|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table 1: Highlights the application of AI and ML techniques in microbiome analysis for predicting atherosclerosis and CVD risk** | | | | | | |
| **Disorder** | **Samples** | **AI/ML/ Other analysis Method** | **Description** | **Limitation** | **Important Findings** | **REF** |
| CVD | 478 CVD, 473 non-CVD participants | Random Forest, Neural Networks, Elastic Net, Decision Tree, Support Vector Machine (SVM) | Supervised ML models were trained on 16S ribosomal RNA sequencing data to classify gut microbiota profiles. Both taxonomic and OTU features were used to differentiate CVD from non-CVD subjects. Feature selection identified the top 25 OTUs that contributed most to CVD classification using fecal 16S metagenomics data. | Gut microbiome can be influenced by diet and medication, which were not fully accounted for. | Random Forest achieved the best results, utilizing the top 25 OTU features to distinguish CVD from non-CVD subjects.  Key bacterial taxa such as *Bacteroides*, *Subdoligranulum*, and *Clostridium* were found to be significantly enriched in CVD patients, suggesting a strong link between these microbes and cardiovascular disease. In contrast, beneficial bacteria like *Faecalibacterium* and *Ruminococcus*, which are known for their anti-inflammatory properties, were more prevalent in non-CVD individuals. | <https://doi.org/10.1161/hypertensionaha.120.15885>. |
| Atherosclerosis | Human: GSE43292 (32 atheroma plaques, 32 intact tissues); GSE120521 (4 unstable, 4 stable plaque samples); GSE155512 (4 atherosclerotic samples) | Random Forest, Weighted Gene Co-expression Network Analysis (WGCNA), Non-negative Matrix Factorization (NMF) | Analyzes gene expression differences in atherosclerotic plaques and identifies key macrophage-related genes (PLEK, IRF8, BTK, CCR1, CD68) linked to gut microbiota. | Focused on specific macrophage genes and limited human sample size. The study relies on existing sequencing datasets without broader validation | Identified gut microbiota-linked macrophage genes (PLEK, IRF8, BTK, CCR1, CD68) involved in immune response and plaque instability, highlighting potential diagnostic markers and therapeutic targets. | <https://doi.org/10.3389/fcimb.2024.1395716>. |
| Dyslipidemia and  Atherosclerosis | 441,016 (UK Biobank dataset for serum lipids); 18,340 individuals for the gut microbiome data from the GWAS (Genome-Wide Association Study). | Mendelian Randomization (MR), Inverse Variance Weighted (IVW), Weighted Median (WM), MR-Egger, MR-PRESSO | Investigates causal relationships between the gut microbiome and lipid levels (LDL, HDL, TG, ApoA, ApoB) using bidirectional MR analysis.  Explores the causal role of the gut microbiome in influencing atherosclerosis-related lipid traits using GWAS and genetic data to infer causality | Confined to European populations; potential confounding factors like diet/environment not fully addressed. | Nine intestinal flora associated with dyslipidemia: Desulfovibrionaceae inversely related to ApoB; Parasutterella and Terrisporobacter linked to higher LDL-C; Oscillospira and Peptococcus negatively correlated with LDL-C; Dorea associated with lower triglyceride levels; Suggests potential for probiotic therapy or fecal transplants.  Christensenellaceae and Ruminococcaceae linked to higher ApoB, increasing atherosclerosis risk; Desulfovibrionaceae showed a protective effect by lowering ApoB; Findings suggest gut microbiome manipulation as a potential therapy for atherosclerosis and lipid imbalances | <https://doi.org/10.1186/s12872-024-03804-3>. |
| Cardiovascular Disease, Ischaemic Heart Disease, Myocardial Infarction, Coronary Atherosclerosis | 3,860 individuals from six ethnicities (Dutch, African-Surinamese, South-Asian Surinamese, Turkish, Moroccan, Ghanaian) in the HELIUS cohort | XGBoost (Gradient-Boosted Trees) for predicting Framingham score; Mendelian Randomization for causal inference | XGBoost used to predict 10-year CVD risk based on gut microbiota composition. MR used to infer causal relationships between gut microbiota and specific cardiovascular outcomes (e.g., ischemic heart disease, myocardial infarction). | Ethnic-specific variability in microbiota relevance; reduced predictive accuracy for Turkish and Ghanaian groups in XGBoost; limited generalizability of MR findings across all ethnic groups. | CMR cluster (*Christensenellaceae*, *Methanobrevibacter*, *Ruminococcaceae*) inversely correlated with triglycerides, lowering CVD risk. *Akkermansia muciniphila* is protective in African-Surinamese; *Ruminococcaceae* UCG-002 in Moroccans. *Ruminiclostridium* 6 and *Bacteroidetes* are protective in African-Surinamese, while *Dorea longicatena* is associated with increased CVD risk. *Ruminococcaceae* UCG-005 and *Lachnospira pectinoschiza* show protective effects in Moroccans. | <https://doi.org/10.1093/cvr/cvae018>. |
| Effect of Dairy Intake on Gut Microbiota and Cardiometabolic Health | 1780 participants aged 45-70 years.  Microbial DNA was extracted from fecal samples, and the V3-V4 hypervariable region of the 16S rRNA gene was amplified and sequenced | Linear Discriminant Analysis Effect Size (LEfSe);  Principal Coordinate Analysis (PCoA) with Bray-Curtis Distance & PERMANOVA | LEfSe was used to identify specific gut microbial biomarkers associated with varying levels of dairy intake (milk, yogurt). PCoA with Bray-Curtis distance and PERMANOVA were used to explore overall microbial community structure in relation to dairy consumption. | Population specificity limits generalizability to other demographics; single time-point data may not capture long-term dietary changes; observational design prevents establishing causality and cannot control for unmeasured confounding factors; geographical focus on one city necessitates multi-centre and longitudinal studies for validation. | Higher dairy intakewas positively associated with increased gut microbial diversity.  Beneficial bacteria such as *Bifidobacterium* and *Streptococcus* were enriched, while lower dairy intake correlated with *Enterobacteriaceae*.  Greater microbial diversity was linked to improved lipid profile and cardiometabolic health.  *2-hydroxy-3-methylbutyric acid*, *L-alanine* were inversely associated with microbial diversity and positively linked to triglycerides, | <https://doi.org/10.1016/j.ebiom.2021.103284>. |
| Acute Coronary Syndrome (ACS) and Gut Microbiota Imbalance | Fecal samples from different groups | Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA)  Empirical Analysis of Digital Gene Expression Data in R (edgeR) | OPLS-DA analyzed metabolite data and gut microbiota diversity (alpha and beta) to identify peaks and Amplicon Sequence Variants (ASVs). edgeR identified differentially abundant ASVs across groups. | Sample size, diversity, and potential confounding factors like diet not fully controlled. | Statin treatment altered gut microbiota, reducing pathogenic (*Parabacteroides merdae*) and increasing beneficial taxa (*Bifidobacterium longum subsp. longum*, *Anaerostipes hadrus*, *Ruminococcus obeum*). Chronic therapy improved clinical outcomes, lowering adverse events and readmissions. Changes in taxa were linked to disease severity and correlated with fatty acid and isoprenoid pathways. A multi-omics approach integrated microbiome and metabolomic analyses for deeper insights into statins' roles in ACS. | <https://doi.org/10.7150%2Fthno.55946>. |
| Atherosclerosis and Cardiometabolic Disease | Apolipoprotein E knockout model; Human: 30 patients with carotid atherosclerosis and 20 controls | Random Forest, Cross-omics analysis (metabolomics + 16S rRNA sequencing) | Investigates antibiotics-induced gut dysbiosis in atherosclerosis and cardiometabolic diseases, emphasizing shifts in gut microbiota, serum metabolome, and metabolic diversity. Focuses on disrupted tryptophan and lipid metabolism pathways | Limited bacterial families and pathways examined; human cohort restricted to Caucasians, and long-term antibiotic effects not fully addressed. | Antibiotics-induced gut dysbiosis exacerbated atherosclerosis by altering tryptophan and lipid metabolism, with loss of Clostridia and Bacteroidetes driving metabolic shifts. Tryptophan supplementation partially reversed these effects in mice. Similar microbiota and metabolic disruptions in humans linked long-term antibiotic use to elevated cardiovascular risk. | <https://doi.org/10.1016/j.molmet.2020.100976>. |