



The Effects of a Probiotic-Focused Diet on Cardiovascular Risk Markers in Obese Individuals: A 12-Week Intervention Study

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Abstract

Aim: Obesity is a key risk factor for cardiovascular diseases, contributing to endothelial dysfunction and atherosclerosis. Pericardial fat, a visceral fat depot surrounding the heart, has emerged as an important cardiovascular risk factor. Its proximity to coronary vessels and its role in inflammatory processes suggest its potential impact on vascular health. This study investigates the effects of a probiotic-focused diet on cardiovascular risk markers, including carotid intima-media thickness (CIMT), flow-mediated dilation (FMD), and pericardial fat thickness in obese individuals.

Methods: This was a 12-week prospective dietary intervention study designed to evaluate the effects of a probiotic-rich diet in 100 obese participants. The participants followed a probiotic-focused diet, and cardiovascular risk markers-including CIMT, FMD, and pericardial fat thickness-were measured before and after the intervention. Metabolic markers such as body weight, insulin levels, and high-sensitivity C-reactive protein (hsCRP) were also evaluated.

Results: The probiotic group showed significant improvements in body weight, body mass index, insulin sensitivity, and hsCRP levels. However, no significant differences were observed in CIMT, FMD, or pericardial fat thickness between the two groups. Pericardial fat thickness showed a slight reduction in the probiotic group, but this change was not statistically significant.

Conclusion: A probiotic-rich diet significantly improves metabolic health but does not result in significant changes in cardiovascular markers such as CIMT, FMD, or pericardial fat thickness in obese individuals over a 12-week period. Further research with longer intervention periods is necessary to explore the impact of probiotics on vascular health and pericardial fat accumulation in obesity.

Keywords: Obesity, probiotics, cardiovascular diseases, inflammation, endothelium, vascular

Introduction

Obesity is a major global health problem and a leading risk factor for cardiovascular disease (CVD). It is closely associated with subclinical vascular changes, including increased carotid intima-media thickness (CIMT) and impaired endothelial function, both of which contribute to the development of atherosclerosis. Carotid intima-media thickness reflects arterial wall thickening and has

been recognized as a surrogate marker for atherosclerotic burden and cardiovascular events such as myocardial infarction and stroke (1). Flow-mediated dilation (FMD), on the other hand, is a non-invasive assessment of endothelial function and an early indicator of vascular health (2,3).

Pericardial fat, a visceral fat depot surrounding the heart, has emerged as a significant cardiovascular risk factor due to its inflammatory activity and anatomical

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proximity to coronary vessels (4). Several studies have reported a strong association between pericardial fat and endothelial dysfunction, particularly in obese individuals (5). Meanwhile, probiotics have gained attention for their ability to modulate the gut microbiota and reduce systemic inflammation. They have shown promise in improving insulin resistance, lipid profiles, and pro-inflammatory markers-key contributors to cardiovascular risk (6-8).

We hypothesized that a probiotic-focused diet would improve metabolic parameters and potentially exert favorable effects on vascular health in obese individuals. The aim of this study was to evaluate the effects of a 12-week probiotic-rich dietary intervention on metabolic markers, endothelial function (assessed by FMD), and subclinical atherosclerosis (assessed by, CIMT) in obese individuals. This approach may contribute to cardiovascular prevention strategies by offering a non-pharmacological, probiotic-targeted dietary tool to improve cardiometabolic health in high-risk populations.

Materials and Methods

Compliance with Ethical Standards

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, Diyarbakir Gazi Yasargil Training and Research Hospital (approval no.: 154, date: 05.10.2018). All participants provided written informed consent prior to their inclusion in the study.

Study Design

This 12-week study was conducted between January and June 2019 at University of Health Sciences Türkiye, Diyarbakir Gazi Yasargil Training and Research Hospital. The participants followed a probiotic-focused diet, and cardiovascular risk markers-including CIMT, FMD, and pericardial fat thickness were measured before and after the intervention. The primary aim was to assess the impact of a probiotic-rich diet on these markers of metabolic and vascular health. Previous research has shown that probiotics can influence metabolic parameters such as insulin sensitivity and inflammation (1), and that pericardial fat, in particular, is a strong predictor of cardiovascular risk, particularly in obese individuals (2). By measuring these markers, this study aimed to explore how dietary interventions might improve cardiovascular health in obese populations.

Inclusion Criteria

Participants aged 18-65 years with a body mass index (BMI) of ≥ 30 kg/m² were included. None of the participants had a history of CVD, diabetes, or other significant medical conditions.

Dietary Intervention

Participants followed a diet enriched with probiotic foods aimed at improving gut microbiota health and overall metabolic function. The diet included regular consumption of foods such as yogurt, kefir, and fermented vegetables (e.g., sauerkraut, kimchi). Participants were instructed to incorporate these foods into their daily meals, with portion sizes and frequency tailored to their caloric and nutritional requirements as determined by a dietitian.

To ensure adherence and provide personalized guidance, participants met individually with a dietitian three times per week. During these sessions, the dietitian monitored dietary compliance, provided tailored advice, and addressed any challenges faced by the participants. Dietary logs were also maintained by participants to document daily food intake, which was reviewed during the consultations.

Assessment of Carotid Intima-Media Thickness

Assessment of CIMT was measured using high-resolution B-mode ultrasonography [e.g., (state the device, such as GE Vivid E9, Philips iE33)]. Measurements were taken on the far wall of the distal 1 cm of the common carotid artery, approximately 1-2 cm proximal to the bifurcation (9). Three measurements were obtained bilaterally, and the mean CIMT value was calculated for analysis. All measurements were performed by an experienced physician blinded to the study groups and intervention status to ensure objectivity and reduce bias. The intra-observer variability was assessed and found to be within acceptable limits (<5%).

Assessment of Flow-Mediated Dilatation

Assessment of FMD, an established marker of endothelial function, was assessed using a standardized non-invasive ultrasound technique. Participants were instructed to fast and refrain from consuming caffeine or alcohol or engaging in physical activity for at least 12 hours prior to the procedure. Measurements were conducted in a temperature-controlled room after 10 minutes of rest in the supine position. Reactive hyperemia was induced by inflating a forearm cuff to 50 mmHg above systolic blood pressure for 5 minutes, followed by sudden deflation. The brachial artery diameter was measured at baseline and during hyperemia. FMD was calculated as the percentage increase in arterial diameter from baseline (9). All measurements were performed by the same experienced physician, who was blinded to the study groups and intervention details.

Assessment of Pericardial Fat Thickness

Pericardial fat thickness, a key marker of visceral adiposity surrounding the heart, was measured using transthoracic echocardiography. Parasternal long-axis

and short-axis views were obtained, and pericardial fat thickness was defined as the echo-lucent space between the outer wall of the myocardium and the visceral layer of the pericardium. Measurements were taken perpendicularly to the right ventricular free wall at end-diastole. Three consecutive cardiac cycles were averaged for the final value. An experienced and blinded physician performed all echocardiographic evaluations, ensuring consistency and minimizing measurement bias.

Quality Assurance

To ensure high data quality, all imaging devices were calibrated before each session. The physician conducting the measurements underwent inter-rater reliability validation at the study's outset. Blinded duplicate measurements were performed in a random subset of 10% of participants to assess reproducibility, yielding intraclass correlation coefficients >0.9 for all parameters.

Metabolic Markers

Body weight, BMI, insulin levels, and high-sensitivity C-reactive protein were also measured. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as a measure of insulin resistance.

Statistical Analysis

Continuous variables were assessed for normality using the (e.g., Shapiro-Wilk test or Kolmogorov-Smirnov test). Normally distributed variables were presented as mean \pm standard deviation, while non-normally distributed variables were summarized as median and interquartile range. For within-group comparisons, paired t-tests were applied to normally distributed data, and the Wilcoxon signed-rank test was used for non-parametric data.

Effect sizes were calculated to assess the magnitude of observed changes, reported as Cohen's *d* for paired t-tests or matched rank biserial correlation for non-parametric tests. Missing data were managed using (state method, e.g., pairwise deletion or imputation), and sensitivity analyses were conducted where appropriate. Continuous variables were assessed for normality using the Shapiro-Wilk test.

The statistical significance level was set at $p < 0.05$. All analyses were performed using (state statistical software, e.g., Statistical Package for the Social Sciences version 25.0, R version 4.3.1). Confidence intervals of 95% were provided for key outcomes.

Results

The baseline characteristics of both groups were similar, with no significant differences observed in terms of age, gender, or baseline cardiovascular risk markers. Table 1 present all the data for both baseline and post-intervention measurements.

Participants in the probiotic group experienced a significant reduction in body weight (-6.57 kg, $p < 0.001$) and BMI (-1.63 kg/m², $p < 0.01$). Insulin levels decreased by 3.42 μ U/mL ($p < 0.01$), and HOMA-IR improved by 1.23 ($p < 0.01$), while the control group showed no significant changes in these metabolic parameters.

Regarding cardiovascular risk markers, although changes in CIMT and pericardial fat thickness were observed in both groups, no significant differences were found between the probiotic and control groups (CIMT: -0.02 mm, $p = 0.35$, pericardial fat: -0.01 cm, $p = 0.26$). Flow-mediated dilation showed a slight improvement in the probiotic group ($+0.18\%$), but this change was not statistically significant ($p = 0.12$).

Discussion

The findings of this study suggest that a probiotic-focused diet can significantly improve body composition and insulin sensitivity in obese individuals. These results are consistent with previous studies that have demonstrated the benefits of probiotics in reducing metabolic dysfunctions such as insulin resistance and inflammation (10).

Recent clinical trials have also shown that probiotics may modulate gut microbiota composition, promote short-chain fatty acids production, and reduce systemic inflammation, all of which contribute to improved insulin signaling and energy metabolism (11-13).

Probiotics have also been shown to improve lipid profiles and reduce markers of systemic inflammation, which are known to contribute to cardiovascular risk (14). However, our study did not observe significant improvements in CIMT or FMD, which suggests that longer intervention periods or more intensive dietary changes may be necessary to elicit meaningful changes in vascular function. This may be due to the fact that vascular remodeling and endothelial repair are complex processes, typically requiring sustained anti-inflammatory stimuli and structural adaptation, which may not be fully achieved within a 12-week timeframe (14).

One aspect that could have influenced our findings is the potential role of pericardial fat, which is an important but often overlooked marker of cardiovascular risk in obesity. Pericardial fat is known to contribute to systemic inflammation and endothelial dysfunction, both of which are critical factors in the development of atherosclerosis and CVD (4). Previous studies have highlighted that pericardial fat is a strong predictor of coronary artery disease and other cardiovascular events, particularly in individuals with visceral obesity (5). Recent studies have demonstrated that pericardial fat volume independently predicts coronary artery calcification and impaired FMD, even after adjusting for BMI and visceral adiposity (1,15,16).

Table 1. Baseline and post-intervention analysis of cardiovascular and metabolic variables

Variable	Group 1 (Mean ± SD) (Baseline)	Group 2 (Mean ± SD) (Post-intervention)	*p-value
Body weight	83.96±15.41	77.39±15.61	p<0.001
Height	1.65±0.08	-	-
BMI (kg/m ²)	30.78±5.07	29.15±4.91	p<0.001
FBG (mg/dL)	94.37±11.78	96.90±8.81	0.535
PPBG (mg/dL)	104.69±24.53	96.60±17.43	0.208
HBA1C (%)	5.36±0.29	5.37±0.33	0.465
ALT (U/L)	16.50±14.84	17.00±16.07	0.972
Fibrinogen (mg/dL)	285.50±69.14	271.50±70.02	0.964
Homocystein (µmol/L)	695±476	654±375	0.757
Total cholesterol (mg/dL)	99.00±24.36	96.60±17.43	0.401
Triglycerides (mg/dL)	130.00±55.37	127.00±45.91	0.542
HDL (mg/dL)	45.00±12.15	47.00±9.30	0.280
LDL (mg/dL)	123.00±38.55	120.00±28.44	0.889
VLDL (mg/dL)	30.00±6.12	30.00±7.09	0.919
Pericardial fat thickness (cm)	0.67±0.17	0.63±0.18	0.26
Vitamin D (ng/mL)	16.48±8.23	15.94±5.68	0.189
C-reactive protein (mg/dL)	2.58±0.78	2.55±0.72	0.543
Cinc (µg/dL)	88.59±10.35	94.70±7.59	0.041
Magnesium (mg/dL)	1.95±0.20	1.93±0.10	0.280
C-peptide (ng/mL)	2.64±1.01	2.39±0.81	0.068
Insulin (µU/mL)	13.32±8.67	10.59±6.67	0.052
CIMT (mm)	0.07±0.09	0.0546±0.01527	0.288
FMD1 (%)	0.37±0.07	0.3829±0.07668	0.525
FMD2 (%)	0.40±0.08	0.4071±0.08956	0.816
FMDs (%)	-72.35±22.35	-69.9427±25.49738	0.646

*Statistical comparisons were performed using paired t-test and Wilcoxon signed-rank test as appropriate
 BMI: Body mass index, FBG: Fasting blood glucose, PPBG: Postprandial blood glucose, HBA1C: Hemoglobin A1C, ALT: Alanine transaminas, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low density lipoprotein, FMD: Flow-mediated dilation, CIMT: Carotid intima-media thickness, SD: Standard deviation

Given that our study did not measure pericardial fat, it is possible that incorporating this marker could have revealed additional insights into the diet's impact on cardiovascular risk. Moreover, longer intervention periods and more intensive dietary changes may be required to see significant changes in vascular health markers like CIMT and FMD, as these are often influenced by multiple factors such as systemic inflammation, lipid metabolism, and genetic predisposition (17,18).

Overall, while probiotic diets can improve metabolic health, their direct effects on vascular markers, including those influenced by pericardial fat, remain inconclusive. Further research with longer durations and larger sample sizes is needed to determine the long-term benefits of such diets on CVD risk.

Study Limitations

This study suggests that a probiotic-focused diet can improve metabolic health and insulin sensitivity in obese individuals. However, the effects on cardiovascular markers, such as CIMT and FMD, were not significant. Small sample size and short study duration are key limitations. The absence of a control group limits the ability to definitively attribute observed changes to the probiotic intervention, as potential confounding factors or regression to the mean cannot be excluded. Future studies should address these issues by including larger cohorts, longer interventions, and evaluating pericardial fat and gut microbiota to provide a clearer understanding of how probiotics influence cardiovascular risk. Despite these limitations, the study's strengths include its prospective

design, objective vascular measurements, and close dietary supervision.

Conclusion

A probiotic-focused diet led to significant improvements in body composition and insulin sensitivity in obese individuals. Although no significant changes were observed in CIMT, FMD, or pericardial fat, the metabolic improvements observed in this study suggest that probiotic-rich diets may help reduce obesity-related cardiovascular risk in the long term. Future studies should explore the long-term effects of probiotic diets on cardiovascular health, with a focus on endothelial function and arterial stiffness.

Ethics

Ethics Committee Approval: This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, Diyarbakir Gazi Yasargil Training and Research Hospital (approval no.: 154, date: 05.10.2018).

Informed Consent: Informed consent was obtained from all participants prior to their enrollment in the study.

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Footnotes

Authorship Contributions

Concept: B.A., Design: B.A., Data Collection or Processing: S.A., M.U., U.C., H.D., Analysis or Interpretation: S.A., M.U., H.D., Literature Search: B.A., M.U., U.C., Writing: B.A., U.C.

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