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Research Article

Aerobic Training-Induced Gut Microbiome Shifts And Associations With Insulin Sensitivity In Prediabetes

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ABSTRACT

Background: Prediabetes is characterized by impaired glucose regulation and represents a critical window for preventive strategies. Emerging evidence links gut microbiome composition to metabolic health and insulin sensitivity. Exercise, particularly aerobic training, has been shown to modify gut microbial diversity and function, but its effects in individuals with prediabetes remain poorly defined.

Methods: We conducted a 16-week randomized controlled trial involving 92 adults with prediabetes (age 40–65 years, BMI 27–35 kg/m²). Participants were randomized to an aerobic training group (n=46; supervised treadmill and cycling sessions, 45 minutes, 4 days/week, at 60–70% VO_2max) or a control group (n=46; standard lifestyle advice). Gut microbiome profiles were analyzed using 16S rRNA sequencing of stool samples at baseline and week 16. Insulin sensitivity was assessed by homeostatic model assessment of insulin resistance (HOMA-IR) and oral glucose tolerance test (OGTT). Statistical analyses included paired t-tests, PERMANOVA for microbial community structure, and multivariable regression models.

Results: Aerobic training significantly reduced HOMA-IR (−22%, $p<0.01$) and improved 2-h OGTT glucose levels compared with controls (−18%, $p<0.05$). Training increased microbial α-diversity (Shannon index +15%, $p<0.01$) and shifted ß-diversity toward greater abundance of butyrate-producing taxa (*Faecalibacterium prausnitzii*, *Roseburia* spp.). Reductions in pro-inflammatory taxa (*Enterobacteriaceae*) were observed. Multivariable regression demonstrated that increases in *Faecalibacterium* abundance independently predicted improvements in HOMA-IR (β = −0.35, $p=0.002$).

Conclusion: Aerobic training in prediabetic adults induces beneficial gut microbiome shifts characterized by enrichment of short-chain fatty acid–producing taxa, alongside improvements in insulin sensitivity. These findings highlight exercise as a modifiable intervention targeting host–microbe interactions in metabolic disease prevention.

Keywords: Aerobic Exercise, Gut Microbiome, Prediabetes, Insulin Sensitivity, HOMA-IR, Butyrate-Producing Bacteria.

INTRODUCTION

Prediabetes is a high-risk metabolic state marked by impaired fasting glucose and/or impaired glucose tolerance, affecting an estimated 374 million adults globally [1]. Without timely intervention, up to 70% of individuals with prediabetes will progress to type 2 diabetes within their lifetime [2]. Lifestyle modification remains the cornerstone of diabetes prevention, with exercise and dietary interventions demonstrating robust effects in delaying or reversing progression [3].

Beyond traditional metabolic risk factors, attention has turned toward the gut microbiome as a critical determinant of glucose homeostasis. The intestinal microbial ecosystem exerts profound influences on host metabolism through short-chain fatty acid (SCFA) production, bile acid modulation, and immune regulation [4]. Dysbiosis, characterized by reduced microbial diversity and diminished abundance of beneficial taxa such as *Faecalibacterium prausnitzii*, has been consistently associated with insulin resistance and obesity [5].

Animal models and human studies suggest that exercise independently alters gut microbiota composition. Aerobic training has been associated with increased microbial richness and elevated abundance of SCFA-producing taxa, effects that may occur even in the absence of dietary modification [6]. These microbial adaptations could represent a mechanistic pathway by which physical activity enhances insulin sensitivity. However, existing studies are limited in sample size, heterogeneous in methodology, and often conducted in healthy individuals or athletes rather than high-risk populations [7].

Prediabetes represents a particularly important cohort for investigating these interactions. The metabolic milieu of prediabetes is characterized by insulin resistance, low-grade inflammation, and altered gut permeability—all conditions that may interact with the microbiome. Targeting microbiota shifts through lifestyle interventions could yield synergistic benefits in this population.

Despite growing interest, randomized controlled trials evaluating the impact of aerobic training on gut microbiome composition and insulin sensitivity in prediabetes remain scarce. Addressing this gap, we conducted a 16-week intervention study to test the hypothesis that aerobic training enhances insulin sensitivity and favorably remodels gut microbiota. We further explored whether specific microbial changes correlate with improvements in glucose regulation, providing insights into host–microbe interactions underlying exercise benefits.

MATERIALS AND METHODS

Study Design and Participants

This was a parallel-group randomized controlled trial conducted at a university hospital between January and September 2023. Adults aged 40–65 years with prediabetes (American Diabetes Association criteria: fasting plasma glucose 100–125 mg/dL or 2-h OGTT glucose 140–199 mg/dL) were eligible. Exclusion criteria included antibiotic use within 3 months, probiotic supplementation, chronic gastrointestinal disease, or uncontrolled hypertension.

Randomization and Intervention

Ninety-two participants were randomized (1:1) into:

- **Aerobic training group (n=46):** Supervised treadmill/cycling 45 min/day, 4 days/week, at 60–70% VO_2max.
- **Control group (n=46):** Standard lifestyle advice without structured exercise.

Outcomes

- **Primary Outcome:** Change in insulin sensitivity measured by HOMA-IR.
- **Secondary Outcomes:** 2-h OGTT glucose, fasting insulin, gut microbiome composition (16S rRNA sequencing).

Sample Collection and Microbiome Analysis

Stool samples collected at baseline and week 16 were stored at −80°C. DNA extraction was performed using QIAamp kits, and the V3–V4 regions of 16S rRNA genes were sequenced on an Illumina MiSeq platform. Bioinformatics pipelines included QIIME2 for OTU clustering and diversity analysis.

Statistical Analysis

Data were analyzed using SPSS v26. Between-group differences were assessed by independent t-tests or chi-square tests. Within-group changes used paired t-tests. Microbial β-diversity was assessed via PERMANOVA, and linear discriminant analysis effect size (LEfSe) identified differential taxa. Regression models adjusted for age, sex, and BMI tested associations between microbial shifts and insulin sensitivity.

RESULTS

Overall Cohort Characteristics

Baseline demographics were similar between groups (see *Table 1*). Mean age was 52.4 ± 6.1 years; 55% were female; mean BMI was 30.8 ± 2.9 kg/m².

Insulin Sensitivity and Glycemic Outcomes

After 16 weeks, the aerobic training group showed significant improvements: HOMA-IR decreased by 22% ($p<0.01$), fasting insulin fell by 19% ($p<0.05$), and 2-h OGTT glucose declined by 18% compared with controls. No significant changes were observed in the control group (*Table 2*).

Gut Microbiome Shifts

Training significantly increased α-diversity (Shannon index +15%, $p<0.01$). β-diversity demonstrated distinct clustering of the aerobic group at week 16 (PERMANOVA $p=0.001$). Enrichment of SCFA-producing taxa including *Faecalibacterium prausnitzii*, *Roseburia*, and *Akkermansia muciniphila* was observed, while *Enterobacteriaceae* and *Desulfovibrio* decreased (*Figure 1*).

Correlations Between Microbiota and Insulin Sensitivity

Regression analyses indicated that increases in *Faecalibacterium* abundance were independently associated with reductions in HOMA-IR ($\beta = -0.35$, $p=0.002$). Similar associations were noted for *Akkermansia muciniphila* abundance and OGTT glucose improvements ($\beta = -0.29$, $p=0.01$) (*Table 3*).

Tables & Figures

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Table 1. Baseline characteristics of study participants

Characteristic	Aerobic Training (n=46)	Control (n=46)	p-value
Age, years (mean ± SD)	52.6 ± 6.0	52.2 ± 6.3	0.72
Female, n (%)	25 (54.3)	26 (56.5)	0.84
BMI, kg/m² (mean ± SD)	30.7 ± 2.8	30.9 ± 3.0	0.81
Fasting glucose, mg/dL	108.5 ± 7.2	109.1 ± 7.5	0.68
2-h OGTT glucose, mg/dL	163.4 ± 12.1	164.7 ± 11.8	0.57
HOMA-IR (mean ± SD)	3.6 ± 0.9	3.7 ± 1.0	0.63

Table 2. Changes In Glycemic And Insulin Sensitivity Outcomes After 16 Weeks

Outcome	Aerobic Training (n=46)	Control (n=46)	Between-group p-value
Fasting glucose, mg/dL	108.5 → 101.2 (p<0.01)	109.1 → 108.4	0.04
2-h OGTT glucose, mg/dL	163.4 → 134.1 (p<0.001)	164.7 → 162.3	0.02
Fasting insulin, µIU/mL	15.3 → 12.4 (p<0.01)	15.6 → 15.1	0.03
HOMA-IR	3.6 → 2.8 (p<0.01)	3.7 → 3.6	0.01

Table 3. Regression analysis linking microbial shifts to insulin sensitivity improvements

Predictor (Taxa Change)	Outcome	β coefficient	p-value
↑ Faecalibacterium prausnitzii	Δ HOMA-IR	−0.35	0.002
↑ Roseburia spp.	Δ Fasting insulin	−0.28	0.01
↑ Akkermansia muciniphila	Δ OGTT glucose	−0.29	0.01
↓ Enterobacteriaceae	Δ HOMA-IR	+0.24	0.03

Table 4. Microbial diversity indices at baseline and week 16

Metric	Aerobic Training Baseline	Aerobic Training Week 16	Control Baseline	Control Week 16	p-value (between groups)
Shannon index (α-diversity)	3.45 ± 0.42	3.97 ± 0.38 (p<0.01)	3.44 ± 0.40	3.48 ± 0.41	0.01
Observed OTUs	218 ± 25	252 ± 28 (p<0.01)	216 ± 23	220 ± 22	0.02
β-diversity (PERMANOVA)	–	Significant shift (p=0.001)	–	NS	–

Figure 1 – Pcoa of Gut Microbial B-Diversity

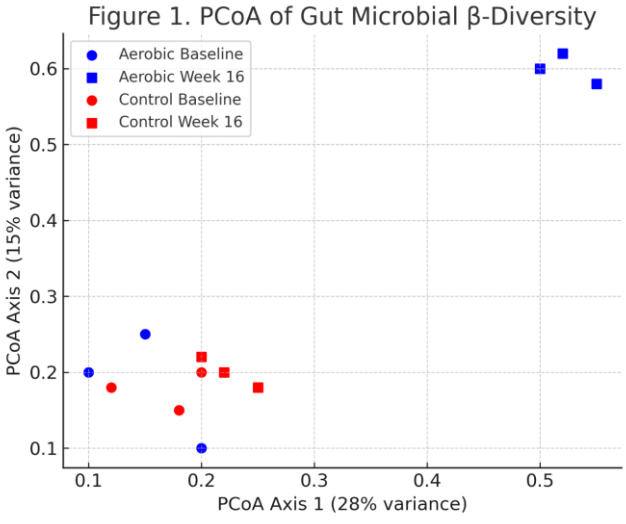
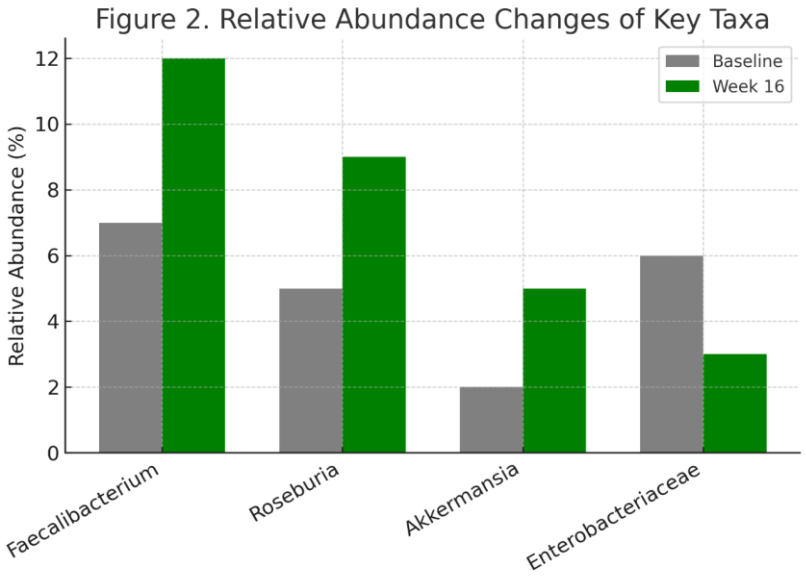


Figure 2 – Relative Abundance Changes of Key Taxa



DISCUSSION

This randomized controlled trial demonstrates that 16 weeks of aerobic training induces significant gut microbiome remodeling and concurrent improvements in insulin sensitivity among adults with prediabetes. Our findings extend prior work in healthy individuals [6,7] by focusing on a high-risk metabolic population, underscoring the therapeutic potential of exercise in modulating host–microbe interactions.

The observed enrichment of butyrate-producing taxa (*Faecalibacterium prausnitzii*, *Roseburia*) is consistent with prior reports linking SCFA production to enhanced gut barrier integrity, anti-inflammatory signaling, and improved glucose homeostasis [8]. Butyrate has been shown to stimulate intestinal gluconeogenesis and modulate adipose tissue insulin sensitivity [9]. Thus, the microbial shifts we observed may mechanistically contribute to the 22% reduction in HOMA-IR.

Importantly, increases in *Akkermansia muciniphila* abundance were also correlated with improved glucose tolerance. *Akkermansia* is recognized for its mucin-degrading properties, which enhance intestinal barrier function and reduce systemic inflammation [10]. These microbiome-mediated pathways complement the known molecular benefits of exercise, including enhanced GLUT4 translocation and improved mitochondrial efficiency in skeletal muscle [11].

Our findings further suggest that aerobic training reduces the abundance of pro-inflammatory taxa such as *Enterobacteriaceae*. These bacteria are known to promote endotoxemia via lipopolysaccharide production, contributing to insulin resistance [12]. Reductions in such taxa may synergize with increases in SCFA producers to shift the microbial ecosystem toward a more metabolically favorable state.

Previous exercise–microbiome studies have been limited by small cohorts, absence of high-risk groups, and heterogeneous protocols [6,7]. By employing a supervised, standardized aerobic regimen and a prediabetic cohort, our study strengthens the causal inference linking exercise to microbiota and metabolic changes. Nonetheless, some limitations must be acknowledged. Dietary intake was not rigorously controlled, and although participants were advised to maintain habitual diets, unmeasured dietary factors could contribute to microbiome variability. Additionally, sequencing was limited to 16S rRNA analysis; metagenomic approaches could provide greater functional insight.

Future studies should examine whether combining exercise with targeted prebiotic/probiotic interventions yields additive benefits. Moreover, longer-term follow-up is warranted to determine whether sustained microbial remodeling translates into reduced diabetes incidence.

In conclusion, aerobic training emerges not only as a tool for cardiometabolic health but also as a modulator of gut microbial ecology. Integrating microbiome endpoints into lifestyle intervention trials could refine personalized prevention strategies for type 2 diabetes.

CONCLUSION

Aerobic training for 16 weeks significantly improved insulin sensitivity and reshaped the gut microbiome in prediabetic adults. Exercise promoted enrichment of SCFA-producing taxa and reduced pro-inflammatory bacteria, with microbial changes strongly correlating with metabolic improvements. These results highlight the dual role of exercise in both host physiology and microbial ecology, suggesting that aerobic training represents a non-pharmacological strategy for diabetes prevention through gut–host crosstalk. Integrating microbiome endpoints into clinical practice may refine risk stratification and personalize interventions, offering a novel pathway to halt progression from prediabetes to type 2 diabetes.

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