



Safety of 8-h time restricted feeding in adults with obesity

Journal:	<i>Applied Physiology, Nutrition, and Metabolism</i>
Manuscript ID	apnm-2018-0389.R1
Manuscript Type:	Rapid communication
Date Submitted by the Author:	04-Sep-2018
Complete List of Authors:	Gabel, Kelsey; University of Illinois at Chicago College of Applied Health Sciences, Nutrition Hoddy, Kristin; University of Illinois at Chicago College of Applied Health Sciences Varady, Krista; University of Illinois at Chicago College of Applied Health Sciences
Keyword:	time-restricted feeding, safety, weight-loss, Intermittent Fasting, adverse events, obese adults
Is the invited manuscript for consideration in a Special Issue? :	Not applicable (regular submission)

SCHOLARONE™
Manuscripts

1 **RAPID COMMUNICATION**

2 **Safety of 8-h time restricted feeding in adults with obesity**

3

4 Kelsey Gabel, Kristin K. Hoddy, Krista A. Varady

5 Department of Kinesiology and Nutrition, University of Illinois at Chicago, Chicago, IL

6

7 **Correspondence and reprint requests:**

8 Krista Varady, PhD

9 Associate Professor of Nutrition

10 Department of Kinesiology and Nutrition

11 University of Illinois at Chicago

12 1919 West Taylor Street, Room 532, Chicago, IL, 60612

13 Tel: 312-996-7897, Email: varady@uic.edu

14

15 **Running head:** Safety of time restricted feeding

16 **Funding source:** University of Illinois Chicago Campus Research Board Pilot Grant

17 **Trial registration:** Clinicaltrials.gov NCT02948517

18

19 **Abstract**

20 This study examines the safety of time restricted feeding (TRF; 8-h feeding window/16-h fasting
21 window daily) in obese adults. Twenty-three subjects participated in an 8-h TRF intervention for
22 12 weeks. Self-reported adverse events, body image perception, complete blood count and
23 disordered eating patterns did not change from baseline to week 12. These findings suggest
24 that consuming food within an 8-h window can safely facilitate weight loss in subjects with
25 obesity.

26

27 **Key Words:** Intermittent fasting, time restricted feeding, weight-loss, safety, adverse events,
28 obese adults

Draft

29 **Introduction**

30 Intermittent fasting regimens involve periods fasting followed by periods of eating freely. The
31 most common forms of intermittent fasting are alternate day fasting (500 calorie fast days
32 alternated with ad libitum feast days) and the 5:2 diet (two 500 calorie fast days and 5 ad
33 libitum feast days per week). Time restricted feeding (TRF) is a newer form of intermittent
34 fasting and involves shortening the eating window to 4-10 h/d. The most common form of TRF
35 is 16:8 during which subjects consume all food within 8 hours and water fast during the
36 remaining 16 hours. Accumulating evidence suggests that TRF is an effective means of
37 decreasing body weight while maintaining lean mass in normal weight and overweight subjects
38 (Gill and Panda 2015; Moro et al. 2016; Tinsley et al. 2017). More recently, it's been shown that
39 TRF may also be effective for weight loss in adults with obesity (Gabel K 2017). Although TRF
40 appears to have beneficial effects on body weight, the safety of this diet has been questioned.
41 For instance, increased frequency of constipation, irritability and fatigue are common safety
42 concerns with all forms intermittent fasting (unpublished observations). Additionally, consistent
43 dietary restriction has been postulated to increase disordered eating behaviors (Conceicao et
44 al. 2013; Elran-Barak et al. 2015; Yanovski and Sebring 1994). Accordingly, this study was
45 undertaken to determine the effects of TRF on certain safety parameters, including: eating
46 disorder symptoms, body image perception, complete blood count, and frequency of adverse
47 events, in adults with obesity. We hypothesized that TRF would not negatively impact any of
48 these parameters during the 12-week trial.

49 **Methods**

50 **Subject selection**

51 This 12-week study is a secondary analysis of a larger study (Gabel K 2017). The UIC Office for
52 the Protection of Research Subjects approved the experimental protocol, and all participants
53 gave informed consent (IRB #2016-0119). Subjects were recruited from Chicago via
54 advertisements. A total of 40 subjects were assessed for eligibility, 11 subjects were excluded
55 because they did not meet one or more inclusion criteria, and 6 subjects declined to participate
56 after qualifying. Twenty-three subjects began the study. Key inclusion criteria were: BMI
57 between 30 and 45 kg/m²; age between 25 and 65 y; sedentary to moderately active (<7500
58 steps/d); weight stable for 3 months prior to the beginning of the study (< 4 kg weight loss or
59 weight gain); non-diabetic; non-smoker; not a shift worker.

61 **Study design and time restricted feeding protocol**

62 The study consisted of a 2-week baseline period followed by a 12-week TRF intervention period.
63 During baseline, subjects continued with their usual diets and kept their weight stable. During
64 the TRF intervention, subjects were instructed to eat ad libitum within an 8-h window (10:00 to
65 18:00 h daily), and fast from 18:00 to 10:00 h daily. During the 8-h feeding window, subjects
66 were not required to monitor caloric intake. During the fasting period, subjects drank water and
67 calorie-free beverages only.

68

69 Body weight, resting metabolic rate, activity and food intake

70 Body weight was assessed at the beginning of every week to the nearest 0.25 kg using a
71 balance beam scale (HealthOMeter, Boca Raton, FL) at the research center. Resting metabolic
72 rate (RMR) was measured by a handheld open circuit indirect calorimeter in between the 6:00
73 and 9:00 h (MedGem Indirect Calorimeter, Microlife, USA) at the research center. Subjects were
74 instructed to abstain from food, drink, and exercise for 12 h prior to the visit. Timing since the
75 last meal (12 h) was standardized for each subject prior to the RMR measurement. Subjects first
76 rested in a dark room in the supine position for 15 min, then a mouthpiece and nose clip were
77 placed on the subject, and oxygen consumption was measured until it reached a stable flow
78 (approx. 10 min). Subjects were instructed to maintain their activity level throughout the trial.
79 Step counts were measured over 7-d during the baseline period and at week 12 by a pedometer
80 (Yamax Digi-walker SW-200, San Antonio, TX). Intake of energy, macronutrients and timing of
81 food consumption was assessed by a 7-d food record at baseline and week 12.

82

83 Adverse event, eating disorder, body image, and eating behavior questionnaires

84 Gastrointestinal and neurological issues were assessed by an adverse events questionnaire.
85 Eating disorder symptoms were measured using the Multidimensional Assessment of Eating-
86 Disorder Symptoms (MEADS) (Anderson et al. 1999). Body image was assessed by the Body
87 Shape Questionnaire (BSQ) (Dowson and Henderson 2001). Dietary restraint, uncontrolled
88 eating, and emotional eating were assessed by the validated three-factor eating questionnaire
89 (TFEQ) (Stunkard and Messick 1985).

90

91 **Complete blood count and ketones**

92 Twelve-h fasting blood samples were collected between 5:00 and 9:00 h at baseline, week 1,
93 and week 12. Complete blood counts were performed using a BC-5500 automatic blood cell
94 analyzer, and the ketone, β -hydroxybuterate, was measured by the biosensor method
95 (Medisense, Abbott, Bedford, MA).

96

97 **Statistical analyses**

98 All data are presented as mean \pm standard error of the mean (SEM). Statistical analyses were
99 performed using SPSS 24.0 (SPSS Inc., Chicago, IL). ANOVA was used to assess changes in
100 continuous variables over time. McNemar's test was used to assess changes in categorical
101 variables over time. Data were included for the 23 participants who began the study, and
102 means were estimated using an intention-to-treat analysis using last observation carried
103 forward. $P < 0.05$ was considered statistically significant.

104 **Results**

105 **Body weight, resting metabolic rate, activity, and food intake**

106 Body weight significantly ($P < 0.001$) decreased by $2.6 \pm 0.5\%$ after 12 weeks of TRF. Resting
107 metabolic rate did not change over time (baseline: 1431 ± 62 kcal/d; week 1: 1393 ± 82 kcal/d;
108 week 12: 1318 ± 61 kcal/d). Activity level did not change from baseline (6896 ± 723 steps/d) to
109 week 12 (7443 ± 880 steps/d). Before starting the TRF intervention, subjects typically started
110 eating at $8:30 \pm 0:30$ h:min and finished eating by $19:30 \pm 0:30$ h:min. Energy intake decreased
111 ($P < 0.05$) from baseline (1676 ± 114 kcal/d) to week 12 (1335 ± 162 kcal/d). There were no
112 changes in percent energy intake from protein (baseline: $16 \pm 1\%$; week 12: $17 \pm 1\%$),
113 carbohydrates (baseline: $47 \pm 2\%$; week 12: $46 \pm 2\%$) or fat (baseline: $37 \pm 1\%$; week 12: $37 \pm$
114 2%).

116 **Adverse events, eating disorder symptoms, body image, and eating behaviors**

117 Self-reported adverse events (gastrointestinal or neurological) did not change over time (**Table**
118 **1**). Eating disorder symptoms including depression, binge eating, purgative behavior, fear of
119 fatness, restrictive eating, and avoidance of forbidden foods, did not change from baseline to
120 week 12 (**Table 2**). Concerns about body size and shape remained unchanged (**Table 2**).
121 Cognitive restraint, uncontrolled eating and emotional eating did not change over time (**Table**
122 **2**).

123

124

125

126 **Complete blood count and ketones**

127 There were no significant changes in any of the complete blood count parameters over time

128 **(Table 3)**. Beta-hydroxybuterate also remained unchanged over the course of the study

129 (baseline: 1.0 ± 1.1 mmol/L; week 1: 0.9 ± 0.4 mmol/L; week 12: 1.2 ± 1.2 mmol/L).

Draft

130 **Discussion**

131 This study is the first to show that TRF is a safe diet therapy for weight loss as it does not
132 negatively impact eating disorder symptoms, eating behaviors, or measures of overall health,
133 such as complete blood count. Moreover, no gastrointestinal or neurological adverse events
134 were reported with 12 weeks of TRF.

135
136 It has been speculated that fasting or calorie restriction may increase eating disorder
137 symptoms. However, recent findings suggest that this is not the case. For instance, in a previous
138 trial (Williamson et al. 2008), daily calorie restriction did not increase eating disorder symptoms
139 and had no harmful psychological effects. Likewise, alternate day fasting has been shown to
140 have no negative impact on eating disorder symptoms in adults with obesity (Hoddy et al.
141 2015). Indeed, alternate day fasting may have beneficial effects by increasing dietary restraint
142 and improving body image perception (Hoddy et al. 2015; Bhutani S 2013).

143
144 In the present trial, no significant increase in adverse events was reported with 12 weeks of
145 TRF. These results are in line with what has been shown with alternate day fasting. For instance,
146 8-weeks alternate day fasting did not increase the frequency of gastrointestinal events
147 (constipation, diarrhea, water retention or bad breath) in adults with obesity (Hoddy et al.
148 2015). Rates of dizziness, general weakness, or sleep disturbances also did not increase with
149 alternate day fasting (Hoddy et al. 2015). The present trial also demonstrates no change in
150 complete blood count with TRF. Similarly, in a previous trial (Stote et al. 2007), complete blood
151 count did not change when normal weight adult subjects were required to consume all of their

152 food within a 4-h period each day. Taken together, these findings suggest that TRF regimens are
153 well tolerated by normal weight and obese adults.

154

155 There are several limitations to our study. First, we had a small sample size ($n = 23$) which limits
156 our ability to detect a significant difference from pre- to post-treatment for many variables,
157 most notably RMR (effect size = 0.25). Second, we did not utilize a control group. Third, our
158 adverse events questionnaire is not very comprehensive. A more elaborate list of adverse
159 events should be developed to more accurately examine the safety TRF. Fourth, using the
160 MedGem to assess RMR is a limitation as this tool has been shown to overestimate RMR when
161 compared to a traditional indirect calorimeter (Anderson et al. 2014). The MedGem is also
162 limited in that it does not provide measures of respiratory ratio. Fifth, our study was short (12
163 weeks). Longer-term studies will be needed to examine how these measures of safety change
164 over time.

165

166 In summary, these pilot findings suggest that TRF is a safe diet therapy for weight loss. TRF did
167 not have any negative impact on eating disorder symptoms, body image perception, or eating
168 behaviors. No adverse events were reported during the study, and blood chemistry remained
169 unaffected. These findings offer promise for the use of TRF as a safe lifestyle intervention for
170 weight loss in adults with obesity.

171 **Conflict of interest:**

172 The authors declare no conflict of interest.

173

174

Draft

175 **References**

- 176 Anderson, D. A., Williamson, D. A., Duchmann, E. G., Gleaves, D. H., Barbin, J. M. 1999.
177 Development and validation of a multifactorial treatment outcome measure for eating
178 disorders, *Assessment*, 6: 7-20.
- 179 Anderson, E. J., Sylvia, L. G., Lynch, M., Sonnenberg, L., Lee, H., Nathan, D. M. 2014. Comparison
180 of energy assessment methods in overweight individuals, *J. Acad. Nutr. Diet.*, 114: 273-
181 8.
- 182 Bhutani, S., Klempel, M.C., Kroeger, C.M., Aggour, E., Calvo, Y., Trepanowski, J.F., et al. 2013.
183 'Effect of exercising while fasting on eating behaviors and food intake, *Journal of the*
184 *International Society of Sports Nutrition*, 10: 50.
- 185 Conceicao, E. M., Crosby, R., Mitchell, J. E., Engel, S. G., Wonderlich, S. A., Simonich, H. K. et al.
186 2013. Picking or nibbling: frequency and associated clinical features in bulimia nervosa,
187 anorexia nervosa, and binge eating disorder, *Int. J. Eat. Disord.*, 46: 815-8.
- 188 Dowson, J., Henderson, L. 2001. The validity of a short version of the Body Shape
189 Questionnaire', *Psychiatry. Res.*, 102: 263-71.
- 190 Elran-Barak, R., Sztainer, M., Goldschmidt, A. B., Crow, S. J., Peterson, C. B., Hill, L., et al. 2015.
191 Dietary Restriction Behaviors and Binge Eating in Anorexia Nervosa, Bulimia Nervosa
192 and Binge Eating Disorder: Trans-diagnostic Examination of the Restraint Model, *Eat.*
193 *Behav.*, 18: 192-6.
- 194 Gabel, K., Hoddy, K.K., Haggerty, N., Song, J.H., Kroeger, C.M., Trepanowski, J.F., et al. 2017.
195 Effects of 8-hour time restricted feeding on body weight and metabolic disease risk
196 factors in obese adults, *Nutr. Healthy Aging*, In Press.

- 197 Gill, S., Panda, S. 2015. A Smartphone App Reveals Erratic Diurnal Eating Patterns in Humans
198 that Can Be Modulated for Health Benefits, *Cell Metab.*, 22: 789-98.
- 199 Hoddy, K. K., Kroeger, C. M., Trepanowski, J. F., Barnosky, A. R., Bhutani, S., Varady, K.A. 2015.
200 Safety of alternate day fasting and effect on disordered eating behaviors, *Nutr. J.*, 14:
201 44.
- 202 Moro, T., Tinsley, G., Bianco, A., Marcolin, G., Pacelli, Q. F., Battaglia, G., et al. 2016. Effects of
203 eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength,
204 body composition, inflammation, and cardiovascular risk factors in resistance-trained
205 males, *J. Transl. Med.*, 14: 290.
- 206 Stote, K. S., Baer, D. J., Spears, K., Paul, D. R., Harris, G. K., Rumpler, W. V., et al. 2007. A
207 controlled trial of reduced meal frequency without caloric restriction in healthy, normal-
208 weight, middle-aged adults, *Am. J. Clin. Nutr.*, 85: 981-8.
- 209 Stunkard, A. J., Messick, S. 1985. The three-factor eating questionnaire to measure dietary
210 restraint, disinhibition and hunger, *J. Psychosom. Res.*, 29: 71-83.
- 211 Tinsley, G. M., Forse, J. S., Butler, N. K., Paoli, A., Bane, A. A., La Bounty, P. M., et al. 2017.
212 Time-restricted feeding in young men performing resistance training: A randomized
213 controlled trial, *Eur. J. Sport. Sci.*, 17: 200-07.
- 214 Williamson, D. A., Martin, C. K., Anton, S. D., York-Crowe, E., Han, H., Redman, L. et al. 2008. Is
215 caloric restriction associated with development of eating-disorder symptoms? Results
216 from the CALERIE trial, *Health Psychol.*, 27: S32-42.
- 217 Yanovski, S. Z., Sebring, N.G. 1994. Recorded food intake of obese women with binge eating
218 disorder before and after weight loss, *Int. J. Eat. Disord.*, 15: 135-50.

Draft

Table 1.**Self-reported adverse events after 12 weeks of time restricted feeding**

Adverse events	Baseline	Week 1	Week 12	P-Value
Gastrointestinal				
Nausea	0%	0%	6%	1.00
Vomiting	0%	0%	0%	1.00
Diarrhea	0%	0%	12%	1.00
Constipation	17%	29%	24%	1.00
Bad Breath	18%	14%	12%	0.50
Dry Mouth	32%	14%	12%	0.13
Neurological				
Dizziness	9%	0%	18%	1.00
Weakness	14%	0%	6%	0.50
Headache	32%	24%	24%	0.50
Fatigue	14%	10%	12%	1.00
Irritability	23%	19%	6%	0.25
Unhappiness	14%	14%	0%	1.00

Values reported as mean % occurrences at each time point (baseline n = 23; week 1 n = 23; week 12 n = 17).

Baseline values were measured 2 weeks before the start of the intervention (week 1).

P-value: McNemar's test.

Table 2.**Eating disorder symptoms, body shape perception, and eating behaviors after 12 weeks of time restricted feeding**

	Baseline	Week 1	Week 12	P-Value
Eating disorder symptoms				
Depression	32 ± 1	32 ± 1	32 ± 1	0.90
Binge Eating	28 ± 2	27 ± 1	27 ± 1	0.79
Purgative behavior	13 ± 1	11 ± 1	12 ± 1	0.23
Fear of fatness	41 ± 2	39 ± 2	41 ± 2	0.89
Restrictive eating	28 ± 2	27 ± 2	29 ± 2	0.68
Avoidance of forbidden foods	37 ± 2	38 ± 2	38 ± 2	0.93
Body image perception				
Concerns about body size/ shape	47 ± 3	46 ± 3	47 ± 3	0.96
Eating behaviors				
Dietary restraint	17 ± 1	16 ± 1	17 ± 1	0.51
Uncontrolled eating	18 ± 1	18 ± 1	18 ± 1	0.89
Emotional eating	7 ± 1	7 ± 1	6 ± 1	0.96

Values reported as mean ± SEM (baseline n = 23; week 1 n = 23; week 12 n = 17).

Baseline values were measured 2 weeks before the start of the intervention (week 1).

P-value: ANOVA.

Table 3.**Complete blood count after 12 weeks of time restricted feeding**

	Normal range	Baseline	Week 1	Week 12	P-value
White cell count (K/UL)	5-10	5.7 ± 0.7	5.1 ± 0.5	5.1 ± 0.4	0.70
Red cell count (M/UL)	4.2-6.1	4.3 ± 0.2	4.4 ± 0.1	4.4 ± 0.1	0.91
Hemoglobin (g/dL)	12-18	12.5 ± 0.2	12.6 ± 0.2	12.6 ± 0.3	0.95
Hematocrit (%)	37-52	38.1 ± 1.3	38.0 ± 0.7	38.5 ± 0.9	0.99
Mean corpuscular volume (fL)	80-100	89.3 ± 5.1	88.0 ± 2.4	87.8 ± 1.9	0.87
Mean corpuscular hemoglobin (pg)	27-32	29.4 ± 1.6	29.2 ± 0.9	29.1 ± 0.7	0.93
Mean corpuscular hemoglobin concentration (%)	32-36	32.9 ± 0.6	33.1 ± 0.3	33.1 ± 0.2	0.95
Red blood cell distribution (%)	11-15	14.4 ± 0.5	13.8 ± 0.3	13.9 ± 0.3	0.69
Platelet count (K/UL)	150-450	202.7 ± 12.8	218.8 ± 8.8	212.1 ± 9.9	0.61
Neutrophil (%)	35-80	56.3 ± 5.6	49.8 ± 3.0	51.9 ± 4.9	0.45
Lymphocyte (%)	18-44	32.3 ± 4.7	38.5 ± 4.2	35.8 ± 3.1	0.47
Monocyte (%)	4.7-12.5	7.2 ± 1.5	7.5 ± 0.6	7.5 ± 0.7	0.96
Eosinophil (%)	0-4	3.7 ± 1.2	3.6 ± 0.6	3.5 ± 0.6	0.99
Basophil (%)	0-1.2	0.8 ± 0.2	0.7 ± 0.2	1.1 ± 0.2	0.27
Neutrophil count (K/UL)	1.8-7.7	3.3 ± 0.6	2.7 ± 0.4	2.8 ± 0.3	0.59
Lymphocyte count (K/UL)	0.8-4.8	1.7 ± 0.3	1.9 ± 0.2	1.8 ± 0.2	0.67
Monocyte count (K/UL)	0.2-0.9	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	0.94
Eosinophil count (K/UL)	0.0-0.8	0.2 ± 0.1	0.2 ± 0.0	0.2 ± 0.0	0.68
Basophil count (K/UL)	0-0.1	0.1 ± 0.0	0.0 ± 0.0	0.1 ± 0.0	0.39

Values reported as mean ± SEM (baseline n = 23; week 1 n = 23; week 12 n = 17).

Baseline values were measured 2 weeks before the start of the intervention (week 1).

P-value: ANOVA.