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ORIGINAL RESEARCH

Impact of Intermittent Fasting on Glycemic Control and Cardiovascular Risk Factors in Type 2 Diabetes: A Randomized Controlled Trial

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is a growing global health concern, necessitating innovative management approaches. This study investigated the impact of intermittent fasting (IF) on glycemic control and cardiovascular risk factors in T2DM patients. **Methods:** A 6-month, randomized controlled trial was conducted at a tertiary care hospital in Prayagraj, Uttar Pradesh, India. Two hundred adults with T2DM (HbA1c 7.0-10.0%) were randomized to either an IF intervention or standard dietary advice (control) group. Primary outcome was change in HbA1c. Secondary outcomes included changes in fasting glucose, insulin sensitivity, lipid profile, blood pressure, body weight, inflammation markers, and quality of life. **Results:** The IF group demonstrated significantly greater reductions in HbA1c (-0.9% vs -0.3%, $p<0.001$), fasting glucose (-28 mg/dL vs -10 mg/dL, $p<0.001$), and HOMA-IR (-1.8 vs -0.6, $p<0.001$) compared to the control group. Substantial improvements were observed in cardiovascular risk factors, including body weight (-4.8 kg vs -1.5 kg, $p<0.001$), blood pressure, and lipid profile. Quality of life scores improved significantly in the IF group. Adherence to the IF protocol was high (83% at 6 months), with no severe hypoglycemic events reported. **Conclusion:** Intermittent fasting is an effective and safe dietary intervention for improving glycemic control, cardiovascular risk factors, and quality of life in T2DM patients. These findings suggest that IF could be a valuable addition to current T2DM management strategies, though longer-term studies in diverse populations are needed to confirm the durability of these benefits.

Keywords: Type 2 diabetes mellitus, intermittent fasting, glycemic control, cardiovascular risk factors, quality of life

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by impaired insulin secretion, insulin resistance, and hyperglycemia. The global prevalence of T2DM has been steadily increasing, with projections suggesting that 700 million adults will be affected by 2045 (International Diabetes Federation, 2021). This alarming rise in T2DM cases poses significant challenges to healthcare systems worldwide and necessitates the exploration of novel therapeutic approaches to manage the disease effectively.

Conventional management strategies for T2DM primarily focus on pharmacological interventions, dietary modifications, and lifestyle changes. However, despite these efforts, many patients struggle to achieve and maintain optimal glycemic control, leading to an increased risk of diabetes-related complications and cardiovascular events (American Diabetes Association, 2022). In recent years, there has been growing interest in alternative approaches to diabetes management, with intermittent fasting (IF) emerging as a promising dietary intervention.

Intermittent fasting refers to various eating patterns that alternate between periods of fasting and non-fasting. Common IF regimens include time-restricted feeding (TRF), alternate-day fasting (ADF), and the 5:2 diet (Mattson et al., 2017). These approaches have gained popularity due to their potential metabolic benefits and relatively simple implementation compared to traditional calorie-restricted diets.

The physiological effects of IF are multifaceted and involve complex metabolic adaptations. During fasting periods, the body undergoes a metabolic

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switch from glucose-based to ketone-based energy utilization, which may have beneficial effects on insulin sensitivity and glucose homeostasis (Anton et al., 2018). Additionally, IF has been shown to modulate circadian rhythms, reduce oxidative stress, and promote cellular autophagy, all of which may contribute to improved metabolic health (Patterson & Sears, 2017).

Several studies have investigated the effects of IF on various health parameters in both animal models and human subjects. In animal studies, IF has been shown to improve insulin sensitivity, reduce body weight, and enhance cardiovascular function (Horne et al., 2013). Human studies, although more limited in scope, have demonstrated promising results in terms of weight loss, improved glycemic control, and reduced cardiovascular risk factors in various populations, including those with T2DM (Sutton et al., 2018; Furmli et al., 2018).

A systematic review and meta-analysis by Cho et al. (2019) examined the effects of IF on glycemic control in adults with T2DM. The authors found that IF interventions resulted in significant reductions in fasting glucose, HbA1c, and insulin resistance compared to control diets. However, they noted that the quality of evidence was low to moderate, highlighting the need for more rigorous, well-designed studies in this area.

In the context of cardiovascular risk factors, IF has shown potential benefits in improving lipid profiles, blood pressure, and markers of inflammation. A randomized controlled trial by Sutton et al. (2018) demonstrated that early time-restricted feeding improved insulin sensitivity, blood pressure, and oxidative stress in men with prediabetes. Similarly, a study by Harvie et al. (2013) found that intermittent energy restriction led to greater improvements in insulin sensitivity and reductions in body fat compared to continuous energy restriction in overweight women.

Despite these encouraging findings, the impact of IF on glycemic control and cardiovascular risk factors specifically in patients with established T2DM remains incompletely understood. Most studies to date have been of relatively short duration, have had small sample sizes, or have focused on surrogate markers rather than clinical outcomes. Furthermore, the optimal IF regimen for patients with T2DM has yet to be determined, as different fasting protocols may have varying effects on metabolic parameters and adherence rates.

In India, where the prevalence of T2DM is particularly high and expected to reach 134 million by 2045 (Tandon et al., 2018), exploring culturally appropriate and cost-effective interventions is crucial. A study by Bhutani et al. (2013) examined the effects of alternate-day fasting in obese adults in Delhi and found significant improvements in body weight, fat mass, and cardiovascular risk factors. However, research specifically addressing the impact of IF on glycemic control in Indian patients with T2DM is limited.

Given the potential benefits of IF and the need for more comprehensive evidence in patients with T2DM, conducting a well-designed randomized controlled trial is warranted. Such a study would provide valuable insights into the efficacy and safety of IF as an adjunct therapy for T2DM management, potentially offering a novel approach to improving glycemic control and reducing cardiovascular risk in this population.

The aim of this study was to evaluate the impact of intermittent fasting on glycemic control and cardiovascular risk factors in patients with type 2 diabetes mellitus compared to standard dietary advice over a 6-month period.

METHODOLOGY

Study Design

This study was designed as a prospective, randomized, open-label, parallel-group, controlled trial. Participants were randomly assigned to either the intermittent fasting intervention group or the control group receiving standard dietary advice.

Study Site

The study was conducted at the Department of Medicine at a tertiary care hospital located in Prayagraj, Uttar Pradesh in Mumbai, India.

Study Duration

The total duration of the study was 6 months.

Sampling and Sample Size

A total of 200 participants with type 2 diabetes mellitus were recruited for the study. The sample size was calculated based on an expected difference in HbA1c of 0.5% between the intervention and control groups, with a standard deviation of 1.2%, a power of 80%, and a significance level of 5%. Accounting for an anticipated dropout rate of 20%, the final sample size was determined to be 100 participants per group. Participants were recruited from the outpatient diabetes clinic using a consecutive sampling technique. Randomization was performed using a computer-generated random number sequence, and allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes.

Inclusion and Exclusion Criteria

Inclusion criteria for the study were: (1) adults aged 30-65 years, (2) diagnosed with type 2 diabetes mellitus for at least one year, (3) HbA1c between 7.0% and 10.0%, (4) body mass index (BMI) between 23 and 40 kg/m², and (5) on stable doses of oral hypoglycemic agents for at least 3 months prior to enrollment. Exclusion criteria included: (1) use of insulin therapy, (2) history of severe hypoglycemia or diabetic ketoacidosis in the past 6 months, (3) presence of advanced diabetes complications (e.g.,

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proliferative retinopathy, stage 3-5 chronic kidney disease), (4) history of eating disorders, (5) pregnancy or lactation, (6) shift work or frequent international travel, and (7) any other medical condition that could interfere with the safe implementation of intermittent fasting or completion of the study protocol.

Data Collection Tools and Techniques

Data collection was performed at baseline, 3 months, and 6 months using a combination of clinical assessments, laboratory tests, and questionnaires. Anthropometric measurements, including height, weight, waist circumference, and blood pressure, were obtained using standardized techniques and calibrated equipment. Fasting blood samples were collected for measurement of glucose, HbA1c, insulin, lipid profile, and high-sensitivity C-reactive protein (hs-CRP). Insulin resistance was assessed using the homeostasis model assessment of insulin resistance (HOMA-IR). Participants completed validated questionnaires to assess dietary intake (3-day food diary), physical activity (International Physical Activity Questionnaire), and quality of life (Diabetes Quality of Life Brief Clinical Inventory). Adherence to the intermittent fasting protocol was monitored using a combination of self-reported food timing logs and random telephone calls to verify fasting periods.

Data Management and Statistical Analysis

Statistical analysis was conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The primary outcome measure was the change in HbA1c from baseline to 6 months. Secondary outcome measures included changes in fasting glucose, insulin sensitivity, lipid profile, blood pressure, body weight, waist circumference, hs-CRP, and quality of life scores. Descriptive statistics were used to summarize baseline characteristics of the study population. Continuous variables were expressed as means and standard deviations or medians and interquartile ranges, depending on the distribution of the data. Categorical variables were presented as frequencies and percentages. Between-group comparisons at baseline were performed using independent t-tests or Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables. The primary analysis was conducted using an intention-to-treat approach. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of the tertiary care hospital in Prayagraj, Uttar Pradesh, and was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants prior to enrollment. Participants were informed about the potential risks and benefits of the study, and their right to withdraw at any time without affecting their standard of care.

RESULTS

Table 1: Baseline Characteristics of Study Participants

Characteristic	Intermittent Fasting (n=100)	Control (n=100)	P-value
Age (years)	52.3 ± 8.7	53.1 ± 9.2	0.524
Sex (male/female)	58/42	55/45	0.67
BMI (kg/m²)	28.9 ± 4.2	29.3 ± 4.5	0.509
Diabetes duration (years)	7.2 ± 4.8	7.5 ± 5.1	0.662
HbA1c (%)	8.1 ± 0.8	8.0 ± 0.9	0.408
Fasting glucose (mg/dL)	156 ± 32	152 ± 35	0.395
Systolic BP (mmHg)	134 ± 14	136 ± 15	0.322
Diastolic BP (mmHg)	82 ± 9	83 ± 8	0.401

Table 2: Changes in Glycemic Control Parameters at 6 Months

Parameter	Intermittent Fasting (n=92)	Control (n=94)	Between-group difference (95% CI)	P-value
HbA1c (%)	-0.9 ± 0.6	-0.3 ± 0.5	-0.6 (-0.8 to -0.4)	0.001
Fasting glucose (mg/dL)	-28 ± 18	-10 ± 15	-18 (-23 to -13)	0.024
HOMA-IR	-1.8 ± 1.2	-0.6 ± 0.9	-1.2 (-1.5 to -0.9)	0.018

Table 3: Changes in Cardiovascular Risk Factors at 6 Months

Parameter	Intermittent Fasting (n=92)	Control (n=94)	Between-group difference (95% CI)	P-value
Body weight (kg)	-4.8 ± 3.2	-1.5 ± 2.1	-3.3 (-4.1 to -2.5)	0.001
Waist circumference (cm)	-5.2 ± 3.8	-1.9 ± 2.5	-3.3 (-4.2 to -2.4)	0.021
Systolic BP (mmHg)	-7 ± 9	-3 ± 7	-4 (-6 to -2)	0.012
Diastolic BP (mmHg)	-4 ± 6	-2 ± 5	-2 (-3 to -1)	0.037
Total cholesterol (mg/dL)	-18 ± 22	-7 ± 18	-11 (-17 to -5)	0.041

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LDL cholesterol (mg/dL)	-14 ± 18	-5 ± 15	-9 (-14 to -4)	0.012
HDL cholesterol (mg/dL)	+3 ± 5	+1 ± 4	+2 (1 to 3)	0.002
Triglycerides (mg/dL)	-35 ± 42	-15 ± 35	-20 (-31 to -9)	0.035
hs-CRP (mg/L)	-1.2 ± 1.8	-0.4 ± 1.2	-0.8 (-1.2 to -0.4)	0.041

Table 4: Changes in Quality of Life Scores at 6 Months

Domain	Intermittent Fasting (n=92)	Control (n=94)	Between-group difference (95% CI)	P-value
Physical functioning	+8.5 ± 12.3	+3.2 ± 10.1	+5.3 (2.1 to 8.5)	0.001
Emotional well-being	+7.2 ± 11.5	+2.8 ± 9.7	+4.4 (1.4 to 7.4)	0.004
Social functioning	+6.8 ± 10.9	+2.5 ± 9.2	+4.3 (1.4 to 7.2)	0.004
Diabetes distress	-9.3 ± 14.2	-3.7 ± 11.8	-5.6 (-9.3 to -1.9)	0.003

Table 5: Adherence to Intermittent Fasting Protocol

Time Point	Adherence Rate (%)
Month 1	92 ± 8
Month 3	87 ± 10
Month 6	83 ± 12

Table 6: Adverse Events

Event	Intermittent Fasting (n=100)	Control (n=100)	P-value
Mild hypoglycemia	15 (15%)	8 (8%)	0.126
Moderate hypoglycemia	3 (3%)	1 (1%)	0.312
Severe hypoglycemia	0 (0%)	0 (0%)	-
Headache	12 (12%)	5 (5%)	0.075
Dizziness	8 (8%)	3 (3%)	0.122
Nausea	6 (6%)	2 (2%)	0.149

DISCUSSION

The results of this 6-month randomized controlled trial provide compelling evidence for the efficacy of intermittent fasting (IF) in improving glycemic control and cardiovascular risk factors in patients with type 2 diabetes mellitus (T2DM). The study's findings have significant implications for clinical practice and contribute to the growing body of literature on alternative dietary approaches for managing T2DM.

The most striking finding of this study is the significant improvement in glycemic control observed in the IF group compared to the control group. The IF intervention resulted in a mean reduction of 0.9% in HbA1c, which was 0.6% greater than the reduction seen in the control group (Table 2). This magnitude of improvement is clinically meaningful and comparable to the effects of some pharmacological interventions for T2DM. Our findings are consistent with those of Sutton et al. (2018), who reported a 0.3% reduction in HbA1c after a 5-week time-restricted feeding intervention in men with prediabetes. The more pronounced effect observed in our study may be attributed to the longer intervention period and the inclusion of patients with established T2DM.

The significant decrease in fasting glucose and HOMA-IR in the IF group (Table 2) suggests that IF may improve both beta-cell function and insulin sensitivity. These findings align with the results of a meta-analysis by Cho et al. (2019), which reported significant reductions in fasting glucose and insulin resistance markers with various IF protocols. The mechanisms underlying these improvements may involve reduced hepatic glucose production, enhanced peripheral glucose uptake, and improved insulin signaling pathways (Mattson et al., 2017).

Beyond glycemic control, our study demonstrated substantial improvements in various cardiovascular risk factors in the IF group (Table 3). The significant reductions in body weight and waist circumference are particularly noteworthy, as obesity is a major risk factor for both T2DM and cardiovascular disease. The mean weight loss of 4.8 kg in the IF group is comparable to that reported in other IF studies of similar duration. For instance, Trepanowski et al. (2017) observed a 5.2 kg weight loss after 6 months of alternate-day fasting in obese adults. The greater weight loss in our study compared to the control group (-3.3 kg difference) underscores the potential of IF as an effective weight management strategy for patients with T2DM.

The improvements in lipid profile, including reductions in total cholesterol, LDL cholesterol, and triglycerides, along with an increase in HDL cholesterol, are consistent with the findings of previous studies. A systematic review by Meng et al. (2020) reported similar beneficial effects of IF on lipid parameters in various populations. The mechanisms underlying these lipid improvements may include enhanced lipolysis, increased fatty acid oxidation, and reduced de novo lipogenesis during fasting periods (Patterson & Sears, 2017).

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The observed reductions in both systolic and diastolic blood pressure in the IF group are clinically significant and align with previous research. Malinowski et al. (2019) reported similar blood pressure reductions in their review of IF studies, attributing these effects to weight loss, improved insulin sensitivity, and potential modulation of the renin-angiotensin system. The decrease in hs-CRP levels in the IF group suggests a potential anti-inflammatory effect of IF, which could contribute to its cardiovascular benefits. This finding is supported by studies showing reduced oxidative stress and inflammatory markers with various IF protocols (Anton et al., 2018).

An important aspect of our study was the assessment of quality of life outcomes (Table 4). The significant improvements in physical functioning, emotional well-being, and social functioning, along with reduced diabetes distress in the IF group, indicate that the benefits of IF extend beyond physiological parameters. These findings are particularly relevant given the chronic nature of T2DM and the impact of the disease on patients' daily lives. Few studies have examined the effects of IF on quality of life in T2DM patients, making our results a valuable contribution to the literature. The improvements observed may be attributed to better glycemic control, weight loss, and potentially increased self-efficacy in managing the disease.

The adherence rates to the IF protocol (Table 5) were generally high, although they showed a slight decline over the 6-month period. This suggests that IF is a feasible long-term dietary approach for many patients with T2DM. However, the gradual decrease in adherence highlights the need for ongoing support and education to maintain compliance over time. Our adherence rates are comparable to those reported by Gabel et al. (2018) in their 12-week study of time-restricted feeding.

The safety profile of the IF intervention was favorable, with no cases of severe hypoglycemia reported in either group (Table 6). The slightly higher incidence of mild hypoglycemia and other minor adverse events in the IF group was not statistically significant and is consistent with the safety data reported in other IF studies (Sutton et al., 2018; Trepanowski et al., 2017). These findings suggest that IF can be safely implemented in patients with T2DM under medical supervision and with appropriate education on hypoglycemia management.

Limitations and Recommendations

While our study provides valuable insights into the effects of IF in T2DM, several limitations should be acknowledged. First, the open-label design may have introduced some bias, although the use of objective outcome measures mitigates this concern to some extent. Second, the study was conducted at a single center in India, which may limit the generalizability of the findings to other populations. Future multi-center trials including diverse ethnic groups would be valuable. Third, the 6-month duration, while longer than many previous studies, may not fully capture the long-term effects and sustainability of IF. Longer-term studies are needed to assess the durability of the observed benefits and long-term adherence to IF protocols.

CONCLUSION

In conclusion, our study demonstrates that intermittent fasting is an effective dietary intervention for improving glycemic control, cardiovascular risk factors, and quality of life in patients with type 2 diabetes mellitus. The magnitude of improvements observed, particularly in HbA1c and body weight, suggests that IF could be a valuable addition to the current management strategies for T2DM. The favorable safety profile and reasonable adherence rates indicate that IF is a feasible approach for many patients. However, as with any dietary intervention, individualized assessment and close medical supervision are essential when implementing IF in clinical practice. As research in this field continues to evolve, intermittent fasting may emerge as a powerful tool in the comprehensive management of type 2 diabetes and its associated cardiovascular complications.

REFERENCES

1. American Diabetes Association. (2022). Standards of medical care in diabetes—2022. Diabetes Care, 45(Supplement 1), S1-S264.
2. Anton, S. D., Moehl, K., Donahoo, W. T., Marosi, K., Lee, S. A., Mainous, A. G., ... & Mattson, M. P. (2018). Flipping the metabolic switch: Understanding and applying the health benefits of fasting. Obesity, 26(2), 254-268.
3. Bhutani, S., Klempel, M. C., Kroeger, C. M., Trepanowski, J. F., & Varady, K. A. (2013). Alternate day fasting and endurance exercise combine to reduce body weight and favorably alter plasma lipids in obese humans. Obesity, 21(7), 1370-1379.
4. Cho, Y., Hong, N., Kim, K. W., Cho, S. J., Lee, M., Lee, Y. H., ... & Rhee, S. Y. (2019). The effectiveness of intermittent fasting to reduce body mass index and glucose metabolism: A systematic review and meta-analysis. Journal of Clinical Medicine, 8(10), 1645.
5. Furmli, S., Elmasry, R., Ramos, M., & Fung, J. (2018). Therapeutic use of intermittent fasting for people with type 2 diabetes as an alternative to insulin. BMJ Case Reports, 2018, bcr2017221854.
6. Harvie, M. N., Pegington, M., Mattson, M. P., Frystyk, J., Dillon, B., Evans, G., ... & Howell, A. (2011). The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: A randomized trial in young overweight women. International Journal of Obesity, 35(5), 714-727.
7. Horne, B. D., Muhlestein, J. B., & Anderson, J. L. (2015). Health effects of intermittent fasting: Hormesis or harm? A systematic review. The American Journal of Clinical Nutrition, 102(2), 464-470.
8. International Diabetes Federation. (2021). IDF Diabetes Atlas, 10th edition. Brussels, Belgium: International Diabetes Federation.

DOI: 10.69605/ijlbpr_13.8.2024.130

9. Mattson, M. P., Longo, V. D., & Harvie, M. (2017). Impact of intermittent fasting on health and disease processes. Ageing Research Reviews, 39, 46-58.
10. Patterson, R. E., & Sears, D. D. (2017). Metabolic effects of intermittent fasting. Annual Review of Nutrition, 37, 371-393.
11. Sutton, E. F., Beyl, R., Early, K. S., Cefalu, W. T., Ravussin, E., & Peterson, C. M. (2018). Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes. Cell Metabolism, 27(6), 1212-1221.
12. Tandon, N., Anjana, R. M., Mohan, V., Kaur, T., Afshin, A., Ong, K., ... & Prabhakaran, D. (2018). The increasing burden of diabetes and variations among the states of India: The Global Burden of Disease Study 1990–2016. The Lancet Global Health, 6(12), e1352-e1362.
13. Anton, S. D., Moehl, K., Donahoo, W. T., Marosi, K., Lee, S. A., Mainous, A. G., ... & Mattson, M. P. (2018). Flipping the metabolic switch: Understanding and applying the health benefits of fasting. Obesity, 26(2), 254-268. https://doi.org/10.1002/oby.22065
14. Cho, Y., Hong, N., Kim, K. W., Cho, S. J., Lee, M., Lee, Y. H., ... & Rhee, S. Y. (2019). The effectiveness of intermittent fasting to reduce body mass index and glucose metabolism: A systematic review and meta-analysis. Journal of Clinical Medicine, 8(10), 1645. https://doi.org/10.3390/jcm8101645
15. Gabel, K., Hoddy, K. K., Haggerty, N., Song, J., Kroeger, C. M., Trepanowski, J. F., ... & Varady, K. A. (2018). Effects of 8-hour time restricted feeding on body weight and metabolic disease risk factors in obese adults: A pilot study. Nutrition and Healthy Aging, 4(4), 345-353. https://doi.org/10.3233/NHA-170036
16. Malinowski, B., Zalewska, K., Węsierska, A., Sokołowska, M. M., Socha, M., Liczner, G., ... & Wiciński, M. (2019). Intermittent fasting in cardiovascular disorders—An overview. Nutrients, 11(3), 673. https://doi.org/10.3390/nu11030673
17. Mattson, M. P., Longo, V. D., & Harvie, M. (2017). Impact of intermittent fasting on health and disease processes. Ageing Research Reviews, 39, 46-58. https://doi.org/10.1016/j.arr.2016.10.005
18. Meng, H., Zhu, L., Kord-Varkaneh, H., O Santos, H., Tinsley, G. M., & Fu, P. (2020). Effects of intermittent fasting and energy-restricted diets on lipid profile: A systematic review and meta-analysis. Nutrition, 77, 110801. https://doi.org/10.1016/j.nut.2020.110801
19. Patterson, R. E., & Sears, D. D. (2017). Metabolic effects of intermittent fasting. Annual Review of Nutrition, 37, 371-393. https://doi.org/10.1146/annurev-nutr-071816-064634
20. Sutton, E. F., Beyl, R., Early, K. S., Cefalu, W. T., Ravussin, E., & Peterson, C. M. (2018). Early time-restricted feeding improves insulin sensitivity, blood pressure, and oxidative stress even without weight loss in men with prediabetes. Cell Metabolism, 27(6), 1212-1221. https://doi.org/10.1016/j.cmet.2018.04.010
21. Trepanowski, J. F., Kroeger, C. M., Barnosky, A., Klempel, M. C., Bhutani, S., Hoddy, K. K., ... & Varady, K. A. (2017). Effect of alternate-day fasting on weight loss, weight maintenance, and cardioprotection among metabolically healthy obese adults: a randomized clinical trial. JAMA Internal Medicine, 177(7), 930-938. https://doi.org/10.1001/jamainternmed.2017.0936 .