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Comparing Intermittent Fasting, Clean Ketogenic Diet, and Their Combined Effects on Body Composition, Cardiometabolic Markers, and Metabolic Health: A Three-Arm Randomized Pre-Post Study

Angie MacKewn

amackewn@utm.edu

University of Tennessee at Martin

Julie Floyd

University of Tennessee at Martin

Todd Sherman

University of Tennessee at Martin

Alison Ellis

University of Tennessee at Martin

Anna Dunn

University of Tennessee at Martin

Diana Sanford

University of Tennessee at Martin

Research Article

Keywords:

Posted Date: July 3rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10085509/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

No study has directly compared intermittent fasting alone, a clean ketogenic diet alone, and their combination in a single three-arm design. The purpose of this study was to compare the effects of these three dietary conditions on body composition, cardiometabolic markers, grip strength, and glycemic control over 30 days.

Methods

A cross-study analysis combined data from two sequential pre-post intervention studies at the University of Tennessee at Martin, yielding a three-arm design: intermittent fasting alone (n = 16), clean ketogenic diet alone (n = 22), and combined clean ketogenic diet with intermittent fasting (n = 41). The clean ketogenic diet restricted carbohydrates to 20 grams per day from whole unprocessed sources and eliminated refined sugars, high-fructose corn syrup, and ultra-processed foods. The intermittent fasting protocol employed a 16:8 time-restricted eating window. Paired-samples t-tests examined within-group changes; one-way ANOVAs with Tukey post-hoc comparisons examined between-group differences. Effect sizes are reported as Hedges' g and eta squared. An independent samples t-test compared glycosylated hemoglobin changes between the intermittent fasting and combined groups, and Spearman and Kendall correlations examined associations between fat mass and cardiometabolic change.

Results

All three conditions produced significant within-group reductions in body weight, body fat percentage, fat mass percentage, waist circumference, and hip circumference. Carbohydrate restriction produced significantly greater weight reduction than intermittent fasting alone, $F(2,76) = 12.003$, $p < .001$, $\eta^2 = .240$, and greater fat mass reduction ($p = .002$, $\eta^2 = .144$). Both fasting-containing conditions produced significantly greater bilateral grip strength improvement than the ketogenic diet alone ($p < .05$). The combined protocol produced significantly greater glycosylated hemoglobin reduction than fasting alone, $t(30) = 2.141$, $p = .041$, $g = 0.738$. Fat mass reduction correlated significantly with triglyceride-to-HDL ratio improvement across all 79 participants ($rs = -.250$, $p = .026$).

Conclusions

Carbohydrate restriction produced the greatest weight loss and cardiometabolic improvements, while the addition of a 16:8 fasting window contributed independently to glycemic control and grip strength. These findings support the clean ketogenic diet as a first-line strategy for metabolic syndrome management, with the combined protocol offering additive benefits.

Trial Registration

This study was retrospectively registered at ClinicalTrials.gov on June 16, 2026 (NCT07659093; https://www.clinicaltrials.gov/)

Background

The Metabolic Health Crisis

Metabolic health refers to optimal functioning of the body's energy regulation systems, characterized by five interrelated biomarkers: fasting blood glucose, triglycerides, high-density lipoprotein (HDL) cholesterol, blood pressure, and waist circumference, each maintained within clinically acceptable levels without pharmaceutical intervention [1]. When three or more of these markers fall outside optimal ranges, the resulting condition is considered metabolic syndrome and is characterized by central obesity, dyslipidemia, insulin resistance, and hypertension. The presence of metabolic syndrome significantly elevates the risk of developing type 2 diabetes mellitus (T2DM), cardiovascular disease, stroke, and neurodegenerative conditions, including Alzheimer's dementia [2, 3, 4]. The prevalence of metabolic syndrome has increased rapidly in the last decade, with an estimated 1.54 billion adults affected globally in 2023, although rates vary considerably among populations and age groups [5, 6, 4]. Only 13% of Americans achieve optimal metabolic health across all five markers, and this number declines to just 8% among those who are overweight and less than 1% among those with obesity [1]. These percentages underscore that metabolic dysfunction is not confined to individuals with visible weight concerns but represents a pervasive, underrecognized global health crisis with profound implications for chronic disease burden, healthcare costs, quality of life, and as emerging evidence demonstrates, neurological and cognitive health [6, 5].

Metabolic Inflexibility and the Role of Nutrition

In a metabolically healthy individual, the body shifts readily between carbohydrate and fat oxidation depending on feeding state, fasting duration, and energy demand. In individuals with metabolic syndrome, this switching capacity is impaired even before a formal diabetes diagnosis, with insulin-resistant and pre-diabetic individuals demonstrating impaired fat oxidation in the fasted state and impaired glucose utilization following a meal [7]. This impaired fuel switching, called metabolic inflexibility, drives insulin resistance and promotes fat deposition in skeletal muscle and the liver [8], and appears more pronounced in adults with type 2 diabetes mellitus and worsens as the disease progresses [9]. Mitochondrial dysfunction, characterized by impaired capacity for fuel oxidation and reduced metabolic flexibility at the cellular level, appears to contribute to this impairment and has been shown to respond favorably to carbohydrate restriction. Low-carbohydrate dietary intervention produces the greatest improvements in insulin sensitivity compared to low-fat and Mediterranean diet approaches [7, 8, 10].

Importantly, lifestyle modifications, particularly dietary choices, are considered the primary therapeutic approach for metabolic syndrome, with the greatest evidence supporting strategies that target direct fuel-switching rather than managing downstream symptoms (Castro-Barquero et al., 2020). Diets that reduce carbohydrate intake, modify glycemic load, and alter meal timing have demonstrated particular relevance to insulin resistance and impaired glucose tolerance, the core metabolic defects driving the syndrome, with carbohydrate restriction and time-restricted eating specifically emerging as key strategies capable of restoring metabolic flexibility, reducing visceral adiposity, and improving the cardiometabolic risk profile in affected individuals [11, 12, 13].

Evidence Base for Low-Carbohydrate and Clean Ketogenic Diets

The clean ketogenic diet (CKD) restricts carbohydrate intake to 20 grams per day from whole, unprocessed sources, with macronutrients comprising approximately 70% fat, 20% protein, and 10% carbohydrate, and excludes refined sugars and high-fructose corn syrup [14, 15, 3] and ultra-processed foods [16, 17]. This approach has demonstrated clinically meaningful improvements in the cardiometabolic outcomes measured in the present study. Low-carbohydrate diets have produced significant reductions in triglycerides and increases in HDL cholesterol in randomized controlled trials, with combined mean differences of − 19.91 mg/dL and + 2.49 mg/dL respectively [18]. Additionally, low-carbohydrate diets reduce body weight and fat mass to a greater extent than high-carbohydrate diets without detrimental effects on fat-free mass, suggesting lean tissue is preserved during carbohydrate restriction [19, 20].

With respect to glycemic control, low-carbohydrate dietary intervention has produced significant HbA1c reduction across multiple study designs, including an umbrella meta-analysis finding improvement in 16 of 21 studies among individuals with type 2 diabetes mellitus [21]. A randomized clinical trial published in JAMA Network Open further demonstrated significant HbA1c reductions in adults with elevated untreated HbA1c following a low-carbohydrate dietary intervention [22]. These findings collectively support the CKD as a targeted approach addressing the core defects of metabolic syndrome, including dyslipidemia, excess adiposity, and impaired glycemic regulation, providing a strong foundation for examining its effects alongside time-restricted eating.

Evidence Base for Intermittent Fasting and Time-Restricted Eating

Intermittent fasting (IF), and specifically the 16:8 time-restricted eating (TRE) protocol in which caloric intake is confined to an 8-hour feeding window with a 16-hour fast, has independently demonstrated significant metabolic benefits through mechanisms partially distinct from caloric restriction alone. Sampieri and colleagues [23] found that 16:8 TRE reduced body mass by 2.46% and absolute fat mass by 8.65% without significant changes in lean tissue or caloric intake, supporting IF as a strategy that preferentially targets fat mass while preserving lean tissue. In adults with metabolic syndrome, 8–10-hour TRE produced significant improvements in fasting glucose, cholesterol, and HbA1c compared to standard nutritional counseling alone [24].

Additionally, IF produces its metabolic benefits through mechanisms partially distinct from dietary composition alone, including the activation of autophagy, the cellular process that clears dysfunctional proteins and organelles through mechanistic target of rapamycin (mTOR) suppression during the fasting window [25, 12], circadian alignment of metabolic processes to natural feeding and fasting rhythms, and extension of the fasted ketogenic state, which drives fat oxidation and ketone body production independent of dietary macronutrient composition. These mechanisms complement rather than duplicate those of CKD. Where CKD addresses metabolic substrate by eliminating glucose availability and forcing fat oxidation, IF addresses metabolic timing by extending the fasted window to maximize fat-burning and autophagy activation. This complementarity provides a strong basis for expecting that combining CKD with IF will produce synergistic rather than merely additive improvements in metabolic health [13, 26].

Of particular relevance for the present study, the triglyceride-to-HDL ratio (TG:HDL) serves as a primary cardiometabolic outcome, given its superior sensitivity over individual lipid values for detecting insulin resistance and atherogenic lipid patterns, with values below 2.0 considered optimal and values above 3.5 indicating elevated metabolic risk [27, 28].

Metabolic Health, Neuroinflammation, and Brain Function

The consequences of metabolic syndrome extend well beyond peripheral tissues. Brain insulin resistance, the impaired response of central nervous system tissues to insulin signaling, has been identified as a key pathological hub linking metabolic dysfunction to neuropsychiatric comorbidities, impairing mitochondrial function, increasing neuroinflammation, and disrupting synaptic plasticity in regions critical for mood, memory, and executive function [29]. Clinically, this neurometabolic impairment manifests as brain fog characterized by forgetfulness, poor concentration, perceived cognitive slowness, difficulty following complex information, and emotional dysregulation [30], as well as elevated anxiety, disrupted sleep, and depressed mood, all of which are prevalent in individuals with metabolic syndrome [31, 32]. The underlying mechanism involves chronic inflammation sufficient to breach the blood-brain barrier, triggering microglial activation and the release of pro-inflammatory cytokines that disrupt synaptic function and inhibit neurogenesis [29]. By reversing peripheral insulin resistance through carbohydrate restriction and extended fasting, the dietary interventions examined in the present study may simultaneously reduce this neuroinflammatory burden. Ketone bodies, the primary metabolic product of CKD and extended fasting, provide a more efficient neuronal fuel source than glucose, with beta-hydroxybutyrate shown to improve mitochondrial function, reduce oxidative stress, and support synthesis of dopamine, noradrenaline, and serotonin, neurotransmitters directly implicated in the mood, anxiety, energy, and sleep outcomes reported in the present study [33, 34]. Additionally, IF activates BDNF-mediated neuroplastic pathways through metabolic stress during the fasting window, though human evidence for IF-induced BDNF changes remains mixed across populations and protocols [35, 36]. Recent EEG research provides translatable evidence that dietary metabolic state is detectable in human brain electrophysiology, with a ketogenic condition producing a flatter 1/f aperiodic slope suggesting an enhanced information processing state compared to a glucogenic condition [37]. These findings suggest

that the improvements in energy, mood, anxiety, and sleep outcomes may reflect a neurometabolic shift beyond peripheral metabolic improvement, a hypothesis that future research incorporating objective cognitive assessment and quantitative EEG is positioned to directly examine.

The Research Gap and Purpose of the Present Study

Despite growing evidence supporting CKD and IF independently, a critical gap remains in the existing literature. Recent multi-arm trials have compared these strategies as separate interventions rather than in combination. Monda et al. [38] compared a hypocaloric ketogenic diet, 16:8 TRE, and 5:2 alternate-day fasting protocol in adults with obesity, while Martínez-Montoro et al. [39] compared a ketogenic diet, two forms of TRE, and modified alternate-day fasting against a Mediterranean diet control. Importantly, neither study included a combined CKD + IF arm, which is the essential design feature needed to determine whether combining carbohydrate restriction with time restriction produces synergistic benefits beyond each strategy alone. To date, no study has examined all three conditions while assessing bilateral grip strength, a validated functional marker of metabolic health and insulin resistance that is inversely associated with systemic inflammation, dyslipidemia, and metabolic syndrome [40], and air displacement plethysmography-based body composition, TG:HDL ratio, HbA1c, and psychological outcomes including mood, anxiety, sleep quality, and well-being.

The present study addresses this gap through a cross-study comparison combining data from two sequential studies conducted using identical protocols and measurement instruments, yielding a three-arm design comprising IF (*n* = 16), CKD (*n* = 22), and CKD + IF (*n* = 41). Building on prior work demonstrating superior metabolic and psychological outcomes in CKD + IF compared to CKD [41], the present analysis extends the comparison to a third condition and introduces HbA1c as an additional glycemic outcome. The purpose of this study was to compare the effects of three dietary conditions on body composition, cardiometabolic and glycemic markers, and grip strength over a 30-day intervention period.

Three hypotheses in this investigation:

H1: All three dietary conditions (IF, CKD, and CKD + IF) will produce significant improvements from baseline in body composition, cardiometabolic markers, and glycemic control over the 30-day intervention period.

H2: The CKD + IF group will demonstrate significantly greater improvements than either CKD or IF across primary outcome variables, reflecting the synergistic effect of combining substrate restriction with time restriction.

H3: The IF group will produce measurable but intermediate improvements compared to the two carbohydrate-restricted conditions, particularly on lipid markers and fat mass outcomes, reflecting the independent metabolic benefit of time restriction without dietary substrate modification.

In addition to these primary benefit outcomes, potential harms associated with dietary restriction, including adverse symptoms including fatigue, gastrointestinal disturbance, or hypoglycemia, were monitored through the intervention period.

Methods

2.1 Patient and Public Involvement

This study presents a cross-study pooled analysis combining data from two sequential pre-post intervention studies conducted using identical protocols, measurement instruments, and a 30-day intervention period at the University of Tennessee at Martin. Both studies employed a pre-post design with randomized group assignment. Data were pooled to enable a three-arm comparison across the following conditions: (1) clean ketogenic diet (CKD), (2) combined clean ketogenic diet with intermittent fasting (CKD + IF), and (3) intermittent fasting (IF). The CKD and CKD + IF arms were drawn from a previously published study [41], and the IF arm was drawn from the current study. All procedures, recruitment strategies, measurement instruments, and intervention protocols were standardized across both studies to support comparability of findings. Given that the CKD + IF arm included participants from both Study 1 and Study 2, baseline equivalencies between these subgroups was verified prior to pooling data. No significant differences were observed, allowing for comparability of CKD + IF participants across studies.

The allocation ratio across the three arms was approximately 1:1.4:2.6 (IF:CKD:CKD + IF) reflecting the sequential pooled design rather than prospective equal randomization. The framework of this analysis is exploratory and consistent with a superiority design, examining whether carbohydrate restriction and time restriction produce differential benefits across body composition, cardiometabolic, and glycemic outcomes.

No changes were made to the trial protocols after commencement of either study.

2.1.1 Study Design

Participants or the public were not involved in the design, conduct, reporting, or dissemination planning of this research.

2.2 Participants

Participants were recruited from the University of Tennessee at Martin campus and surrounding community through university-wide email distribution and local community flyers. Eligible participants were adults 18 years of age or older with no reported contraindications to dietary modification. Individuals currently pregnant, breastfeeding, or with a diagnosed eating disorder were excluded. All participants provided written informed consent prior to enrollment and were informed of their right to withdraw at any time without consequence.

The combined sample consisted of 79 participants across three groups, CKD (*n* = 22; 10 males, 12 females; mean age = 41.77, *SD* = 12.82 years), CKD + IF (*n* = 41; 13 males, 28 females; mean age = 46.88, *SD* = 9.30 years), and IF (*n* = 16; 6 males, 10 females; mean age = 49.69, *SD* = 10.49 years). No significant between-group differences in baseline age, sex distribution, body weight, or body fat percentage were observed (all $p > .05$), supporting the comparability of groups prior to intervention. Although baseline age did not differ significantly across groups, a trend toward difference was observed ($p = .064$), and the possibility that age-related variation modestly influenced outcomes cannot be fully excluded.

Both studies received certification as expedited reviews by the Institutional Review Board at the University of Tennessee at Martin prior to data collection. Study 1 (CKD and CKD + IF arms) received IRB approval (No. 2021-872-E05-4065/MacK, Ang). Study 2 (IF arm) received IRB approval (No. 2022-925-E05-4065/MacK, Ang). Both studies were funded by internal faculty development grants from the University of Tennessee at Martin Faculty Development Program.

2.2.1 Randomization

Participants were randomly assigned to dietary conditions using a simple randomization procedure (random number table). No stratification or blocking was employed. A degree of allocation concealment was achieved through procedural separation. The principal investigator generated the random allocation sequence and assigned participants to numbered groups without knowing which group number corresponded to which dietary condition. Enrollment and communication of group assignment to participants was overseen by research assistants.

In Study 1, participants were assigned to either CKD or CKD + IF. In Study 2, participants were assigned to either IF or CKD + IF. The CKD arm was drawn exclusively from Study 1, the IF exclusively from Study 2, and the CKD + IF includes participants from both studies. Due to the nature of dietary interventions, blinding of participants to group assignment was not feasible. Participants were aware of their dietary condition throughout the intervention period. Outcome assessors were not blinded to group assignment. The open-label design is an acknowledged limitation to dietary intervention research. However, the primary outcomes, including, body composition, grip strength, and cardiometabolic were assessed using objective instruments. This reduces the potential for performance or detection bias associated with the unblinded design.

2.3 Dietary Interventions

All participants received standardized dietary instructions at an initial baseline session approximately two weeks prior to the intervention start date. During this session, participants were provided with an approved food list [42] and instructed to gradually reduce intake of refined sugars, high-fructose corn syrup, and ultra-processed foods in the two weeks prior to the intervention to minimize potential metabolic disruption at initiation.

2.3.1 Clean Ketogenic Diet (CKD)

Participants assigned to the CKD group were instructed to follow a strict clean ketogenic diet for 30 days, defined as limiting total daily carbohydrate intake to no more than 20 grams from whole, unprocessed food sources on an approved food list. The CKD excluded packaged or commercially prepared "keto-friendly" products and explicitly eliminated refined sugars, high-fructose corn syrup, and ultra-processed foods. The macronutrient target was approximately 70% fat, 20% protein, and 10% unprocessed carbohydrates. No restrictions were placed on the timing or duration of the daily feeding window in this group.

2.3.2 Combined Clean Ketogenic Diet and Intermittent Fasting (CKD + IF)

Participants in the CKD + IF group adhered to the identical CKD protocol described above with the additional requirement of restricting all caloric intake to an 8-hour feeding window each day, thereby maintaining a 16-hour fasting period (16:8 time-restricted eating). Participants selected their own preferred 8-hour feeding window and were instructed to maintain consistency across the 30-day period. Non-caloric beverages including water, black coffee, and plain tea were permitted during the fasting window.

2.3.3 Intermittent Fasting (IF)

Participants in the IF group followed the same 16:8 time-restricted eating protocol, restricting all caloric intake to an 8-hour feeding window with a 16-hour fast, without any carbohydrate restrictions or macronutrient targets. Participants were instructed to maintain their habitual dietary patterns within the feeding window and were not provided the approved CKD food list. Consistency of the feeding window timing was encouraged throughout the 30-day period.

2.4 Adherence Monitoring

Dietary adherence was monitored throughout the 30-day intervention using daily log sheets on which participants recorded food and fluid intake, mealtimes, and subjective physical and psychological responses before and after eating. Participants were assigned a designated support contact who communicated with them once per week via their preferred method of email or text message to provide encouragement, address questions, and reinforce protocol compliance. Completed daily logs were collected at the post-test session and used to verify adherence. Participants who did not demonstrate at least 80% dietary adherence based on submitted log review were excluded from the final analysis.

2.4.1 Harms Monitoring

Potential adverse side effects associated with dietary restriction were monitored throughout the intervention period. Participants were instructed to report any adverse symptoms, including fatigue, dizziness, gastrointestinal disturbance, or hypoglycemic episodes to their designated weekly support contact. No formal adverse event reporting instrument was used. No adverse events or unintended effects were reported by participants in any group during either study.

2.5 Outcome Measures

The primary outcomes for this study were body, body fat percentage, fat mass percentage, waist circumference, and hip circumference. Each was assessed change from baseline to 30 days using mean differences. Secondary outcomes were triglycerides, HDL cholesterol, TG:HDL ratio, waist-to-hip ratio, bilateral grip strength, and glycosylated hemoglobin (HbA1c). Each was assessed by measuring the change from baseline to 30 days using mean differences.

All outcome measures were collected at baseline (pre-test) and at the conclusion of the 30-day intervention (post-test) by research personnel using identical procedures across both studies. The following variables were assessed at both testing sessions. Psychological measures assessed in both studies are reported separately in a companion analysis.

2.5.1 Body Composition

Body weight, body fat percentage, fat mass, and fat-free mass were assessed using the BOD POD® Body Composition Tracking System (COSMED, Rome, Italy), which employs air displacement plethysmography. Participants were assessed per the manufacturer's recommended procedures. The BOD POD® has demonstrated strong agreement with dual-energy X-ray absorptiometry (DXA) across diverse adult populations and is considered a reference-grade instrument for body composition research.

Waist-to-hip ratio (WHR) was calculated by dividing waist circumference by hip circumference for all participants across both studies, consistent with WHO guidelines [43]. One participant in the IF group was unable to complete BOD POD® assessment due to claustrophobia; body composition for this individual was estimated using ACSM circumference-based prediction equations [44], consistent with the circumference measurement protocol used for all participants in this study.

2.5.2 Grip Strength

Bilateral handgrip strength was assessed using a calibrated hand dynamometer following the standardized protocols outlined in ACSM's Guidelines for Exercise Testing and Prescription [44]. Participants were standing with the elbow flexed at 90° and instructed to squeeze the dynamometer with maximal effort. Three trials were performed for each hand and the maximum value recorded. Grip strength was included as a validated functional marker of skeletal muscle integrity and cardiometabolic health, given its established inverse relationship with systemic inflammation, dyslipidemia, and metabolic syndrome risk, and its association with fall risk in adults over 50 years of age [40, 45]

2.5.3 Lipid Panel: Triglycerides, HDL, and TG:HDL Ratio

Fasting triglyceride and HDL cholesterol concentrations were assessed via fingerstick whole blood using the CardioChek® Plus Professional analyzer (PTS Diagnostics, Indianapolis, IN), a CLIA-waived point-of-care lipid panel device validated for research and clinical settings. The triglyceride-to-HDL ratio (TG:HDL)

was calculated by dividing the fasting triglyceride value by the fasting HDL value. A TG:HDL ratio below 2.0 is considered optimal and values above 3.5 indicate elevated cardiometabolic risk [27, 28].

2.5.4 Glycosylated Hemoglobin (HbA1c)

Glycosylated hemoglobin (HbA1c) was measured via fingerstick whole blood using the A1CNow Plus Professional analyzer (PTS Diagnostics, Indianapolis, IN) at baseline and post-test. HbA1c reflects average blood glucose concentration over the preceding 8–12 weeks and was included as a marker of longer-term glycemic regulation and insulin sensitivity.

2.6 Descriptive Statistics

Descriptive statistics were calculated for all outcome variables at baseline and post-test for each group separately. Means and standard deviations are reported for all continuous variables. Baseline participant characteristics are presented in Table 1. Sex distribution was examined using frequency counts and percentages.

2.7 Sample Size

A formal a priori power analysis was not conducted prior to data collection given the cross-study pooled design combining two sequential studies. Post-hoc power analyses were conducted using G*Power (Version 3.1) for the between-group outcome (body weight change). Using the obtained effect size (η^2 = .240, f = 0.562), α = .05, and N = 79, the achieved power was the One-Way ANOVA was 0.995, indicating the total sample provided more than adequate power to detect the observed effects. Note that due to unequal group sizes (n = 16, 22, 41), G*power calculates power based on the average group size. For the HbA1c independent samples t-test (g = .738, α = .05, and n = 32), achieved power was 0.524, indicating the Study 2 subsample was underpowered for this secondary outcome. This limitation is acknowledged in Section 4.6. No interim analyses were conducted, and no stopping guidelines were prespecified for either study.

2.8 Statistical Analysis

Analyses were conducted on a per-protocol basis, including only participants who completed the full 30-day intervention and demonstrated at least 80% dietary adherence based on submitted daily log review. Participants who did not meet this threshold were excluded prior to analysis.

Assumptions of normality were assessed using the Shapiro-Wilk test and homogeneity of variance was assessed using Levene's test prior to analysis. As assumptions were satisfied for primary outcome variables, parametric tests were used throughout. Where Levene's test indicated a significant violation of homogeneity of variance, Welch's robust F-statistic is reported in place of the standard F. The trial protocol and statistical analysis plan are available from the corresponding author on reasonable request.

Within-group changes from baseline to post-test were examined using paired-samples t-tests for each condition separately. Effect sizes are reported as Hedges' g for all within-group comparisons, with g = 0.2 interpreted as small, g = 0.5 as medium, and g = 0.8 as large.

Between-group differences in the magnitude of change were examined using one-way analyses of variance (ANOVAs) on change scores with group as the between-subjects factor. Where omnibus F-tests indicated significant between-group differences, Tukey's Honest Significant Difference post-hoc comparisons were conducted to identify specific pairwise differences. Effect sizes are reported as eta-squared (η^2), with $\eta^2 = .01$ interpreted as small, $\eta^2 = .06$ as medium, and $\eta^2 = .14$ as large.

As HbA1c was collected in Study 2 only, the between-group comparison for this variable was conducted using an independent samples *t*-test comparing the IF and CKD + IF groups. Spearman's rho was used to examine associations between fat mass percentage change and cardiometabolic marker change for the full sample. Kendall's tau-b was employed for the smaller Study 2 subsample ($n = 32$) given its superior robustness with small samples and tied ranks.

Baseline equivalence across groups was verified prior to analysis using a one-way ANOVA for continuous variables and a chi-square test of independence for sex distribution. All analyses were conducted using IBM SPSS Statistics Version 31 (IBM Corp., Armonk, NY). Statistical significance was set at $\alpha = .05$ for all tests and all tests were two-tailed.

No imputation was performed for missing data. Participants with incomplete post-test outcome data were excluded from the relevant analyses. One participant in the IF group was unable to complete the BOD POD assessment due to claustrophobia, therefore body composition for this individual was estimated using ACSM circumference-based prediction equations as described in 2.5.1 and this participant was retained in body composition analyses.

Within-group paired t-tests, between-group ANOVAs with Tukey post-hoc comparisons, and the HbA1c independent samples t-test were all prespecified prior to analysis. Spearman and Kendall correlation analyses examining associations between fat mass change and cardiometabolic marker change were prespecified. No post-hoc analyses were conducted beyond those described in this section.

2.9 Use of Artificial Intelligence

A large language model (Claude, Anthropic) was used during manuscript preparation to assist with literature searches, formatting references from APA to Vancouver style, and grammatical revision of the text, and the generation of the CONSORT flow diagram figure and checksheet. All scientific content, study design, data analysis, and interpretation of results were performed by the authors. The authors reviewed and verified all AI-assisted content for accuracy prior to submission.

Results

3.1 Participant Characteristics

Study 1 (CKD and CKD + IF arms) were conducted from Sept. 1, 2021, to Nov. 15, 2021, including baseline testing and recruitment beginning Sept.1. There was a two- to three-week dietary transition period, followed by the 30-day intervention period and then post-testing ending Nov. 15. Study 2 (IF and

CKD + IF arms) were conducted from Sept. 15, 2023, to Oct. 30, including baseline testing beginning Sept. 15th, the 30-day intervention beginning Oct. 1 and ending Oct. 30, followed by post testing and the study concluded November 20. The 30-day follow up period for outcome assessment was completed for all participants within each respective study period.

Dietary adherence was assessed based on submitted daily log reviews. In Study 1, mean adherence was 88% in the CKD group and 90% in the CKD + IF group. In Study 2, mean adherence was 95% in the IF group and 83% in the CKD + IF group. Three CKD participants and eight CKD + IF participants were excluded for failing to meet the 80% adherence threshold. No participants in the IF group were excluded for non-adherence. All participants retained in the final analysis demonstrated at least 80% dietary adherence.

A total of 79 participants were included in the final analysis. The IF group comprised 16 participants (6 males, 10 females; mean age 49.69 ± 10.49 years), the CKD group comprised 22 participants (10 males, 12 females; mean age 41.77 ± 12.82 years), and the CKD + IF group comprised 41 participants (13 males, 28 females; mean age 46.88 ± 9.30 years). Groups did not differ significantly at baseline by age, $F(2,76) = 2.85$, $p = .064$, or sex distribution $\chi^2(2) = 1.171$, $p = .557$, supporting the comparability of groups prior to analysis. Baseline body composition, grip strength, and cardiometabolic markers are presented in Table 1.

3.2 Within-Group Pre-Post Changes

Paired-samples *t*-tests were conducted separately for each group to examine pre-to-post changes across all outcome variables. Results, with effect sizes, are presented in Table 2. Assumptions of normality and homogeneity of variance were verified prior to analysis.

Table 2
Pre- and post-intervention means, standard deviations, paired t-test statistics, 95% confidence intervals for mean differences, and effect sizes by dietary group

Variable	Pre M (SD)	Post M (SD)	Mean Diff	95% CI	t	df	p	Hedges' g
Group 1: Intermittent Fasting (n = 16)								
Body weight (lbs)	178.88 (40.19)	176.56 (37.91)	−2.31	[−4.03, − 0.60]	2.878	15	.011	−0.683
Body fat %	34.56 (9.44)	33.21 (8.75)	−1.35	[−2.39, − 0.31]	2.767	15	.014	−0.656
Fat mass %	63.85 (27.93)	61.15 (25.09)	−2.70	[−5.01, − 0.39]	2.495	15	.025	−0.592
Waist (inches)	35.19 (4.59)	34.25 (4.22)	−0.94	[−1.60, − 0.28]	3.053	15	.008	−0.724
Hips (inches)	43.67 (4.71)	42.34 (4.46)	−1.33	[−2.22, − 0.44]	3.171	15	.006	−0.752
WHR	0.805 (0.049)	0.809 (0.059)	+ 0.004	[−0.011, + 0.019]	0.562	15	.582	+ 0.133
Grip left (kg)	55.30 (19.27)	59.53 (22.56)	+ 4.23	[−0.25, + 8.72]	2.011	15	.063	+ 0.477
Grip right (kg)	58.33 (23.05)	61.62 (21.01)	+ 3.30	[−0.03, + 6.62]	2.112	15	.052	+ 0.501
HDL (mg/dL)	60.69 (12.20)	58.75 (13.98)	−1.94	[−5.94, + 2.07]	1.031	15	.319	−0.245

 HbA1c collected in Study 2 only (IF n = 16; CKD + IF n = 16). N/A = not applicable (CKD group, Study 1 only).

95% CI = 95% confidence interval for the mean difference (post − pre). Negative values indicate reduction; positive values indicate increase.

Negative Hedges' g indicates reduction (desired for body composition outcomes). Positive g indicates increase (desired for grip strength).

M = mean; SD = standard deviation; WHR = waist-to-hip ratio; TG:HDL = triglyceride-to-HDL ratio.

Variable	Pre M (SD)	Post M (SD)	Mean Diff	95% CI	t	df	p	Hedges' g
Group 1: Intermittent Fasting (n = 16)								
Triglycerides (mg/dL)	131.56 (72.64)	119.13 (58.68)	−12.44	[−33.54, + 8.66]	1.256	15	.228	−0.298
TG:HDL ratio	2.45 (1.85)	2.28 (1.67)	−0.167	[−0.544, + 0.211]	0.941	15	.361	−0.223
HbA1c (%)□	5.73 (1.57)	5.66 (1.45)	−0.075	[−0.221, + 0.071]	1.093	15	.292	−0.259
Group 2: Clean Ketogenic Diet (n = 22)								
Body weight (lbs)	210.08 (42.96)	197.84 (38.24)	−12.24	[−16.07, − 8.41]	6.643	21	< .001	−1.365
Body fat %	34.35 (9.57)	31.25 (9.85)	−3.10	[−4.32, − 1.89]	5.314	21	< .001	−1.092
Fat mass %	73.44 (31.42)	63.27 (28.67)	−10.17	[−12.96, − 7.37]	7.566	21	< .001	−1.555
Waist (inches)	41.03 (5.77)	38.44 (4.49)	−2.59	[−3.71, − 1.48]	4.832	21	< .001	−0.993
Hips (inches)	45.27 (5.44)	43.70 (4.65)	−1.57	[−2.11, − 1.02]	5.992	21	< .001	−1.231
WHR	0.908 (0.087)	0.882 (0.083)	−0.026	[−0.048, − 0.003]	2.378	21	.027	−0.489

□ *HbA1c collected in Study 2 only (IF n = 16; CKD + IF n = 16). N/A = not applicable (CKD group, Study 1 only).*

95% CI = 95% confidence interval for the mean difference (post − pre). Negative values indicate reduction; positive values indicate increase.

Negative Hedges' g indicates reduction (desired for body composition outcomes). Positive g indicates increase (desired for grip strength).

M = mean; SD = standard deviation; WHR = waist-to-hip ratio; TG:HDL = triglyceride-to-HDL ratio.

Variable	Pre M (SD)	Post M (SD)	Mean Diff	95% CI	t	df	p	Hedges' g
Group 1: Intermittent Fasting (n = 16)								
Grip left (kg)	37.95 (10.08)	37.05 (10.87)	−0.90	[−1.94, + 0.15]	1.785	21	.089	−0.367
Grip right (kg)	38.05 (11.11)	38.85 (11.69)	+ 0.80	[−0.56, + 2.15]	1.224	21	.235	+ 0.252
HDL (mg/dL)	52.91 (8.92)	51.00 (13.81)	−1.91	[−5.98, + 2.16]	0.975	21	.340	−0.200
Triglycerides (mg/dL)	171.36 (98.24)	123.14 (53.92)	−48.23	[−81.65, −14.80]	3.001	21	.007	−0.617
TG:HDL ratio	3.54 (2.76)	2.60 (1.46)	−0.940	[−1.805, −0.074]	2.257	21	.035	−0.464
HbA1c (%)□	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Group 3: Combined CKD + IF (n = 41; HbA1c n = 16)								
Body weight (lbs)	199.04 (50.03)	188.26 (48.05)	−10.77	[−12.79, − 8.76]	10.816	40	< .001	−1.657
Body fat %	34.87 (8.76)	33.13 (9.65)	−1.74	[−2.70, − 0.78]	3.677	40	< .001	−0.563
Fat mass %	70.31 (30.19)	64.04 (29.95)	−6.26	[−8.51, − 4.01]	5.629	40	< .001	−0.863
Waist (inches)	39.09 (6.51)	36.90 (6.29)	−2.19	[−2.80, − 1.58]	7.264	40	< .001	−1.113

□ *HbA1c collected in Study 2 only (IF n = 16; CKD + IF n = 16). N/A = not applicable (CKD group, Study 1 only).*

95% CI = 95% confidence interval for the mean difference (post − pre). Negative values indicate reduction; positive values indicate increase.

Negative Hedges' g indicates reduction (desired for body composition outcomes). Positive g indicates increase (desired for grip strength).

M = mean; SD = standard deviation; WHR = waist-to-hip ratio; TG:HDL = triglyceride-to-HDL ratio.

Variable	Pre M (SD)	Post M (SD)	Mean Diff	95% CI	t	df	p	Hedges' g
Group 1: Intermittent Fasting (n = 16)								
Hips (inches)	44.90 (5.73)	43.33 (5.05)	−1.58	[−2.11, −1.05]	6.043	40	< .001	−0.926
WHR	0.871 (0.100)	0.851 (0.101)	−0.020	[−0.034, −0.006]	2.847	40	.007	−0.436
Grip left (kg)	46.64 (25.57)	50.17 (27.92)	+ 3.53	[+2.24, + 4.82]	5.535	40	< .001	+ 0.848
Grip right (kg)	49.00 (26.09)	52.52 (28.19)	+ 3.51	[+2.28, + 4.75]	5.738	40	< .001	+ 0.879
HDL (mg/dL)	60.93 (14.94)	62.24 (14.29)	+ 1.32	[−2.16, + 4.80]	0.765	40	.449	+ 0.117
Triglycerides (mg/dL)	173.49 (129.71)	123.20 (82.43)	−50.29	[−70.25, −30.34]	5.093	40	< .001	−0.780
TG:HDL ratio	3.34 (3.12)	2.23 (1.95)	−1.109	[−1.592, −0.625]	4.634	40	< .001	−0.710
HbA1c (%)□	5.33 (0.41)	5.03 (0.39)	−0.306	[−0.484, −0.129]	3.672	15	.002	−0.871
□ *HbA1c collected in Study 2 only (IF n = 16; CKD + IF n = 16). N/A = not applicable (CKD group, Study 1 only).*								
95% CI = 95% confidence interval for the mean difference (post − pre). Negative values indicate reduction; positive values indicate increase.								
Negative Hedges' g indicates reduction (desired for body composition outcomes). Positive g indicates increase (desired for grip strength).								
M = mean; SD = standard deviation; WHR = waist-to-hip ratio; TG:HDL = triglyceride-to-HDL ratio.								

All three dietary conditions produced significant reductions in body weight, body fat percentage, fat mass percentage, waist circumference, and hip circumference, $p < .05$. Effect sizes were medium to very large across these outcomes, with CKD (Hedges' $g = 1.365$ for weight) and CKD + IF ($g = 1.657$ for

weight) showing particularly strong effects. The IF group also produced significant within-group improvements in body composition outcomes, though with smaller effect sizes (g = 0.683 for weight).

Grip strength improved significantly for both the left and right hand in the CKD + IF group, grip left, $t(40) = 5.535$, $p < .001$, $g = 0.848$; grip right, $t(40) = 5.738$, $p < .001$, $g = 0.879$, representing large effects. The IF group showed a trend toward grip improvement, grip left, $p = .063$; grip right, $p = .052$. No significant within-group grip strength changes were observed in the CKD group.

Table 1
Baseline participant characteristics by dietary group

Variable	**IF (n = 16)**	**CKD (n = 22)**	**CKD + IF (n = 41)**
Age (years, M ± SD)	49.69 ± 10.49	41.77 ± 12.82	46.88 ± 9.30
Sex (male/female)	6/10	10/12	13/28
Body weight (lbs, M ± SD)	178.88 ± 40.19	210.08 ± 42.96	199.04 ± 50.03
Body fat % (M ± SD)	34.56 ± 9.44	34.35 ± 9.57	34.87 ± 8.76
Fat mass % (M ± SD)	63.85 ± 27.93	73.44 ± 31.42	70.31 ± 30.19
Waist (inches, M ± SD)	35.19 ± 4.59	41.03 ± 5.77	39.09 ± 6.51
Hips (inches, M ± SD)	43.67 ± 4.71	45.27 ± 5.44	44.90 ± 5.73
WHR (M ± SD)	0.81 ± 0.05	0.91 ± 0.09	0.87 ± 0.10
Grip left (kg, M ± SD)	55.30 ± 19.27	37.95 ± 10.08	46.64 ± 25.57
Grip right (kg, M ± SD)	58.33 ± 23.05	38.05 ± 11.11	49.00 ± 26.09
HDL (mg/dL, M ± SD)	60.69 ± 12.20	52.91 ± 8.92	60.93 ± 14.94
Triglycerides (mg/dL, M ± SD)	131.56 ± 72.64	171.36 ± 98.24	173.49 ± 129.71
TG:HDL ratio (M ± SD)	2.45 ± 1.85	3.54 ± 2.76	3.34 ± 3.12
HbA1c (%)□ (M ± SD)	5.73 ± 1.57	N/A	5.33 ± 0.41

□ *HbA1c was collected in Study 2 only (IF and CKD + IF groups; n = 32 total).*

M = mean; SD = standard deviation; WHR = waist-to-hip ratio; TG:HDL = triglyceride-to-HDL cholesterol ratio; IF = intermittent fasting; CKD = clean ketogenic diet.

Cardiometabolic improvements were most pronounced in the CKD and CKD + IF groups. Triglycerides decreased significantly in CKD, $t(21) = 3.001$, $p = .007$, $g = 0.617$; and CKD + IF, $t(40) = 5.093$, $p < .001$, $g = 0.780$, but not in IF, $p = .228$. The TG:HDL ratio improved significantly in CKD, $t(21) = 2.257$, $p = .035$, $g = 0.464$; and CKD + IF, $t(40) = 4.634$, $p < .001$, $g = 0.710$, but not in IF, $p = .361$. WHR declined significantly in

CKD and CKD + IF (both $p < .05$) but not in IF ($p = .582$). HDL did not change significantly within any group (all $p > .05$).

HbA1c was collected in Study 2 only, comparing IF and CKD + IF; $n = 16$ per group. A significant HbA1c reduction was observed in the CKD + IF group, $t(15) = 3.672$, $p = .002$, $g = 0.871$, representing a large effect and a mean reduction of 0.306 percentage points over 30 days. HbA1c did not change significantly in the IF group, $t(15) = 1.093$, $p = .292$.

3.3 Between-Group Differences in Magnitude of Change

Separate ANOVAs examined whether the magnitude of change differed across the three dietary conditions. Where Levene's test indicated violation of homogeneity of variance, Welch's robust F-statistic is reported. Results of significant and selected non-significant analyses are presented in Table 3.

Body weight change differed significantly across groups, $F(2, 76) = 12.003$, $p < .001$, $\eta^2 = .240$, with CKD (adjusted $M = -12.24$ lbs.) and CKD + IF (adjusted $M = -10.77$ lbs.) producing significantly greater weight loss than IF (adjusted $M = -2.31$ lbs.; both $p < .001$). CKD and CKD + IF did not differ significantly from each other, $p = .681$, suggesting carbohydrate restriction was the primary mechanism producing greater weight loss in this sample regardless of the addition of a time-restricted eating window.

Fat mass change also differed significantly across groups, $F(2, 76) = 6.373$, $p = .003$, $\eta^2 = .144$. The CKD group ($M = -10.17\%$) demonstrated significantly greater fat mass reduction than the IF group ($M = -2.70\%$; $p = .002$). The CKD + IF group ($M = -6.26\%$) did not differ significantly from either condition.

Grip strength in the left hand differed significantly across groups, Welch $F(2,33.37) = 15.829$, $p < .001$, $\eta^2 = .157$. Both the IF group ($M = +4.23$ kg; $p = .006$) and the CKD + IF group ($M = +3.53$ kg; $p = .003$) showed significantly greater left grip improvements than the CKD group ($M = -0.90$ kg). IF and CKD + IF did not differ from each other, $p = .880$. A similar pattern emerged for right grip strength, where CKD + IF demonstrated significantly greater improvement than CKD, Welch $F(2, 33.87) = 4.730$, $p = .015$, Tukey $p = .049$.

Table 3
One-way ANOVA results for between-group differences in change scores with Tukey HSD post-hoc comparisons and eta-squared effect sizes with 95% confidence intervals

Outcome	F(2, 76)	p	η² (95% CI)	Tukey HSD pairwise comparisons	Welch F
Body weight	12.003	< .001	.240 [.081, .377]	IF < CKD (p < .001); IF < CKD + IF (p < .001); CKD = CKD + IF (p = .681)	27.172**
Fat mass %	6.373	.003	.144 [.020, .276]	CKD > IF (p = .002); CKD + IF = IF; CKD = CKD + IF	9.311**
Grip left	7.103	.001	.157 [.027, .291]	IF > CKD (p = .006); CKD + IF > CKD (p = .003); IF = CKD + IF	15.829**
Grip right	3.061	.053	.075 [.000, .191]	CKD + IF > CKD (p = .049)	4.730*
Waist	3.362	.040	.081 [.000, .200]	CKD > IF (p = .037); CKD + IF = IF; CKD = CKD + IF	5.656**
Hips	0.159	.853	.004 [.000, .046]	None	—
WHR	2.337	.104	.058 [.000, .167]	None	—
Body fat %	2.360	.101	.058 [.000, .167]	None	—
HDL	1.051	.355	.027 [.000, .114]	None	—
TG:HDL ratio	2.169	.121	.054 [.000, .161]	None (trend: CKD + IF > IF)	—
Triglycerides	1.413	.250	.036 [.000, .131]	ns between groups; within-group significant in CKD and CKD + IF	—

 Levene's test indicated violation of homogeneity of variance (p < .05); Welch's robust F-statistic reported with adjusted degrees of freedom.

 Levene's test p = .013; Welch F reported.

** p < .05; ** p < .01. η² = eta-squared. ns = not significant; — = not applicable.*

95% CI for η² from SPSS ANOVA effect sizes output. Groups: 1 = IF; 2 = CKD; 3 = CKD + IF.

Changes in waist circumference differed significantly across groups, $F(2, 76) = 3.362$, $p = .040$, $\eta^2 = .081$, Welch $F = 5.656$, $p = .007$. The CKD group produced significantly greater reductions ($M = -2.59$ inches) than the IF group ($M = -0.94$ inches, $p = .037$). No other pairwise comparisons reached significance. Hip circumference, WHR, body fat percentage, TG:HDL ratio, triglycerides, and HDL did not differ significantly between groups in magnitude of change (all $p > .05$).

3.4 HbA1c (IF versus CKD + IF)

As HbA1c was collected only in Study 2, between-group comparison was limited to the IF and CKD + IF groups ($n = 16$ per group). An independent samples t-test revealed that CKD + IF produced significantly greater HbA1c reductions than IF, $t(30) = 2.141$, $p = .041$, Hedges' $g = 0.738$, with mean A1c changes of −0.306% (CKD + IF) versus − 0.075% (IF), a mean difference of 0.231 percentage points (95% CI: 0.011, 0.452). See Table 4.

Table 4
HbA1c comparison between IF and CKD + IF (Study 2 only; n = 16 per group) with 95% confidence intervals

Group	N	Pre HbA1c M (SD)	Post HbA1c M (SD)	Mean Diff (95% CI)	t	df	p	Hedges' g
IF	16	5.73 (1.57)	5.66 (1.45)	−0.075 [−0.221, + 0.071]	1.093	15	.292	−0.259
CKD + IF	16	5.33 (0.41)	5.03 (0.39)	−0.306 [−0.484, −0.129]	3.672	15	.002	−0.871
Between-group diff				+ 0.231 [+ 0.011, + 0.452]	2.141	30	.041	+ 0.738

Rows 1–2: within-group paired t-test results. Row 3: between-group independent samples t-test result.

95% CI = 95% confidence interval for the mean difference. g = Hedges' correction.

CKD group was not in Study 2 and therefore has no HbA1c data.

3.5 Summary of Findings

Across within-group analyses, all three dietary conditions produced significant improvements in body weight, body fat percentage, fat mass percentage, waist circumference, and hip circumference. Carbohydrate-restricted conditions additionally improved triglycerides, TG:HDL ratio, and WHR within

groups. CKD + IF uniquely produced significant bilateral grip strength improvements and the largest HbA1c reduction. Between-group analyses indicated that carbohydrate restriction was the primary mechanism producing greater weight loss and fat mass reduction compared to time restriction alone. Grip strength improvement was greater in the IF and CKD + IF groups than in CKD, suggesting that time restriction may contribute independently to functional muscle outcomes. HbA1c reductions were significantly greater in CKD + IF than IF, supporting the additive glycemic benefit of combining both dietary strategies.

3.6 Correlational Analyses

Spearman correlations were conducted to examine associations between fat mass percentage change and cardiometabolic marker change. Fat mass percentage change was significantly correlated with TG:HDL ratio changes across the full sample ($r_s = -.250$, $p = .026$, $n = 79$). Participants who achieved greater fat mass reduction also demonstrated greater reductions in TG:HDL ratio, consistent with the established mechanistic relationship between adipose tissue loss and cardiometabolic risk improvement. The association between fat mass percentage change and HbA1c change was examined using Kendall's tau-b given the smaller Study 2 sample size, and was not statistically significant ($\tau b = .100$, $p = .434$, $n = 32$), a finding likely reflecting insufficient statistical power to detect a small effect in this subsample.

3.7 Adverse Events

No adverse events or unintended effects were reported by participants in any group during the 30-day intervention period. No participants required medical attention because of participation. One participant experience claustrophobia during the BOD POD assessment and completed body composition measurement using an alternative method as described in Section 2.5.1, but this was not treated as an adverse event.

Discussion

The present study used a three-arm pre-post design to compare the effects of intermittent fasting, a clean ketogenic diet, and their combination on body composition, cardiometabolic markers, grip strength, and glycemic control in 79 participants. The dietary groups were comparable at baseline by age and sex distribution, supporting comparability prior to analysis. All three dietary conditions produced significant within-group improvements in body weight, body fat percentage, fat mass percentage, and waist and hip circumference over 30 days. Carbohydrate restriction produced greater weight loss and fat mass reduction, while the addition of a 16:8 intermittent fasting window produced additive glycemic benefit and significantly improved bilateral grip strength, with implications for both metabolic syndrome management and future neuropsychological investigation.

4.1 Body Weight and Fat Mass: The Central Role of Carbohydrate Restriction

The most robust between-group finding was the significantly greater weight loss in the CKD and CKD + IF groups compared to IF, with a large effect size, $F(2, 76) = 12.003$, $p < .001$, $\eta^2 = .240$. CKD also produced significantly greater fat mass percentage reduction than IF ($p = .002$), with a large effect ($\eta^2 = .144$). These findings are consistent with a 2026 meta-analysis of energy-matched randomized controlled trials confirming that low-carbohydrate diets reduce body weight and fat mass to a significantly greater extent than high-carbohydrate diets without detrimental effects on fat-free mass [19] and extend that evidence to a three-arm comparison including a time-restricted condition.

The superior body composition outcomes in carbohydrate-restricted conditions reflect the multi-layered design of the CKD protocol, which targets metabolic dysfunction through three distinct mechanisms. Restricting total carbohydrate intake to 20 grams per day from whole unprocessed sources reduces circulating insulin levels and promotes adipose tissue lipolysis. The elimination of refined sugars and high-fructose corn syrup reduces hepatic lipid accumulation and improves insulin sensitivity through fructose-specific metabolic pathways [14, 15]. Finally, the removal of ultra-processed foods addresses a third pathway, given the dose-dependent association between ultra-processed food exposure and cardiovascular and metabolic risk [17]. Together, these elements of the CKD protocol address the root causes of metabolic syndrome rather than managing symptoms alone. This is further supported by the significant correlation between fat mass percentage change and TG:HDL ratio changes across the full sample ($rs = -.250$, $p = .026$), confirming that greater fat mass reduction was associated with greater cardiometabolic risk improvement, regardless of dietary condition.

Notably, CKD and CKD + IF did not differ significantly on body weight reduction ($p = .681$) or fat mass percentage, suggesting that the addition of a 16:8 fasting window did not produce additional body composition benefit beyond carbohydrate restriction alone over 30 days. This finding should be interpreted cautiously, as the short intervention window may be insufficient to reveal synergistic effects that would emerge over longer periods, particularly for visceral adipose tissue reduction, which cannot be distinguished from subcutaneous fat using BOD POD methodology. Future research incorporating dual-energy X-ray absorptiometry would allow direct quantification of visceral fat and provide a more sensitive test of this question.

4.2 Cardiometabolic Markers: The Specific Benefits of Eliminating Refined Carbohydrates

Cardiometabolic improvements were observed in the CKD and CKD + IF groups but not in the IF group. Triglycerides and the TG:HDL ratio improved significantly and WHR declined in both carbohydrate-restricted conditions but not in IF alone. These patterns indicate that carbohydrate restriction is the primary mechanism producing cardiometabolic improvement, with the descriptive pattern for TG:HDL change across groups suggesting a dose-response relationship: IF = − 0.167, CKD = − 0.940, CKD + IF = − 1.109.

The elimination of refined sugars and high-fructose corn syrup in the CKD protocol has mechanistic significance beyond general carbohydrate restriction. When dietary carbohydrate is restricted, the liver

loses its primary precursor for triglyceride synthesis, leading to reductions in VLDL secretion and circulating triglycerides [18], while HFCS elimination specifically addresses hepatic de novo lipogenesis and fructose-driven insulin resistance, with clinically significant changes occurring within two weeks of exposure [14]. These findings suggest that carbohydrate quality matters as much as quantity in metabolic syndrome management, and that the absence of significant between-group TG:HDL differences on the ANOVA (p = .121) likely reflects limited statistical power in the IF group (n = 16) rather than a true null effect.

HDL cholesterol did not change significantly within any group, consistent with the known lag in lipoprotein particle remodeling, which typically requires 12 or more weeks to stabilize following dietary change [27]. Future research with longer follow-up periods would be expected to reveal HDL increases as triglyceride reductions are sustained over time.

4.3 Grip Strength: The Independent Contribution of the Intermittent Fasting Window

Grip strength improved significantly in both IF-containing conditions but not in the CKD group, and between-group analyses confirmed that the magnitude of improvement in both IF and CKD + IF was significantly greater than in CKD. The absence of a difference between IF and CKD + IF indicates that a fasting window, rather than carbohydrate restriction, was the common element producing this outcome.

Grip strength is a validated functional marker of skeletal muscle integrity inversely associated with systemic inflammation, dyslipidemia, metabolic syndrome risk, and body fat percentage [40, 46], and lower grip strength in older adults has been independently associated with elevated inflammatory markers including CRP and TNF-α and increased fall risk [47, 48, 45]. Its improvement in IF-containing conditions but not CKD alone suggests that extending the daily fasted state produces functional benefits beyond dietary modification. Extended fasting activates autophagy through mTOR suppression, clearing dysfunctional proteins within muscle cells and potentially improving contractile function [25, 12], while the fasted hormonal environment of reduced insulin and elevated growth hormone pulsatility may additionally support anabolic processes during the feeding window.

These findings suggest a practical clinical distinction. Carbohydrate restriction alone appears sufficient for body weight and lipid panel improvement, while the addition of a 16:8 fasting window provides meaningful incremental benefit for grip strength. Future research should incorporate DXA-based regional lean mass assessment and longer follow-up to determine whether this functional strength benefit reflects preservation of appendicular skeletal muscle index, a clinically relevant outcome for aging adults with metabolic syndrome, and whether resistance exercise combined with CKD + IF produces additive improvements in both functional strength and cardiometabolic markers.

4.4 Glycemic Control: Combining Carbohydrate Restriction with Time Restriction

The HbA1c comparison between IF and CKD + IF was among the most clinically significant findings in this study. CKD + IF produced a mean HbA1c reduction of 0.306% over 30 days compared to 0.075% in IF, a statistically significant difference, $t(30) = 2.141$, $p = .041$, $g = 0.738$, 95% CI: 0.011, 0.452, with a large within-group effect size in the CKD + IF group, $t(15) = 3.672$, $p = .002$, $g = 0.871$. Given that HbA1c reflects average blood glucose over the preceding 8 to 12 weeks, a measurable reduction in just 30 days indicates a rapid and substantial shift in glycemic regulation. For context, most medications used to treat type 2 diabetes mellitus produce reductions of 0.5 to 1.0% over 3 to 6 months.

The superior HbA1c improvement in CKD + IF reflects the combined action of two complementary strategies. Carbohydrate restriction removes the primary dietary source of blood sugar spikes, while the 16:8 fasting window reduces the total time the body spends in a high-insulin state and improves the body's ability to use glucose effectively [49, 50]. The non-significant HbA1c change in IF ($p = .292$) combined with the significant between-group difference suggests that what one eats matters more than when one eats for glycemic control over 30 days, while combining both strategies produces greater benefit than either alone [13]. The association between fat mass change and HbA1c change was not significant in the Study 2 subsample ($\tau b = .100$, $p = .434$, $n = 32$), likely due to the small sample size rather than a true absence of relationship.

4.5 Metabolic Health, Neuroinflammation, and the Case for Future Neuropsychological Investigation

The cardiometabolic improvements documented across conditions suggest that both CKD and CKD + IF began restoring metabolic flexibility, the capacity to shift efficiently between carbohydrate and fat oxidation that is fundamentally impaired in metabolic syndrome [8, 9]. This is significant because metabolic inflexibility does not remain confined to peripheral tissues. Brain insulin resistance, defined as the impaired response of central nervous system tissues to insulin signaling, has been identified as a key pathological hub linking peripheral metabolic dysfunction to neuropsychiatric comorbidities, impairing mitochondrial function, increasing neuroinflammation, and disrupting synaptic plasticity in regions critical for mood, memory, and executive function [29]. The reductions in triglycerides, TG:HDL ratio, body fat, and HbA1c documented in the CKD and CKD + IF groups represent a meaningful reduction in the metabolic conditions that sustain this neuroinflammatory cascade.

The elimination of refined sugars and high-fructose corn syrup in the CKD protocol is particularly relevant here, as fructose metabolism in the brain promotes neuroinflammation through elevated uric acid production and metabolic signaling linked to Alzheimer's disease pathology [3]. This aspect of the CKD protocol targets a direct pathway to central insulin resistance and neuroinflammation that general caloric restriction does not address. The cardiometabolic improvements observed here, particularly the TG:HDL and HbA1c reductions in the CKD + IF group, suggest that the neuroinflammatory burden in these participants was already shifting downward over 30 days. Additionally, the carbohydrate restriction and the extended fasting in the CKD and CKD + IF conditions would have promoted ketone body

production, providing the brain with beta-hydroxybutyrate as an alternative fuel source shown to improve mitochondrial function, reduce oxidative stress, and support neurotransmitter synthesis [33].

A companion analysis examining self-reported cognitive and psychological outcomes in the same participant sample is currently underway, including measures of mood, anxiety, perceived stress, energy, sleep quality, short-term and long-term memory, and brain fog. Testing whether participants who achieved greater cardiometabolic improvements also reported greater psychological benefit will provide a direct empirical link between the metabolic findings reported here and the neurological consequences of metabolic improvement. Future research incorporating quantitative EEG assessment would allow objective neurophysiological verification of these cognitive benefits, building on recent evidence that a ketogenic dietary state produces measurable changes in neuronal aperiodic activity consistent with enhanced information processing [37]. Combined with DXA-based body composition assessment and a validated neuropsychological test battery, this represents the logical next step in characterizing the full neurological impact of reducing refined carbohydrates and extending the daily fasted window.

4.6 Limitations

Several limitations should be acknowledged when interpreting these findings. First, the cross-study pooled design draws data from two sequential studies conducted at different times. Although groups did not differ significantly at baseline by age or sex distribution, a trend toward age difference was observed, with Study 2 participants averaging approximately six years older than Study 1 participants, which may have modestly influenced outcomes, particularly grip strength given known age-related variation in muscle function. Additionally, given that the CKD + IF arm included participants from both Study 1 and Study 2, baseline equivalence between these subgroups was verified prior to pooling and no significant differences were found, allowing for the combination of the CKD + IF participants across studies.

Second, dietary adherence was monitored through self-reported daily food logs and participants were required to demonstrate at least 80% adherence to remain in the final analysis. While this threshold strengthens confidence in the findings, self-reported logs remain subject to under-reporting, recall bias, and social desirability effects. Future studies should incorporate objective dietary biomarkers or digital food diary applications to improve adherence verification.

Third, the BOD POD provides valid and reliable whole-body estimates of fat mass and fat-free mass but cannot distinguish visceral from subcutaneous adipose tissue. The improvements in waist circumference and TG:HDL ratio in the carbohydrate-restricted groups are consistent with visceral fat reduction, but this cannot be confirmed without dual-energy X-ray absorptiometry. The next phase of this research will incorporate DXA body composition assessment to directly quantify visceral adipose tissue and provide a more complete picture of the regional body composition changes produced by these dietary interventions.

Fourth, one participant in the IF group was unable to complete BOD POD assessment due to claustrophobia, and body composition for this individual was estimated using ACSM circumference-

based prediction equations, introducing minor measurement inconsistency for that participant.

Finally, the 30-day intervention period is relatively short for characterizing the full metabolic trajectory of these interventions. HDL changes, visceral fat redistribution, and the full glycemic response typically require 12 or more weeks to stabilize. The between-group A1c and correlational analyses were additionally limited by the Study 2 subsample size (n = 32, 16 per group), which yielded achieved power of 0.524, which is insufficient to reliably detect effects of observed magnitude. The significant between-group differences should be interpreted cautiously and replication in a larger sample size is needed. Longitudinal studies with extended follow-up, larger samples, and the DXA and EEG assessments described above would allow a more complete characterization of both the metabolic and neurological benefits of these dietary strategies.

Conclusions

This three-arm comparison demonstrates that reducing dietary refined carbohydrates through a clean ketogenic diet produces the greatest improvements in body weight, fat mass, triglycerides, and TG:HDL ratio over 30 days. The elimination of refined sugars, high-fructose corn syrup, and ultra-processed foods carries independent mechanistic significance beyond general macronutrient restriction, targeting the specific foods and ingredients most directly linked to insulin resistance, dyslipidemia, and neuroinflammation. The addition of a 16:8 fasting window produced meaningful incremental benefits not achieved by carbohydrate restriction alone, including greater HbA1c reduction and bilateral grip strength improvement, suggesting that extending the daily fasted period contributes independently to both glycemic regulation and muscle function. The significant correlation between fat mass reduction and TG:HDL improvement further supports the mechanistic link between adipose tissue loss and cardiometabolic risk reduction, regardless of dietary strategy.

The cardiometabolic improvements documented here extend beyond metabolic health. By reducing insulin resistance, dyslipidemia, and hyperglycemia, these dietary strategies reduce the neuroinflammatory burden linking metabolic dysfunction to cognitive impairment, disrupted mood, impaired memory, and brain fog. A companion analysis of psychological and cognitive outcomes in the same sample will test this hypothesis directly. Future research incorporating quantitative EEG and objective neuropsychological assessment will provide independent neurophysiological verification. Given growing evidence linking metabolic syndrome and brain insulin resistance to Alzheimer’s disease and other neurodegenerative conditions [3, 29], dietary strategies that reduce refined carbohydrates and extend the daily fasted window may represent not only a first-line intervention for metabolic syndrome but a meaningful pathway for reducing neurological disease risk in a population where both are rising.

Abbreviations

ACSM
American College of Sports Medicine

ADP
Air displacement plethysmography
BDNF
Brain-derived neurotrophic factor
CKD
Clean ketogenic diet
CKD + IF
Combined clean ketogenic diet and intermittent fasting
DXA
Dual-energy X-ray absorptiometry
EEG
Electroencephalography
HbA1c
Glycosylated hemoglobin
HDL
High-density lipoprotein cholesterol
HFCS
High-fructose corn syrup
IF
Intermittent fasting
IRB
Institutional Review Board
mTOR
Mechanistic target of rapamycin
NCT
National Clinical Trial
T2DM
Type 2 diabetes mellitus
TG
HDL:Triglyceride-to-HDL ratio
TRE
Time-restricted eating
WHR
Waist-to-hip ratio

Declarations

Ethics Approval and Consent to Participate

Both studies were reviewed and approved as expedited reviews by the Institutional Review Board at the University of Tennessee at Martin prior to data collection. Study 1 (CKD and CKD+IF arms) received IRB

approval (No. 2021-872-E05-4065/MacK, Ang). Study 2 (IF arm) received IRB approval (No. 2022-925-E05-4065/MacK, Ang). All participants provided written informed consent prior to enrollment and were informed of their right to withdraw at any time without consequence. All procedures were conducted in accordance with the ethical standards of the institutional review board and with the 1964 Helsinki Declaration and its later amendments.

Consent for Publication

Not applicable. No individual participant data, images, or identifying information are reported in this manuscript.

Availability of Data and Materials

The de-identified individual participant datasets supporting the conclusions of this article are available from the corresponding author on reasonable request. Data will be provided in Microsoft Excel format or SPSS Version 31 data file with an accompanying data dictionary. Statistical analysis code (IBM SPSS Statistics Version 31 syntax files) is available from the corresponding author on request.

Competing Interests

The authors declare no competing interests.

Funding

Both studies were funded by internal faculty development grants from the University of Tennessee at Martin Faculty Development Program. The funding body had no role in the design of the study, data collection, analysis, interpretation of data, or writing of the manuscript.

Authors' Contributions

A.M. conceived the study design, led data collection for both studies, conducted the statistical analyses, and drafted the manuscript. J.F. contributed to study design, data collection, and manuscript review. T.S. contributed to data collection, interpretation of results, and manuscript review. A.E. contributed to data collection and manuscript review. A.D. contributed to data collection and manuscript review. D.S. contributed to study design, statistical consultation, and critical revision of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors wish to thank all participants for their commitment and dedication throughout the 30-day intervention period, and the student research assistants at the University of Tennessee at Martin who assisted with data collection.

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Figures

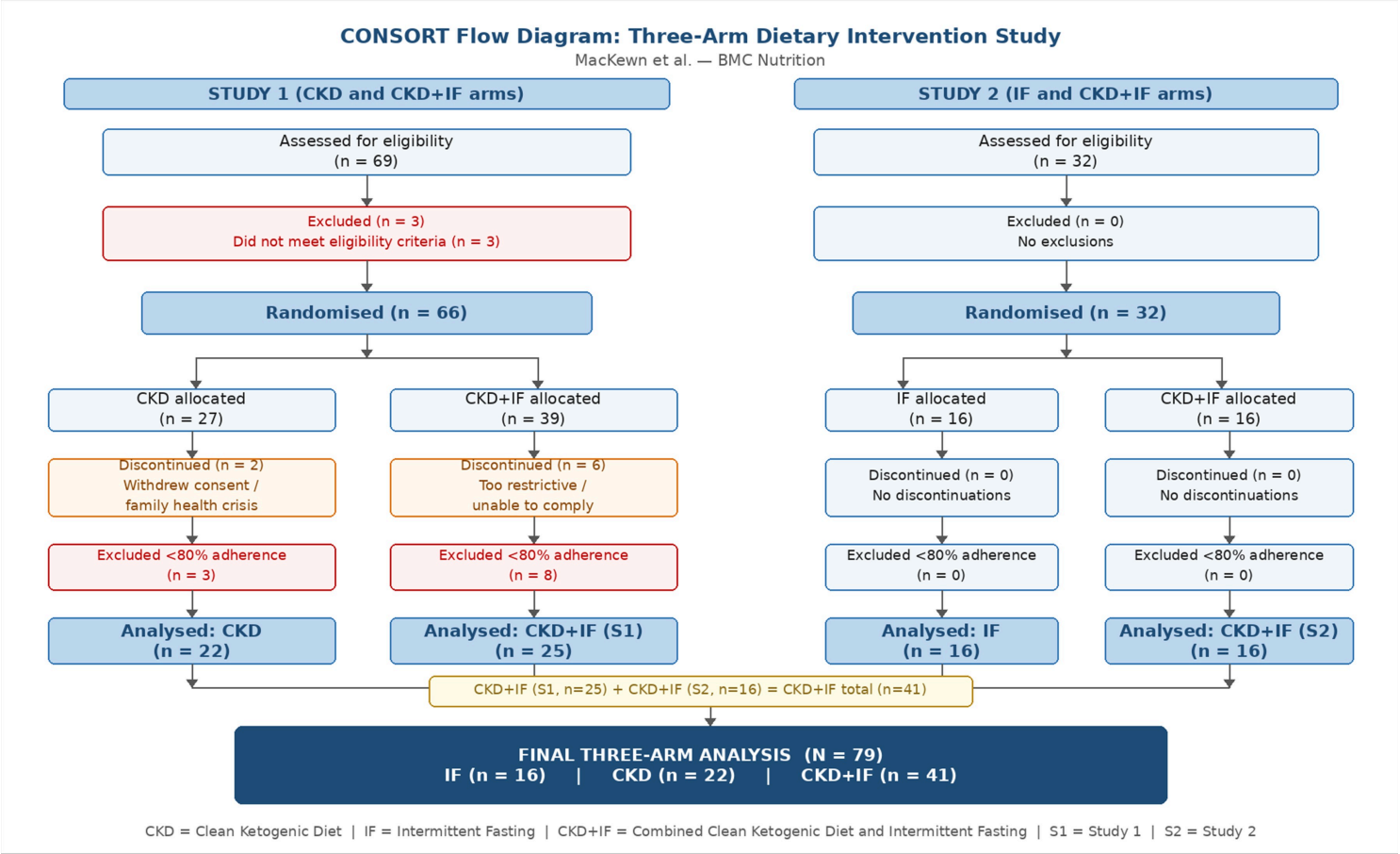


Figure 1

CONSORT flow diagram depicting participant enrollment, allocation, adherence, and analysis across Study 1 (CKD and CKD+IF arms, 2021) and Study 2 (IF and CKD+IF arms, 2023). CKD = clean ketogenic diet; IF = Intermittent fasting; CKD+IF = combined clean ketogenic diet and intermittent fasting