Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults

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ABSTRACT

Background: The ability of modified alternate-day fasting (ADF; ie, consuming 25% of energy needs on the fast day and ad libitum food intake on the following day) to facilitate weight loss and lower vascular disease risk in obese individuals remains unknown.

Objective: This study examined the effects of ADF that is administered under controlled conditions compared with self-implemented conditions on body weight and coronary artery disease (CAD) risk indicators in obese adults.

Design: Sixteen obese subjects (12 women, 4 men) completed a 10-wk trial, which consisted of 3 phases: 1) a 2-wk control phase, 2) a 4-wk weight loss/ADF controlled food intake phase, and 3) a 4-wk weight loss/ADF self-selected food intake phase.

Results: Dietary adherence remained high throughout the controlled food intake phase (days adherent: 86%) and the self-selected food intake phase (days adherent: 89%). The rate of weight loss remained constant during controlled food intake (0.67 ± 0.1 kg/wk) and self-selected food intake phases (0.68 ± 0.1 kg/wk). Body weight decreased (P < 0.001) by 5.6 ± 1.0 kg (5.8 ± 1.1%) after 8 wk of diet. Percentage body fat decreased (P < 0.01) from 45 ± 2% to 42 ± 2%. Total cholesterol, LDL cholesterol, and triacylglycerol concentrations decreased (P < 0.01) by 21 ± 4%, 25 ± 10%, and 32 ± 6%, respectively, after 8 wk of ADF, whereas HDL cholesterol remained unchanged. Systolic blood pressure decreased (P < 0.05) from 124 ± 5 to 116 ± 3 mm Hg.

Conclusion: These findings suggest that ADF is a viable diet option to help obese individuals lose weight and decrease CAD risk. This trial was registered at clinicaltrials.gov as UIC-004-2009. Am J Clin Nutr 2009;90:1138–43.

INTRODUCTION

Obese individuals are at greater risk of developing coronary artery disease (CAD) (1). A decrease in energy intake by means of dietary restriction has been shown to lower the risk of CAD in obese populations (2). The most common form of dietary restriction implemented is daily calorie restriction (CR), which requires individuals to decrease their energy intake by 15–40% of baseline needs each day (3). Another form of dietary restriction used, although far less commonly, is alternate-day fasting (ADF) (4). ADF regimens were created to increase adherence to dietary restriction protocols because these regimens only require energy restriction every other day rather than every day, as with CR. ADF regimens consist of a “feed day” (ad libitum food intake for 24 h) alternated with a “fast day” (complete fast for 24 h). Modified ADF regimens that allow for the consumption of 20–25% of energy needs on the fast day have also been implemented.

To date, 3 ADF studies in humans have been performed (5–7). Results from the 2 trials performed in normal-weight men and women indicate that 2–3 wk of ADF (complete fast on the fast day) significantly lowered body weight by 2.5% from baseline (5, 6). Decreases in triacylglycerol concentrations and increases in HDL-cholesterol concentrations were also observed (5, 6). Findings from the third trial conducted in overweight adults showed that 8 wk of modified ADF (20% restriction on the fast day) significantly lowered body weight by ≈8% from baseline (7). This trial also showed LDL-cholesterol and triacylglycerol reductions of 10% and 40%, respectively, when posttreatment values were compared with baseline (7). Whether or not these weight loss and cardioprotective effects can be reproduced in obese individuals by using ADF remains unknown.

Nutrition intervention studies often provide participants with food to ensure that the trial is carefully controlled for energy intake and macronutrient distribution (8). At the conclusion of the study, when food is no longer provided, the individual generally returns to their baseline food intake/meal pattern. In some trials, dietary counseling is provided to the participant at the end of the study to aid the subject in maintaining his or her newly acquired healthy eating regimen (9). The ability of an obese individual to maintain an ADF regimen by providing the subject with dietary counseling, after a period of controlled food intake, is of great interest but has yet to be tested.

Accordingly, this study examined the ability of ADF to facilitate weight loss and beneficially modulate key indicators of CAD risk in obese men and women. Additionally, this study compared the degree of weight loss that could be achieved by ADF during a period of controlled food intake compared with a period of self-selected food intake combined with dietary counseling.

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SUBJECTS AND METHODS

Subjects

Subjects were recruited from the greater Chicago area by means of advertisements placed in community centers and libraries. A total of 52 individuals expressed interest in the study, but only 20 were deemed eligible to participate after the pre- 
liminary questionnaire and body mass index (BMI; in kg/m²) 
assessment (Figure 1). Key inclusion criteria were as follows: age 35–65 y, BMI between 30 and 39.9, weight stable for 3 mo before the beginning of the study (ie, <5 kg weight loss or weight gain), nondiabetic, no history of cardiovascular disease, lightly active [ie, <3 h/wk of light-intensity exercise at 2.5–4.0 metabolic equivalent tasks for 3 mo before the study (10)], nonsmoker, and not taking weight loss or lipid- or glucose-
lowering medications. Perimenopausal women were excluded from the study, and postmenopausal women (absence of menses for >2 y) were required to maintain their current hormone replacement therapy regimen for the duration of the study. The experimental protocol was approved by the Office for the Protection of Research Subjects at the University of Illinois, Chicago, and all volunteers gave their written informed consent to participate in the trial.

Study design

A 10-wk trial, which consisted of 3 consecutive intervention phases, was implemented to test the study objectives. The 3 consecutive phases were as follows: 1) 2-wk preloss control phase, 2) 4-wk weight loss/ADF controlled food intake phase, and 3) 4-wk weight loss/ADF self-selected food intake phase.

Phase 1: preloss control protocol

During the first phase, subjects were required to keep their body weight stable by maintaining their usual eating and exercise habits. As such, each subject served as his or her own control.

Phase 2: weight loss/ADF controlled food intake protocol

The second phase consisted of a 4-wk controlled food intake ADF period. The baseline energy requirement for each subject was determined by the Mifflin equation (11). All subjects consumed 25% of their baseline energy needs on the “fast” day (24 h) and then consumed food ad libitum on each alternate “feed” day (24 h). During this controlled food intake phase, subjects were provided with a calorie-restricted meal on each fast day, and consumed food ad libitum at home on the alternate day. All meals were prepared in the metabolic kitchen of the Human Nutrition Research Center at the University of Illinois, Chicago, and were provided as a 3-d rotating menu. The nutrient composition of the provided fast day meal is shown in Table 1. On the ad libitum food intake day, subjects were instructed to limit fat intake to <30% of energy needs by choosing low-fat meat and dairy options. The feed/fast days began at midnight each day, and all fast day meals were consumed between 1200 and 1400 to ensure that each subject was undergoing the same duration of fasting. On each fast day, the subjects were allowed to consume energy-
free beverages, tea, coffee, and sugar-free gum and were encouraged to drink plenty of water.

Phase 3: weight loss/ADF self-selected food intake protocol

The third phase consisted of a 4-wk ADF self-selected food intake period in conjunction with weekly dietary counseling. During this phase, subjects still consumed 25% of their baseline energy needs on the fast day and consumed food ad libitum on the feed day. However, during this period, no food was provided to the subjects. Instead, subjects met with a registered dietitian at the beginning of each week to learn how to maintain the ADF regimen on their own at home. During each counseling session, the diettitian worked with the subject to develop individualized fast day meal plans. These plans included menus, portion sizes, and food lists that were consistent with their food preferences and prescribed calorie levels for the fast day. During these sessions, subjects were also instructed how to make healthy food choices on the ad libitum food intake days by choosing low-fat meat and

![Figure 1. Study flowchart. ADF, alternate-day fasting.](https://academic.oup.com/ajcn/article-abstract/90/5/1138/4598070/52 Subjects were screened)
dairy options. Subjects were asked to consume fast day meals between 1200 and 1400.

**Blood collection protocol**

Twelve-hour fasting blood samples were collected between 0700 and 0900 at baseline (day 1), at the end of phase 1 (day 14), at the end of phase 2 (day 41: feed day; day 42: fast day), and at the end of phase 3 (day 69: feed day; day 70: fast day). The subjects were instructed to avoid exercise, alcohol, and coffee for 24 h before each visit. Blood was centrifuged for 15 min at 520 × g at 4°C to separate plasma from red blood cells and was stored at –80°C until analyzed.

**Analyses**

*Adherence to ADF diets*

During phase 2 (controlled food intake phase), subjects were instructed to eat only the fast day food provided and to report any extra food item consumed by using an “extra food log.” During phase 3, subjects were provided with individualized meal plans that were consistent with their food preferences and prescribed calorie levels for the fast day. Subject was asked to report any extra food item consumed on the fast day that did not comply with their prescribed plan by using the extra food log. The log was collected and reviewed by study personnel each week. If the log indicated that the subject ate an extra food item on a fast day, that day was labeled as “not adherent.” If the log revealed that the subject did not eat any extra food item, that day was labeled as “adherent.” Adherence data were assessed each week as 1) absolute adherence (number of days adherent with diet) and 2) percentage adherence calculated by applying the following formula:

\[
\%\text{Adherence} = \frac{\text{no. fast days adherent}}{\text{no. fast days in week}} \times 100 \quad (I)
\]

**Weight loss and percentage body fat assessment**

Body weight measurements were taken to the nearest 0.5 kg at the beginning of every week with subjects wearing light clothing and without shoes by using a balance beam scale at the research center (HealthOMeter; Sunbeam Products, Boca Raton, FL). BMI was assessed as kilograms divided by meters squared. Percentage body fat was assessed in triplicate after the weigh-in by using a tetra-polar bioelectrical impedance analyzer (Omron HBF-500; Omron Health Care, Bannockburn, IL) (12). The within-group CV for percentage body fat was 2.7%.

**Plasma lipid profile, blood pressure, and heart rate determination**

Plasma total cholesterol, HDL-cholesterol, and triacylglycerol concentrations were measured in duplicate by using enzymatic kits, standardized reagents, and standards (Biovision Inc, Mountainview, CA) and analyzed by using a microplate reader (iMark Microplate Reader; Bio-Rad Laboratories Inc, Richmond, CA). The concentration of LDL cholesterol was calculated by using the Friedewald, Levy, and Fredrickson equation (13). The within-group CVs for total cholesterol, HDL-cholesterol, and triacylglycerol concentrations were 3.1%, 2.6%, and 2.5%, respectively. Blood pressure and heart rate were measured in triplicate with the subject in a seated position after a 10-min rest.

**Statistics**

Results are presented as means ± SEMs. Tests for normality were included in the model. Sample size was calculated by assuming a 10% change in LDL-cholesterol concentrations, with a power of 80% and an α risk of 5%. One-factor analysis of variance was performed to determine an overall P value for each variable.

Bonferroni correction was used to assess significance. Relations between continuous variables were assessed by using simple regression analyses as appropriate. Data were analyzed by using SPSS software (version 17.0 for Mac OS X; SPSS Inc, Chicago, IL).

**RESULTS**

**Subject dropout and baseline characteristics**

Twenty subjects commenced the study, with 16 completing the entire 10-wk trial. Two subjects dropped out due to time constraints, whereas 2 others dropped out due to inability to comply with the ADF protocol. Baseline characteristics of the subjects who completed the entire 10-wk trial are shown in Table 2.

**Adherence to ADF diets**

During the ADF controlled food intake phase, subjects were adherent with the provided fast day meals (ie, no extra food items consumed) for 3.8 ± 0.1 of 4 d during week 3, 2.6 ± 0.1 of 3 d during week 4, 3.6 ± 0.1 of 4 d during week 5, and 2.1 ± 0.2 of 3 d during week 6. During the ADF self-selected food intake phase, subjects were adherent with prescribed kcal goal for 3.5 ± 0.2 of 4 d during week 7, 2.5 ± 0.2 of 3 d during week 8, 3.8 ± 0.1 of 4 d during week 9, and 2.8 ± 0.1 of 3 d during week 10. When expressed as percentage adherence (Figure 2), there was no drop in adherence over the course of the controlled food intake phase or the self-selected food intake phase. Moreover, no changes in physical activity habits were reported over the course of the trial; thus, changes in body weight and clinical parameters may be attributed primarily to change in diet.

**TABLE 2**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>46.0 ± 2.4†</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>4/12</td>
</tr>
<tr>
<td>Ethnicity (n)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>8</td>
</tr>
<tr>
<td>White</td>
<td>2</td>
</tr>
<tr>
<td>Hispanic</td>
<td>6</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>96.8 ± 5.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168.2 ± 2.3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.8 ± 1.0</td>
</tr>
<tr>
<td>Exercise level (h/wk)²</td>
<td>2.4 ± 0.3</td>
</tr>
</tbody>
</table>

† Mean ± SEM; measured at screening appointment (all such values).

² Defined as number of hours per week of light aerobic exercise at 2.5–4.0 metabolic equivalent tasks. Activity level was self-reported.
weight loss was related to percentage of days adherent to diet per week \( (r = 0.43, P < 0.05) \).

### Changes in plasma lipids by ADF

Mean plasma lipid concentrations over the 10-wk trial are presented in Table 3 (values presented in the text are an average of the food intake and fast days). Total cholesterol concentrations were lowered \( (P < 0.001) \) by 18.0 ± 4.3% after completion of the controlled food intake phase and by 21.2 ± 4.3% after completion of the self-selected food intake phase. Lowered LDL cholesterol \( (P < 0.01) \) was noted after 4 and 8 wk of ADF \( (26.0 \pm 8.2\% \text{ and } 24.8 \pm 9.6\%, \text{respectively}) \). HDL-cholesterol concentrations were not affected by the ADF diet. Circulating triacylglycerol concentrations were lowered \( (P < 0.01) \) by 25.3 ± 7.0% after the controlled food intake phase and further lowered \( (P < 0.01) \) by 32.2 ± 6.4% after the self-selected food intake phase. No differences between food intake and fast day values were observed for any lipid parameter. Decreases in LDL cholesterol were associated with decreased body weight \( (r = 0.48, P < 0.05) \) posttreatment. Decreased triacylglycerol concentrations were related to reductions in body weight \( (r = 0.45, P < 0.05) \) and percentage body fat \( (r = 0.38, P < 0.05) \) at the end of the study.

### Changes in blood pressure and heart rate by ADF

The effects of 8 wk of ADF on blood pressure and heart rate were also assessed. Systolic blood pressure was lowered \( (P < 0.05) \) by 4.4 ± 1.8% after completion of the controlled food intake phase and by 5.1 ± 1.6% after completion of the self-selected food intake phase (Figure 3). No differences between food intake and fast day values were observed for systolic blood pressure. Diastolic blood pressure values at baseline \( (80.3 \pm 7.0 \text{ mm Hg}) \) did not differ from those at week 6 \( (79.2 \pm 2.1 \text{ mm Hg}) \) or those at week 10 \( (78.8 \pm 2.5 \text{ mm Hg}) \). Heart rate was significantly lowered \( (P < 0.05) \) from baseline after 8 wk of diet (Figure 3). Changes in body weight, BMI, and percentage body fat were not related to blood pressure or heart rate values.

### DISCUSSION

This study is the first to show that ADF is an effective dietary intervention to help obese individuals lose weight and lower CAD risk. Specifically, we show here that an ADF regimen, which allowed participants to consume 25% of their energy needs on the fast day, resulted in a mean weight loss of 5.8% from baseline after only 8 wk of treatment. Decreases in several key biomarkers for CAD risk, such as total cholesterol, LDL cholesterol, triacylglycerols, systolic blood pressure, and heart rate, were also observed. Additionally, we show here that a similar rate of weight loss was achieved during the ADF controlled food intake period when compared with the ADF self-selected food intake period. These data suggest that subjects were able to maintain the ADF meal pattern when preparing their own meals at home (ie, when removed from a clinically controlled environment).

Although CR is more frequently implemented than ADF to facilitate weight loss \( (4, 14) \), many obese patients find it difficult to adhere to CR because food intake must be limited every day by 15–40% of baseline needs \( (15–17) \). ADF regimens were created to increase adherence to dietary restriction protocols because...
these regimens require energy restriction only every other day (4). In the present study, we measured the ability of obese subjects to adhere to their fast day energy goal. Our data show that adherence to ADF was high (days per week adherent: ≈ 85%) and that this level of adherence remained constant throughout the 8-wk trial. We also show here that adherence to the ADF protocol was similar between the controlled food intake phase and the self-selected food intake phase. These findings suggest that obese individuals are capable of self-selecting foods to meet their individual fast day energy goals. It should be noted, however, that the subjects met weekly with a registered dietitian.

In view of this, future studies should examine the ability of obese subjects to adhere to ADF regimens without the help of a dietitian. Such data would be more indicative of the efficacy of the ADF regimen for weight loss in the general population. It should also be noted that of the 20 subjects initially recruited to partake in the study, 2 individuals dropped out due to inability to comply with the fast day diet protocol. Thus, on the basis of these findings, it is possible that this dietary restriction protocol may not be well tolerated by 10% (or possibly more) of the obese population. Nevertheless, dropout rate data from ADF trials with larger sample sizes (eg, n = 68 subjects, calculated with a power of 80% and an α risk of 5%) are still required before solid conclusions can be reached. It should also be noted that this trial was not controlled. The need for a randomized controlled trial to test similar hypotheses is clearly warranted.

Decreases in body weight are directly related to degree of dietary adherence (17–20). In the present ADF study, obese subjects lost an average of 0.68 kg/wk, which corresponded to a total weight loss of 5.6 kg over 8 wk (95% CI: −7.4, −3.8). Because rate of weight loss was correlated to percentage weekly adherence, it can be assumed that the high adherence rate to ADF diets played a significant role in the total weight loss achieved. We also show here that rate of weight loss remained constant after the subjects switched from the ADF controlled food intake phase to the ADF self-selected food intake phase. Thus, the ADF diet may be an effective dietary strategy to help obese individuals achieve a stable, healthy rate of weight loss, even during periods of self-implementation. We predicted that subjects would lose a total of 4.5 kg fat mass after 8 wk (on the basis of a 75% decrease in energy intake on the fast day, with no change in energy intake on the feed day). The actual fat mass lost (5.4 kg) exceeded our predictions. This indicates that these subjects were also limiting their energy intake on the feed day, which may have occurred because the subjects knew they were enrolled in a weight loss trial. Our weight loss findings are similar to those of Johnson et al (7) (8% weight loss after 8 wk of ADF in overweight individuals). However, the trial by Johnson et al (7) takes precedence both in time and study design because it was a randomized controlled trial study. The degree of weight loss achieved by the present ADF regimen is also comparable to that of short-term CR trials (14, 21, 22). In view of these similar effects on body weight, ADF may be considered a suitable alternative to CR to help obese individuals lose weight. A study that directly compares the effects of ADF to that of CR on body weight and body
composition is undoubtedly an important next step in the ADF field. It must also be noted, however, that the degree of weight loss achieved by ADF may not be sustainable long term. Whether or not obese individuals are able to adhere to ADF over the long term and experience sustained weight loss will be an important focus of future research.

Beneficial modulations in several key CAD risk indicators were also noted in response to ADF. Total and LDL-cholesterol concentrations decreased by 21% and 25%, respectively, after 8 wk of diet. Triglyceride concentrations were also lowered by 32% when baseline values were compared with posttreatment values. These modulations in LDL-cholesterol and triglyceride concentrations are similar to those observed by Johnson et al (7).

We also show that improvements in plasma LDL-cholesterol and triglyceride concentrations were correlated to changes in body weight and percentage body fat posttreatment. Thus, the degree of weight loss achieved by this ADF regimen most likely played a major role in the degree to which these plasma lipids were altered (23). No changes in HDL-cholesterol concentrations were observed throughout the trial. This lack of effect of ADF on HDL cholesterol is not surprising because this cardioprotective lipid parameter is generally augmented only in response to exercise training (24). An important next step in the ADF field will be to incorporate an exercise program into this lifestyle regimen. Perhaps with the addition of physical activity, HDL-cholesterol concentrations will increase, thus beneficially modulating the entire lipid profile. Findings from the majority of CR trials also report no change in HDL cholesterol after short durations of treatment (21, 22, 25). Lipid variable measurements were assessed on consecutive food intake and fast days at the end of each diet phase (after a 12-h fasting blood draw). Results reveal that consumption of food or fasting the day before the lipid assessment has no effect on lipid concentrations. Findings from the present study also show that 8 wk of ADF in obese individuals may reduce systolic blood pressure and heart rate. In view of the powerful association of high blood pressure with risk of CAD (26, 27), this finding further supports the cardioprotective actions of ADF.

In summary, our findings indicate that ADF may be implemented as an effective diet strategy to help obese individuals lose weight and to confer protection against CAD. ADF should therefore be considered a viable option for obese patients who wish to lose weight through dietary restriction but who are unable to adhere to daily CR.

The authors’ responsibilities were as follows—KAV: designed the experiment, analyzed the data, and wrote the manuscript; SB and ECC: conducted the clinical trial, performed the laboratory analyses, and assisted with the preparation of the manuscript; and MCK: coordinated food preparation and distribution, provided technical assistance during the analysis phase of the experiment, and assisted with the preparation of the manuscript. The authors had no conflicts of interest to report.

REFERENCES