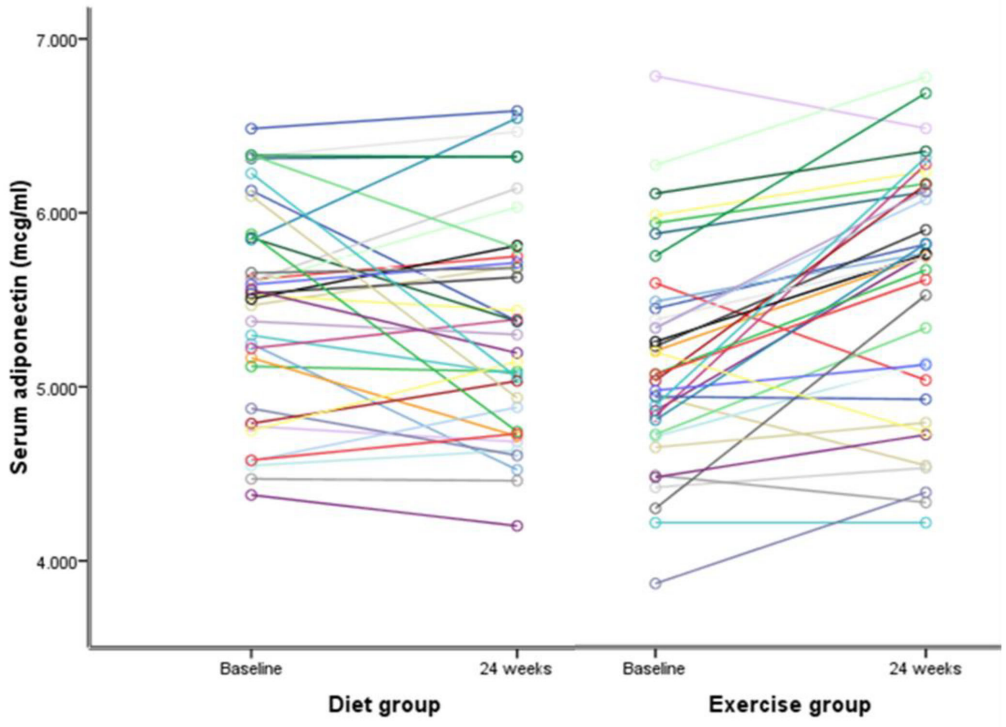

Figure 3 — Changes in serum adiponectin after 24 weeks of diet- or exercise-induced weight loss in obese men.

reductions in chemerin and fat mass are consistent with previous combined weight loss interventions (Blüher et al., 2012; Kim et al., 2014; Lee et al., 2013), underscoring the links between adiposity and chemerin production. Chemerin messenger RNA (mRNA) expression increases with adipocyte size (Sell et al., 2010) and is lower in lean compared with obese and diabetic individuals (Chakaroun et al., 2012) while changes in production of other adipokines, particularly adiponectin, may also influence chemerin production (Suzuki et al., 2012). We found that baseline chemerin concentration and insulin resistance (HOMA-IR), and reductions in both after fat mass loss, were also significantly correlated, as in previous lifestyle intervention studies (Kim et al., 2014; Lee et al., 2013). In particular, the reduction of ~8% in serum chemerin in our exercise group was comparable to the 7–10% reduction in chemerin that was significantly associated with improvement in insulin sensitivity after 12 weeks of moderate-intensity exercise in the study of Chakaroun et al. Direct links between insulin and chemerin production were demonstrated in human adipose cells where insulin infusion stimulated chemerin synthesis (Tan et al., 2009) and in human skeletal muscle cells where administration of chemerin increased insulin resistance (Bauer et al., 2012) and impaired insulin receptor signaling and glycogen synthase kinase 3 phosphorylation (Sell et al., 2009). In our study, improvement in insulin sensitivity, in addition to being associated with reduction in adiposity, may thus also be directly mediated by chemerin reduction as shown by association of reductions in chemerin and HOMA-IR after correction for fat mass loss.

In contrast to studies that found that at least 10% weight loss is required to reduce inflammatory markers (Christiansen et al., 2010; Forsythe et al., 2008), we found that CRP was significantly decreased with modest (<5%) reduction in weight and adiposity. Associations between baseline chemerin and CRP concentrations, and reductions after fat mass loss, are likely related to the link between chemerin and increased adipose tissue macrophage infiltration (Hart & Greaves, 2010) and expression of CRP, interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) (Lehrke et al., 2009). Chemerin mRNA expression increases with the number of macrophages in adipose tissue (Sell et al., 2010), and proinflammatory cytokines up-regulate chemerin in adipocytes (Parlee et al., 2010), while stimulation of macrophages by chemerin increases proinflammatory cytokines (Mariani & Roncucci, 2015) and vice-versa (Kralisch et al., 2009). Greater reduction in CRP with exercise is consistent with the observation that regular exercise reduces systemic inflammation, as demonstrated by the inverse relationship between serum CRP and physical activity in population studies (Kasapis & Thompson, 2005) and reduction in CRP, IL-6, and TNF-α in obese individuals after 3 months to 3 years of exercise programs (Huang et al., 2013). Changes in adiponectin and chemerin, which were not measured in these studies, may mediate these metabolic benefits.

Adiponectin increased significantly with exercise but not caloric restriction, an additional metabolic advantage of physical activity, and occurred with modest (~4%) weight loss, in contrast with studies that found that adiponectin increased with weight loss exceeding 5–10% (Christiansen et al., 2010; Madsen et al., 2008) but not with smaller reductions (Auerbach et al., 2013; Kim et al., 2014; Ryan et al., 2003; Simpson & Singh, 2008). The ~8% increase in adiponectin level in our exercise group was similar to the 11% rise in adiponectin that was associated with significant improvement in systemic inflammation in obese adults who lost at least 10% of baseline weight through dieting (Madsen et al., 2008). Similarly, 12 weeks of exercise (~270 min/week) increased adiponectin by more than 15% without significant caloric restriction in participants with fatty liver disease (Oh et al., 2013) and changed high-molecular weight adiponectin by ~10% in obese older adults in association with reduction in systemic inflammation, hepatic insulin resistance, and serum fetuin-A and leptin (Malin et al., 2014). However, adiponectin did not change with a similar duration of combined lifestyle modification (Kim et al., 2014; Lee et al., 2013). The reduction of leptin in association with decrease in fat mass concurs with previous observations (Blüher et al., 2012; Kim et al., 2014; Klimcakova et al., 2010; Lee et al., 2013).

Our diet group lost more weight in the first 2 months but regained weight before stabilizing at a lower level than baseline while weight decreased steadily in the exercise group after the first month. Lower-than-expected weight loss may have been due to unsupervised exercise and underestimation of intake. Weight regain may have been due to suboptimal diet compliance from neurohormonal changes with caloric restriction, decreased muscle mass, and adaptive thermogenesis leading to greater-than-expected reductions in BMR and nonexercise energy expenditure (Müller & Bosy-Westphal, 2013). In contrast, regular exercise has been shown to attenuate the biological drive to regain weight in animal models through decreased appetite and increased fat and glucose oxidation (MacLean et al., 2009) and may improve the coupling between energy intake and expenditure (Müller & Bosy-Westphal, 2013) that maintains energy balance after caloric restriction.

Our study was limited by the lack of a control group that exercised without fat mass loss (though our aim was to compare the effects of diet with exercise prescribed to induce weight loss), relatively short follow-up, and the small number of participants. Dual-energy X-ray absorptiometry or computed tomography would be more sensitive for body composition measurement. Activity diaries show low correlation with doubly-labeled water (DLW) techniques, which are the gold standard for measurement of energy expenditure (Strath et al., 2013), though DLW measurements are time-consuming and costly and may, like diaries, be affected by changes when under observation (Strath et al., 2013). Total adiponectin was measured, rather than proportions of high- (associated with insulin sensitivity) and low-molecular weight forms that may respond differently to dieting and exercise (Auerbach et al., 2013; Malin et al., 2014). Measurement of active (proinflammatory) and inactive (anti-inflammatory)

chemerin bioforms could further our understanding of differential effects of diet and exercise on chemerin for reducing inflammation (Mariani & Roncucci, 2015). Blood sampling at more frequent points would allow evaluation of effects of weight variations.

In conclusion, exercise prescribed to induce weight loss in obese Asian men was associated with greater reductions in fat mass, serum chemerin, resistance, and inflammation and increase in adiponectin, compared with a similar degree of energy restriction from dieting. Improved adipokine profile in the exercise group was possibly due to increased activity per se and/or greater reduction in adiposity. Our findings underscore the metabolic benefits of regular exercise in obese individuals.

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Author contributions: JK, RC, and RT designed the study. JK, SD, DC, and SY collected data. JK performed statistical analysis. JK, SD, RC, and RT interpreted the data and prepared the manuscript. All authors reviewed the paper.

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