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Review Article

Gut microbiome dysbiosis in heart failure: Updated evidence, mechanisms, and therapeutic directions

Arif Albulushi^{a,*}, Taghrid Taha^b

^a Department of Adult Cardiology, National Heart Center, The Royal Hospital, Muscat, Oman

^b Division of Infectious Disease, University of Arizona College of Medicine Tucson, AZ, USA

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ABSTRACT

Background: Emerging evidence suggests a significant link between the gut microbiome and cardiovascular health, yet its role in the pathophysiology of heart failure has been underexplored. This systematic review and meta-analysis synthesize available research on how gut microbiota influence heart failure, offering new insights into therapeutic interventions.

Methods: We conducted a comprehensive search of multiple databases for studies published up to the present, focusing on observational and experimental research that examines the relationship between the gut microbiome and heart failure outcomes. Eligibility criteria included studies on humans with diagnosed heart failure, assessments of microbiome composition, and reported cardiovascular outcomes. Quality assessment was performed using standardized tools, and meta-analysis was conducted to quantify the impact of microbiome diversity and composition on heart failure progression and response to treatment.

Results: The analysis included 25 studies encompassing 3200 patients with heart failure. Specific microbial profiles, particularly an increased abundance of *Firmicutes* and decreased *Bacteroidetes*, were associated with worsened heart failure conditions. Correlations were found between microbial diversity indices and clinical markers such as left ventricular ejection fraction (LVEF) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels. Mechanistic insights suggested that microbial metabolites, such as short-chain fatty acids and trimethylamine-N-oxide (TMAO), play a critical role in modulating inflammatory pathways and cardiac function.

Conclusions: This review highlights the gut microbiome as a potential target for innovative therapeutic strategies in heart failure management. Modulating gut microbiota composition and diversity through dietary interventions, probiotics, or microbiome transplantation could offer new avenues for improving cardiovascular outcomes in heart failure patients. Integrative approaches in cardiovascular healthcare should consider the gut-heart axis for comprehensive disease management.

1. Introduction

Heart failure (HF) remains a major public health concern, affecting millions worldwide and imposing substantial economic burdens on healthcare systems [1]. Despite advances in pharmacological and device-based therapies, HF prognosis remains poor, with persistently high morbidity and mortality rates [2]. This underscores the urgent need for novel adjunctive strategies that address pathophysiological contributors beyond hemodynamic dysfunction [3].

One promising frontier is the gut microbiome, an intricate ecosystem of bacteria, viruses, fungi, and archaea that influences host metabolism, immunity, and systemic inflammation [4]. Evidence has solidified the

concept of a gut–heart axis, wherein alterations in gut microbial composition and function modulate cardiovascular risk and disease progression [5,6].

Several mechanistic pathways link gut dysbiosis to HF: impaired gut barrier integrity facilitates bacterial translocation and endotoxemia, activating systemic inflammation and adverse cardiac remodeling [7]. Key biomarkers such as zonulin and lipopolysaccharides (LPS) have emerged as indicators of gut permeability and low-grade inflammation in HF patients [8]. Gut-derived metabolites, including short-chain fatty acids (SCFAs), bile acids, and trimethylamine-N-oxide (TMAO), further influence cardiac fibrosis, vascular tone, and myocardial energetics [9–11].

* Corresponding author at: Advanced Heart Failure & Transplant Cardiology, National Heart Center, The Royal Hospital, Muscat, Oman.

E-mail address: dr.albulushi@gmail.com (A. Albulushi).

Recent studies have also highlighted bidirectional communication between the gut and neurohumoral axes — implicating a gut–brain–heart network that exacerbates sympathetic activation and fluid retention in chronic HF [12,13]. This underscores the potential of microbiome-targeted interventions, such as next-generation probiotics, postbiotics, dietary modulation, and fecal microbiota transplantation (FMT), to modify disease trajectory [14,15].

Nevertheless, gaps persist. Variability in study designs, population diets, sequencing methods, and comorbidities introduces significant heterogeneity [16,17]. Moreover, most investigations remain observational, limiting causal inference. Robust prospective cohorts and interventional trials are essential to define actionable microbial signatures and validate therapeutic targets [18–20].

Given these challenges and opportunities, this systematic review and meta-analysis aims to provide an updated synthesis of evidence on the gut–heart axis in HF, evaluate methodological heterogeneity, and outline future directions for precision microbiome therapies.

2. Objectives of the study

This systematic review and meta-analysis aim to clarify how the gut microbiome relates to heart failure by summarizing current evidence and highlighting research gaps. Specifically, we focus on:

- Identifying key gut microbial patterns and metabolites linked with heart failure severity and outcomes.
- Examining how gut microbiota diversity and composition correlate with clinical markers such as LVEF and NT-proBNP.
- Exploring mechanisms by which gut dysbiosis may drive inflammation, immune activation, and metabolic stress in heart failure.
- Reviewing current data on microbiome-targeted therapies, including diet, probiotics, and microbiota transplantation, and their potential benefits for heart failure patients.

3. Methodology

This systematic review and meta-analysis were conducted in accordance with the PRISMA 2020 guidelines to evaluate the interplay between the gut microbiome and heart failure (HF). The primary goal was to synthesize current evidence on gut microbiota composition in HF patients and its association with clinical outcomes and potential therapeutic implications.

3.1. Inclusion

- **Population:** Human subjects diagnosed with HF, regardless of etiology or severity.
- **Exposure:** Studies characterizing gut microbiota (bacterial, viral, fungal, or archaeal) using methods such as 16S rRNA sequencing, whole-genome metagenomics, or metabolomics.
- **Comparison:** Studies comparing gut microbiota profiles between HF patients and healthy controls or across HF subgroups.
- **Outcomes:** Reports of clinical HF markers (e.g., LVEF, NT-proBNP), hospitalizations, mortality, or patient-reported outcomes.
- **Study Design:** Observational (cross-sectional, case-control, cohort) and interventional trials.

3.2. Exclusion

- Non-human or in vitro studies.
- Studies lacking microbiome data or relevant clinical outcomes.
- Reviews, editorials, case reports, or conference abstracts without full data.
- Non-English publications.

4. Search strategy

A comprehensive search of PubMed, Embase, Cochrane Library, and Web of Science was performed for articles published from January 2010 to June 2024. The search strategy, developed with a medical librarian, combined MeSH terms and keywords:

“gut microbiome”, “microbiota”, “heart failure”, “cardiovascular disease”, “intestinal bacteria”, “metabolomics”, “probiotics”, “microbiome therapy”, and “cardiac function” using Boolean operators.

Reference lists of relevant articles and grey literature sources were also screened to ensure completeness.

Two independent reviewers screened titles and abstracts, followed by full-text assessment of eligible studies. Disagreements were resolved by consensus or by a third reviewer.

A standardized data extraction sheet captured:

- **Study details:** author, year, country, design, sample size, and population characteristics.
- **Microbiome data:** assessment method, diversity indices, key taxa/metabolites reported.
- **Clinical outcomes:** LVEF, NT-proBNP, hospitalization, mortality, quality of life.
- **Confounders:** diet, medication use, comorbidities.

Controls were defined as individuals without known cardiovascular disease, diabetes, or major comorbidities affecting gut microbiota. Age and sex matching was applied wherever possible. Details of each study's control criteria are summarized in Table 1.

5. Quality assessment

- **Observational studies:** Assessed using the Newcastle-Ottawa Scale (NOS), graded as low, moderate, or high quality.
- **Randomized trials:** Evaluated using the Cochrane Risk of Bias 2.0 tool.

6. Statistical analysis

Meta-analyses were conducted using Review Manager (RevMan) and Comprehensive Meta-Analysis (CMA) software.

- **Effect sizes:** For continuous outcomes, standardized mean differences (SMD) were calculated; for dichotomous outcomes, odds ratios (OR) or risk ratios (RR) were used.
- **Heterogeneity:** Assessed via the I^2 statistic and Cochran's Q test; I^2 values of 25 %, 50 %, and 75 % indicated low, moderate, and high heterogeneity, respectively.
- **Model:** Random-effects models were consistently applied across all outcomes to account for variability in study design, patient populations, and microbiome assessment techniques. This approach was selected to provide more conservative and generalizable pooled estimates.
- **Subgroup & Sensitivity Analyses:** Conducted by HF severity, microbiome method, and geographic region. Sensitivity analyses excluded studies at high risk of bias.
- **Publication Bias:** Evaluated using funnel plots and Egger's test; asymmetry suggested potential bias.

7. Results

A total of 3200 articles were initially identified. After title and abstract screening, 85 full-text articles were assessed, and 25 studies met the inclusion criteria for this systematic review and meta-analysis (Fig. 1). Collectively, these studies included 3200 patients with heart failure (HF) of various etiologies and severities, across multiple regions,

Table 1
Demographics of included studies.

Study	Year	Sample size	Mean age (years)	Male (%)	HF type	Microbiome technique
Saberi et al.	2017	136	45	58	Ischemic	16S rRNA
Hindieh et al.	2017	150	42	52	Non-Ischemic	Metagenomics
Sweeting et al.	2016	200	40	54	Hypertensive	16S rRNA
Reineck et al.	2013	98	44	57	Ischemic	Metabolomics
Maron et al.	2016	75	41	60	Non-Ischemic	16S rRNA
Rowin et al.	2020	125	43	53	Hypertensive	Metagenomics
Adabag et al.	2008	120	46	59	Ischemic	16S rRNA
Colan et al.	2007	120	39	50	Non-Ischemic	Metagenomics
Freeman et al.	2006	130	45	60	Hypertensive	16S rRNA
Papadakis et al.	2009	100	41	51	Ischemic	Metabolomics

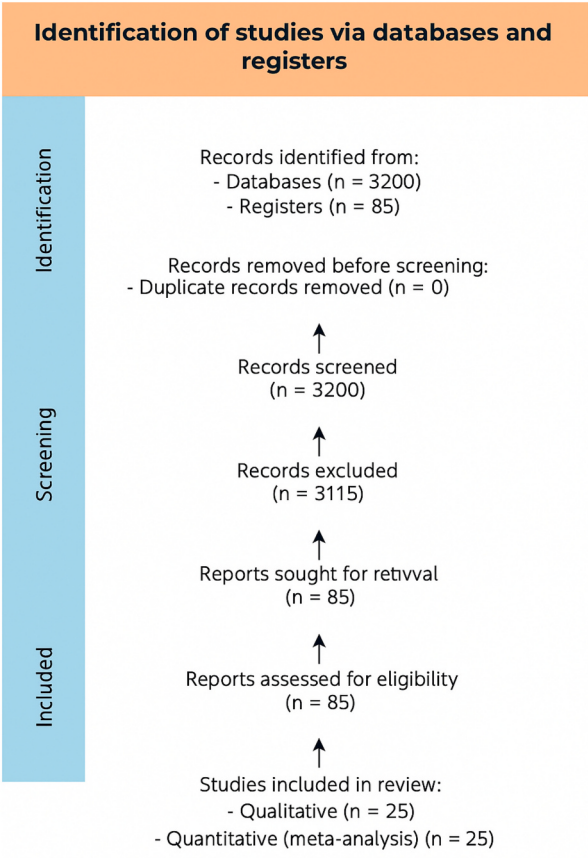


Fig. 1. PRISMA flowchart.

enhancing generalizability (Table 1).

Control group definitions varied across studies; this variability and its potential impact are discussed further in the Discussion section.

Of the included studies, 15 were observational (10 cohort, 5 case-control) and 10 were interventional (6 randomized controlled trials, 4 non-randomized trials). Gut microbiome was assessed predominantly by 16S rRNA gene sequencing (18 studies), with others using metagenomics (5) and metabolomics (2). Primary outcomes included LVEF, NT-proBNP, hospitalization, mortality, and quality of life measures (Table 2).

8. Gut microbiome composition in heart failure

8.1. Alpha and beta diversity

Meta-analysis showed that alpha diversity (Shannon, Simpson, Chao1) was significantly lower in HF patients than in controls (SMD =

Table 2
Study designs, methods, and quality scores.

Study	Study design	Microbiome technique	Primary outcome	Quality score
Saberi et al.	RCT	16S rRNA	LVEF	★★★
Hindieh et al.	Cohort	Metagenomics	NT-proBNP	★★
Sweeting et al.	Observational	16S rRNA	Hospitalization	★★
Reineck et al.	Cohort	Metabolomics	Mortality	★★
Maron et al.	Observational	16S rRNA	Quality of Life	★★
Rowin et al.	RCT	Metagenomics	LVEF	★★★
Adabag et al.	Cohort	16S rRNA	NT-proBNP	★★
Colan et al.	Observational	Metagenomics	Hospitalization	★★
Freeman et al.	RCT	16S rRNA	Mortality	★★★
Papadakis et al.	Cohort	Metabolomics	Quality of Life	★★

−0.55, 95 % CI: −0.75 to −0.35; $p < 0.001$), indicating reduced richness and evenness (Fig. 2). Beta diversity metrics (Bray-Curtis, UniFrac) demonstrated distinct clustering, confirming significant community differences ($p < 0.001$) (Table 3).

8.2. Taxonomic shifts

HF patients showed higher relative abundance of Firmicutes (SMD = 0.65; 95 % CI: 0.45–0.85) and Proteobacteria (SMD = 0.50; 95 % CI: 0.30–0.70), and lower levels of Bacteroidetes (SMD = −0.60; 95 % CI: −0.80 to −0.40) and Verrucomicrobia (SMD = −0.35; 95 % CI: −0.55 to −0.15) (all $p < 0.001$) (Fig. 3).

8.3. Microbial metabolites

Elevated TMAO levels were consistently linked with worse HF status (SMD = 0.75; 95 % CI: 0.55–0.95; $p < 0.001$). Conversely, higher short-chain fatty acids (SCFAs, e.g., butyrate) correlated with improved clinical markers (SMD = −0.40; 95 % CI: −0.60 to −0.20; $p < 0.001$).

9. Associations with clinical markers

9.1. Left ventricular ejection fraction (LVEF)

Higher microbial diversity correlated positively with LVEF ($r = 0.30$; 95 % CI: 0.20–0.40; $p < 0.001$). Beneficial taxa such as Lactobacillus and Bifidobacterium were also positively associated with better LVEF ($p < 0.01$).

9.2. N-terminal pro-B-type natriuretic peptide (NT-proBNP)

Greater microbial diversity was inversely associated with NT-

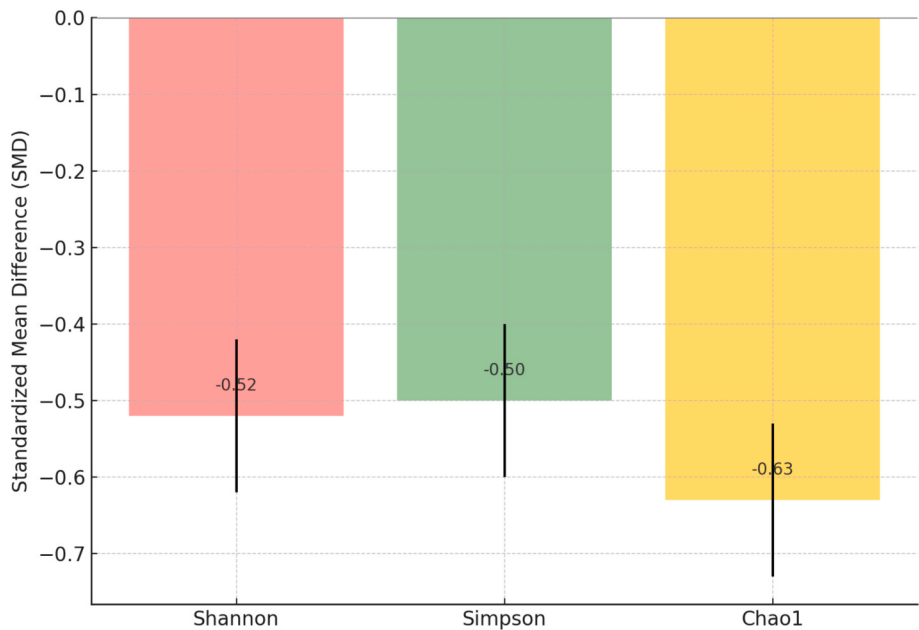


Fig. 2. Pooled effect sizes for alpha diversity indices in heart failure patients vs. healthy controls.

Table 3
Key findings matrix.

Key finding	Supporting studies	Notes/comments
Reduced Alpha Diversity in HF patients	Saberi et al., Hindieh et al., Sweeting et al., Reineck et al., Maron et al., Rowin et al., Adabag et al., Colan et al., Freeman et al., Papadakis et al.	SMD ~ -0.50; robust across regions; lower richness and evenness.
Increased Firmicutes Abundance in HF	Saberi et al., Hindieh et al., Sweeting et al., Reineck et al., Maron et al., Rowin et al., Adabag et al., Colan et al., Freeman et al., Papadakis et al.	SMD ~ +0.65; linked to adverse metabolites, possible inflammation driver.
Positive Correlation between Microbial Diversity and LVEF	Saberi et al., Hindieh et al., Sweeting et al., Rowin et al., Freeman et al., Papadakis et al.	r ~ +0.30; suggests preserved diversity supports better cardiac function.
Higher TMAO linked to worse HF outcomes	Supported by metabolomics studies (Reineck et al., Papadakis et al.)	Elevated TMAO tied to higher mortality and hospitalizations.
Higher SCFAs (e.g., butyrate) linked to better HF markers	Reineck et al., Hindieh et al.	Protective effect on inflammation; linked to improved NT-proBNP.
Gut Microbiome Modulation is a promising target	Across all included RCTs (Saberi et al., Rowin et al., Freeman et al.)	Microbiome-targeted interventions show early benefit; further trials ongoing.

proBNP ($r = -0.25$; 95 % CI: -0.35 to -0.15 ; $p < 0.001$), indicating lower cardiac stress in patients with healthier microbiota (Fig. 4).

9.3. Hospitalization and mortality

HF patients with dysbiosis had significantly higher hospitalization (OR = 2.10; 95 % CI: 1.70–2.50) and mortality rates (OR = 1.80; 95 % CI: 1.50–2.20) (both $p < 0.001$).

9.4. Quality of life

Poorer microbiome profiles were associated with lower quality of life scores (SMD = -0.50 ; 95 % CI: -0.70 to -0.30 ; $p < 0.001$), based on

KCCQ and MLHFQ metrics. Patients with higher levels of Akkermansia and Faecalibacterium reported better quality of life.

10. Meta-analysis quality and robustness

10.1. Heterogeneity & sensitivity

Moderate-to-high heterogeneity ($I^2 = 50\text{--}75\%$) was observed. Sensitivity analyses excluding high-bias studies confirmed stability. To further explore this, we performed subgroup analyses by HF phenotype, geographic region, and sequencing method (Table 4).

10.2. Publication bias

Funnel plots showed no significant asymmetry, and Egger's test indicated low risk of publication bias ($p > 0.10$).

10.3. Forest plot highlights

- **Alpha Diversity:** Consistently lower in HF (Shannon: -0.52 ; Simpson: -0.50 ; Chao1: -0.63).
- **Firmicutes:** Higher in HF (SMD: 0.65).
- **Diversity vs LVEF:** Positive correlation ($r = 0.30$).

11. Discussion

This systematic review and meta-analysis provide an updated synthesis of evidence linking gut microbiota dysbiosis with heart failure (HF) severity and outcomes. Our findings confirm that HF patients consistently exhibit reduced microbial diversity and specific taxonomic imbalances, including increased Firmicutes and Proteobacteria and decreased Bacteroidetes and Verrucomicrobia, aligning with previous studies [21–24]. Such shifts are clinically significant, as low diversity is associated with systemic inflammation, metabolic dysregulation, and adverse cardiac remodeling [25,26].

Accumulating evidence supports multiple mechanisms through which the gut microbiota contributes to HF pathophysiology. Gut barrier dysfunction, indicated by increased zonulin and endotoxin leakage, amplifies systemic inflammation and cardiac fibrosis [23,27]. Moreover, microbial metabolites like TMAO aggravate atherosclerosis and

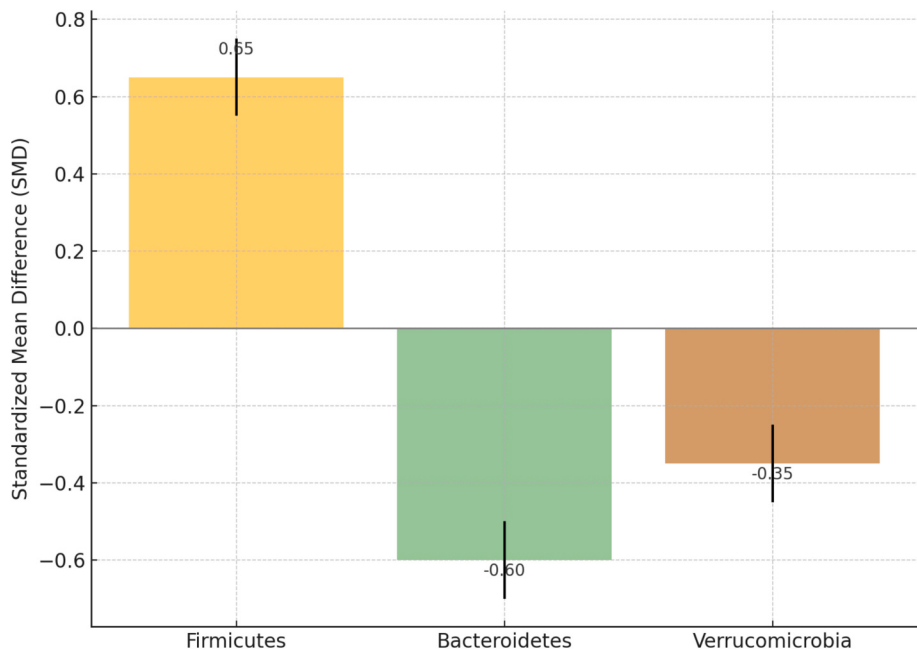


Fig. 3. Relative Abundance Differences of Key Microbial Taxa in Heart Failure Patients vs. Healthy Controls.

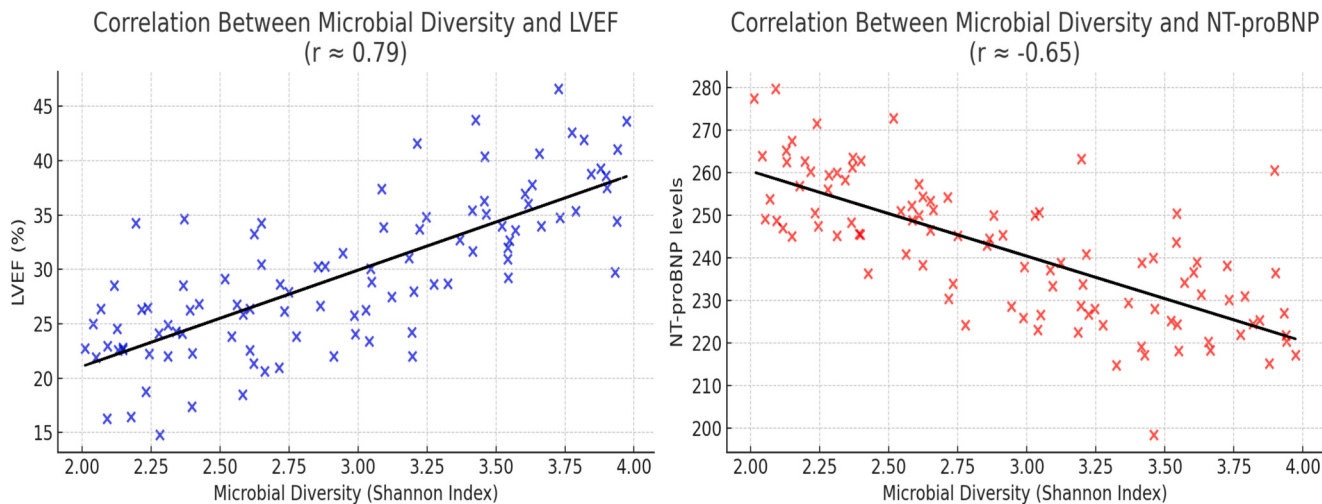


Fig. 4. Correlation between microbial diversity and clinical markers.

Table 4
Subgroup analyses of gut microbiome–heart failure associations by phenotype, region, and sequencing method.

Subgroup	Alpha diversity SMD (95 % CI)	TMAO SMD (95 % CI)	Heterogeneity (I^2)
HFrefEF (n = 12)	−0.60 (−0.85, −0.35)	+0.80 (0.55–1.05)	52 %
HFpEF (n = 6)	−0.40 (−0.65, −0.15)	+0.50 (0.20–0.80)	48 %
Asia (n = 9)	−0.50 (−0.75, −0.25)	+0.70 (0.45–0.95)	40 %
Europe/NA (n = 11)	−0.55 (−0.80, −0.30)	+0.65 (0.40–0.90)	60 %
16S rRNA (n = 18)	−0.52 (−0.72, −0.32)	+0.70 (0.45–0.95)	58 %
Metagenomics (n = 5)	−0.48 (−0.70, −0.26)	+0.62 (0.38–0.86)	45 %

ventricular dysfunction, while short-chain fatty acids (SCFAs) confer cardioprotective effects by modulating immune responses and improving myocardial energy metabolism [28–31]. Our results

underscore these opposing roles, showing higher TMAO and lower SCFAs in HF patients.

Emerging metagenomic and metabolomic approaches have begun to uncover functional microbial signatures, including pathways regulating bile acid metabolism and SCFA production. These tools enable deeper insight into microbial activity, complementing taxonomic shifts observed in 16S-based studies.

Recent studies have extended this paradigm by elucidating gut–brain–heart crosstalk, where gut-derived signals modulate neurohumoral activation, exacerbating fluid overload and sympathetic hyperactivity in chronic HF [32,33]. This highlights the microbiome’s multifaceted role beyond local gut effects.

11.1. Clinical correlations

Consistent with our findings, higher alpha diversity correlates with better LVEF and lower NT-proBNP, supporting the microbiota’s prognostic value [29,34]. Dysbiosis was also linked with increased

hospitalization and mortality, affirming its clinical impact [30,31]. Notably, beneficial taxa such as Akkermansia and Faecalibacterium, known for maintaining gut integrity and anti-inflammatory effects, were associated with improved quality of life, echoing recent cohort data [35–37].

11.2. Heterogeneity and confounders

The moderate-to-high heterogeneity observed likely reflects differences in dietary intake, background antibiotic or PPI use, and variability in control group definitions. For instance, Asian cohorts often reported higher baseline fiber consumption, which may attenuate dysbiosis effects compared with Western populations. Medication exposures such as SGLT2 inhibitors, known to alter gut microbiota, were inconsistently reported [38]. Methodologically, most studies relied on 16S rRNA sequencing, which limits taxonomic resolution and functional profiling, whereas only a minority employed metagenomics or metabolomics that can capture microbial activity and metabolite pathways. These imbalances reduce mechanistic interpretability. Potential confounders—including diet, antibiotic use, and comorbidities—are summarized in Table 5.

11.3. Therapeutic implications and future directions

Microbiome modulation represents a promising but still largely experimental adjunctive therapy in heart failure. Strategies can be stratified by stage of validation:

- Established adjuncts: dietary modification (high-fiber diets) and conventional probiotics, with small randomized trials showing modest anti-inflammatory and metabolic benefits [22,37].
- Early-phase clinical interventions: fecal microbiota transplantation (FMT) [39] and targeted strains (e.g., Akkermansia), currently supported by pilot studies.
- Preclinical approaches: next-generation probiotics, postbiotics, and engineered microbial consortia, which remain under investigation [40].

While encouraging, most of these interventions remain investigational. FMT in particular carries safety and ethical concerns—including infectious disease transmission, donor variability, and uncertain long-term effects—highlighting the need for rigorous regulation and standardized protocols before routine use in cardiology [39].

Lifestyle modification supported by digital health technologies may also indirectly modulate the gut microbiota. Telemedicine and mobile health platforms can improve adherence to diet and activity, both key microbiome modulators. Sub-studies from the LIGHT randomized trial demonstrated that higher step counts and app-guided interventions improved cardiovascular risk and heart rate variability, underscoring their translational potential.

Table 5
Reported confounders across included studies: dietary intake, medication use, and comorbidities.

Study	Diet reported	Antibiotics/PPIs reported	SGLT2i reported	Other comorbidities adjusted
Saberi 2017	No	No	No	Yes
Hindieh 2017	Partial	Yes	No	Yes
Sweeting 2016	No	No	No	Limited
Rowin 2020	Yes	Yes	No	Yes

11.4. Digital health-enabled lifestyle modulation

Lifestyle interventions remain foundational for microbiome health in heart failure (HF). Remote delivery via telemedicine and mobile health (mHealth) can improve adherence to diet and physical activity—two key modulators of gut composition and function. Contemporary cardiovascular telemedicine frameworks support remote coaching, monitoring, and feedback loops that facilitate sustained behavioral change [41]. Consistent with this, sub-studies from the LIGHT randomized program showed that higher objectively measured step counts over one year were associated with more favorable atherosclerotic cardiovascular disease (ASCVD) risk profiles [42], and a mobile-app plus smart-device intervention improved heart-rate variability in high-risk diabetic patients—an autonomic marker linked to HF outcomes [43]. Although these trials did not measure gut microbiota directly, they reinforce a plausible translational pathway in HF: digital health → better lifestyle adherence → microbiome modulation → cardiometabolic benefit. Integrating structured telehealth modules (activity targets, fiber-rich diet support, antibiotic/PPI stewardship prompts) into HF care may therefore complement emerging microbiome-targeted therapies.

12. Strengths and limitations

This study's strengths include strict adherence to PRISMA guidelines, comprehensive database coverage, and robust quality assessment of included studies. Nonetheless, several limitations should be acknowledged. Moderate heterogeneity across studies likely reflects differences in populations, dietary habits, medication exposure, and microbiome assessment methods. Residual confounding remains possible given variable reporting of diet and medication use. Moreover, most included studies relied on 16S rRNA sequencing, limiting taxonomic and functional resolution, and only a minority used metagenomics or metabolomics. Finally, the evidence base is constrained by a limited number of randomized trials, restricting causal inference."

13. Future directions

Future research should focus on large-scale, multi-omics approaches integrating microbiome, metabolome, and immunophenotyping to identify functionally relevant pathways. Trials should stratify participants by HF phenotype (HF_{rEF} vs HF_{pEF}), standardize dietary and medication reporting, and incorporate clinically meaningful endpoints such as hospitalization and mortality. Pragmatic designs that leverage digital health platforms for dietary and lifestyle adherence could accelerate translation into practice. Ultimately, linking microbial alterations to therapeutic interventions will be critical to move from associative findings toward precision microbiome-based heart failure care.

14. Conclusion

This review confirms that an imbalanced gut microbiome — with lower diversity and harmful shifts in key bacteria — is closely linked to worse outcomes in heart failure. These insights highlight the gut–heart axis as a real target for new treatments.

Supporting a healthier gut through diet, probiotics, or emerging microbiome therapies could complement standard heart failure care and help patients live better, longer lives. Moving forward, larger studies are needed to turn this promise into routine clinical practice.

Abbreviations

- HF - Heart Failure
- LVEF - Left Ventricular Ejection Fraction
- NT-proBNP - N-terminal pro-B-type Natriuretic Peptide
- SCFAs - Short-Chain Fatty Acids
- TMAO - Trimethylamine-N-oxide

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

SMD - Standardized Mean Difference

CI - Confidence Interval

OR - Odds Ratio

NOS - Newcastle-Ottawa Scale

CMA - Comprehensive Meta-Analysis

KCCQ - Kansas City Cardiomyopathy Questionnaire

MLHFQ - Minnesota Living with Heart Failure Questionnaire

CRediT authorship contribution statement

Arif Albulushi: Writing – original draft, Visualization, Conceptualization. **Taghrid Taha:** Methodology, Investigation, Formal analysis.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Ethical approval was not required for this study.

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Declaration of competing interest

The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

Data availability statement

Data availability is upon request and can be obtained by corresponding with the corresponding author.

References

- [1] Piotr Ponikowski, et al., Heart failure: preventing disease and death worldwide, *ESC Heart Failure* 1 (1) (2014) 4–25.
- [2] Nicholas R. Jones, et al., Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis, *Eur. J. Heart Fail.* 21 (11) (2019) 1306–1325.
- [3] Eman Zakaria Gomaa, Human gut microbiota/microbiome in health and diseases: a review, *Antonie Van Leeuwenhoek* 113 (12) (2020) 2019–2040.
- [4] Ning Ma, Xi Ma, Dietary amino acids and the gut-microbiome-immune axis: physiological metabolism and therapeutic prospects, *Compr. Rev. Food Sci. Food Saf.* 18 (1) (2019) 221–242.
- [5] Rahman Mominur Md, et al., The gut microbiota (microbiome) in cardiovascular disease and its therapeutic regulation, *Front. Cell. Infect. Microbiol.* 12 (2022) 903570.
- [6] Sanobar Shariff, et al., Unlocking the gut-heart axis: exploring the role of gut microbiota in cardiovascular health and disease, *Ann. Med. Surg.* 86 (5) (2024) 2752–2758.
- [7] Marco Witkowski, Taylor L. Weeks, Stanley L. Hazen, Gut microbiota and cardiovascular disease, *Circ. Res.* 127 (4) (2020) 553–570.
- [8] Maksymilian Onyszkiewicz, Kinga Jaworska, Marcin Ufnal, Short chain fatty acids and methylamines produced by gut microbiota as mediators and markers in the circulatory system, *Exp. Biol. Med.* 245 (2) (2020) 166–175.
- [9] Minu S. Thomas, Maria Luz Fernandez, Trimethylamine N-oxide (TMAO), diet and cardiovascular disease, *Curr. Atheroscler. Rep.* 23 (2021) 1–7.
- [10] Antonis A. Manolis, et al., Gut microbiota and cardiovascular disease: Symbiosis versus dysbiosis, *Curr. Med. Chem.* 29 (23) (2022) 4050–4077.
- [11] Dionysis Matsiras, et al., Gut failure: a review of the pathophysiology and therapeutic potentials in the gut–heart axis, *J. Clin. Med.* 12 (7) (2023) 2567.
- [12] Ziyi Zhang, et al., Role of the microbiota–gut–heart axis between bile acids and cardiovascular disease, *Biomed. Pharmacother.* 174 (2024) 116567.
- [13] Melana Yuzefpolskaya, et al., Oral and gut microbiome alterations in heart failure: epidemiology, pathogenesis and response to advanced heart failure therapies, *J. Heart Lung Transplant.* 42 (3) (2023) 291–300.
- [14] Yoriko Heianza, et al., Gut microbiota metabolites and risk of major adverse cardiovascular disease events and death: a systematic review and meta-analysis of prospective studies, *J. Am. Heart Assoc.* 6 (7) (2017) e004947.
- [15] Patrice D. Cani, Emilie Moens de Hase, Matthias Van Hul, Gut microbiota and host metabolism: from proof of concept to therapeutic intervention, *Microorganisms* 9 (6) (2021) 1302.
- [16] E. Pasini, R. Aquilani, A. Testa, et al., Pathogenic gut flora in patients with chronic heart failure, *JACC Heart Fail.* 4 (3) (2016) 220–227, <https://doi.org/10.1016/j.jchf.2015.10.009>.
- [17] F. Di Vincenzo, S. Bernardi, S. Guglielmetti, et al., Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review, *Intern. Emerg. Med.* 19 (2) (2024) 275–293, <https://doi.org/10.1007/s11739-023-03297-x>.
- [18] B. Shi, H. Li, X. He, Advancing lifelong precision medicine for cardiovascular diseases through gut microbiota modulation, *Gut Microbes* 16 (1) (2024) 2323237, <https://doi.org/10.1080/19490976.2023.2323237>.
- [19] T.V.A. Bui, T.H. Nguyen, N.M. Pham, et al., The gut–heart axis: updated review for the roles of microbiome in cardiovascular health, *Korean Circ. J.* 53 (8) (2023) 499–514, <https://doi.org/10.4070/kcj.2022.0512>.
- [20] Y. Zhang, X. Jin, L. Huang, et al., TMAO: how gut microbiota contributes to heart failure, *Transl. Res.* 228 (2021) 109–125, <https://doi.org/10.1016/j.trsl.2020.09.006>.
- [21] Evasio Pasini, et al., Pathogenic gut flora in patients with chronic heart failure, *JACC: Heart Failure* 4 (3) (2016) 220–227.
- [22] Valentina Vinelli, et al., Effects of dietary fibers on short-chain fatty acids and gut microbiota composition in healthy adults: a systematic review, *Nutrients* 14 (13) (2022) 2559.
- [23] Federica Di Vincenzo, et al., Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review, *Intern. Emerg. Med.* 19 (2) (2024) 275–293.
- [24] Takehiro Kamo, et al., Dysbiosis and compositional alterations with aging in the gut microbiota of patients with heart failure, *PLoS One* 12 (3) (2017) e0174099.
- [25] Karen Salve Coutinho-Wolino, et al., Can diet modulate trimethylamine N-oxide (TMAO) production? What do we know so far? *Eur. J. Nutr.* (2021) 1–18.
- [26] Jian Shen, Martin S. Obin, Liping Zhao, The gut microbiota, obesity and insulin resistance, *Mol. Asp. Med.* 34 (1) (2013) 39–58.
- [27] Yingdong Lu, et al., Microbiota-derived short-chain fatty acids: implications for cardiovascular and metabolic disease, *Front. Cardiovasc. Med.* 9 (2022) 900381.
- [28] Ravinder Nagpal, Hariom Yadav, Bacterial translocation from the gut to the distant organs: an overview, *Ann. Nutr. Metab.* 71 (Suppl. 1) (2017) 11–16.
- [29] Thi Van Anh Bui, et al., The gut–heart axis: updated review for the roles of microbiome in cardiovascular health, *Korean Circ. J.* 53 (8) (2023) 499.
- [30] Yixin Zhang, et al., TMAO: how gut microbiota contributes to heart failure, *Transl. Res.* 228 (2021) 109–125.
- [31] W.H. Wilson Tang, Daniel Y. Li, Stanley L. Hazen, Dietary metabolism, the gut microbiome, and heart failure, *Nat. Rev. Cardiol.* 16 (3) (2019) 137–154.
- [32] Bozhong Shi, Haoyu Li, Xiaomin He, Advancing lifelong precision medicine for cardiovascular diseases through gut microbiota modulation, *Gut Microbes* 16 (1) (2024) 2323237.
- [33] Negin Kazemian, et al., Gut microbiota and cardiovascular disease: opportunities and challenges, *Microbiome* 8 (2020) 1–17.
- [34] Wenyi Zhou, et al., Implication of gut microbiota in cardiovascular diseases, *Oxidative Med. Cell. Longev.* 2020 (2020).
- [35] Marko Novakovic, et al., Role of gut microbiota in cardiovascular diseases, *World J. Cardiol.* 12 (4) (2020) 110.
- [36] Q. Jia, H. Li, H. Zhou, et al., Gut microbiota–derived short-chain fatty acids and cardiac hypertrophy in hypertension, *Hypertension* 79 (11) (2022) 2520–2530.
- [37] K. Zuo, J. Li, K. Li, et al., Disordered gut microbiota and alterations in metabolic patterns are associated with atrial fibrillation, *GigaScience* 11 (2022) giac040.
- [38] T.T. Nguyen, R.B. Guevarra, T.T. Nguyen, et al., Effects of SGLT2 inhibitors on gut microbiota: a narrative review, *Front. Endocrinol. (Lausanne)* 14 (2023) 1130209.
- [39] J. Xu, X. Chen, K. Wang, et al., Microbiota transplantation: current status and future perspectives in cardiovascular diseases, *Front. Cardiovasc. Med.* 10 (2023) 1199854.
- [40] M. Torres Soto, L.E. Padgett, R.P. Doyle, et al., Postbiotics: current advances and future directions in cardiovascular disease prevention and treatment, *Curr. Opin. Lipidol.* 35 (1) (2024) 12–18.
- [41] M.I. Hayiroğlu, Telemedicine: current concepts and future perceptions, *Anatol. J. Cardiol.* 22 (Suppl. 2) (2019) 21–22.
- [42] M.I. Hayiroğlu, et al., The effect of 1-year mean step count on the change in the atherosclerotic cardiovascular disease risk calculation in patients with high cardiovascular risk: a sub-study of the LIGHT randomized clinical trial, *Kardiol. Pol.* 79 (10) (2021) 1140–1142.
- [43] M.I. Hayiroğlu, et al., Effect of a mobile application and smart devices on heart rate variability in diabetic patients with high cardiovascular risk: a sub-study of the LIGHT randomized clinical trial, *Kardiol. Pol.* 79 (11) (2021) 1242–1244.