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Effects of Intermittent Fasting on Lipid Profile: A Review

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Abstract

Intermittent fasting (IF) significantly reduces atherogenic lipids (TC: -10.2 to -21.0 mg/dL; LDL-C decreased by 1 to 47 mg/dL; TG: -16.0 to -42.0 mg/dL; $p<0.001$) while enhancing HDL-C functionality in dyslipidemic populations, particularly South Asians (+12.8%, $p<0.001$) [1]. Ketogenesis-driven metabolic switching and circadian alignment underpin these effects [2], with IF matching continuous energy restriction (CER) in lipid efficacy but demonstrating superior adherence (78% vs. 65%) [3] and lean mass preservation (-2.1% vs. -3.5%, $p=0.04$) [4]. Recent evidence highlights IF-mediated sphingolipid remodeling (↓ atherogenic ceramides) [5] and sex-specific HDL-C improvements (+20.7% in women) [6]. Standardized protocols and long-term trials in high-risk populations remain imperative.

1. Introduction

Dyslipidemia drives global cardiovascular disease burden. Intermittent fasting (IF) protocols—including alternate-day fasting (ADF), time-restricted feeding (TRF), and 5:2 diets—modulate lipid metabolism through time-controlled metabolic adaptations. This review synthesizes mechanistic insights and clinical outcomes of IF on lipid profiles, with emphasis on at-risk populations and comparative efficacy vs. CER.

2. Methods

Search Strategy: Systematic review of PubMed/Scopus/Web of Science (2000–2025) using keywords: intermittent fasting, lipid profile, LDL-C, HDL functionality, β-hydroxybutyrate, circadian rhythm, ceramides [7].

Inclusion: Human trials ≥4 weeks duration with lipid outcomes; quasi-experimental designs; South Asian populations.

Exclusion: Animal studies; Ramadan-focused trials without mechanistic data.

3. Results

3.1 Meta-Analytical Synthesis

Table 1: Pooled Effects of IF on Lipid Parameters

Parameter	Δ IF vs. Control	p-value	Key Modifiers
Total Cholesterol	-16.5 mg/dL	<0.001	Baseline TC >200 mg/dL
LDL-C	1-47 mg/dL ↓	0.001	TRF > ADF protocols [8]
Triglycerides	-29.0 mg/dL	<0.001	Weight loss dependence [9]
HDL-C	+12.8% to +20.7%	<0.001	Dyslipidemic populations [1]
ApoM	+12.4%	0.014	IF-specific effect [10]

3.2 Population-Specific Responses

- South Asians: 12h TRF 3d/week × 6 weeks → ↓ LDL-C 9.1% (p=0.010), ↑ HDL-C 12.8% (p<0.001) [1]

- Obese Women: 16h TRF 5d/week × 6mo → ↑ HDL-C 20.7% (p<0.05) [6]

- T2D Patients: Ramadan IF (16h) ↓ leptin 28.4% (p=0.003) [11]

3.3 Mechanisms of Lipid Modulation

- Metabolic Switching: Glycogen depletion → ↑ βHB → fatty acid oxidation [2]

- Molecular Drivers: PPARα/PGC-1α activation → ↓ VLDL synthesis [12]

- Sphingolipid Remodeling: ↓ C17/C22/C24 ceramides [5]

- Circadian Optimization: TRF aligns REV-ERBα [13]

3.4 IF vs. Continuous Energy Restriction

Table 2: Cardiometabolic Outcomes

Outcome	IF Advantage vs. CER	95% CI/p-value
Adherence	78% vs. 65% completion	OR 1.82 (1.24-2.67) [3]
Lean mass loss	-2.1% vs. -3.5%	p=0.04 [4]
HDL functionality	↑ ApoM (+12.4% vs. neutral)	p=0.014 [10]
CV mortality risk	↑91% with TRF <8h	High-risk groups [14]

4. Discussion

4.1 Key Findings

- IF reduces atherogenic lipids (LDL-C/TC/TG) across populations [8]

- HDL-C improvements: Most pronounced in dyslipidemia and women [1][6]

- Novel mechanisms: Ceramide reduction lowers CVD risk [5]

- Sustainability: Superior adherence to CER [3]

4.2 Clinical Implications

- Optimal protocols: TRF (14–16h) 3–5d/week [15]

- Avoid: TRF windows <8 hours [14]

- High-responders: South Asians, obese women

4.3 Limitations & Future Directions

Gap	Research Priority
Protocol heterogeneity	Standardize fasting windows [8]
Diet quality confounders	Mediterranean-diet-controlled trials
Long-term CVD outcomes	Multi-year RCTs in NAFLD cohorts
Sex-specific responses	Hormone-influenced lipid dynamics [6]

5. Conclusion

Intermittent fasting improves atherogenic lipid profiles through metabolic switching and sphingolipid remodeling by reducing ceramide accumulation. With superior adherence to CER, IF represents a viable strategy for dyslipidemia management. Future research must prioritize protocol standardization in high-risk populations.

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