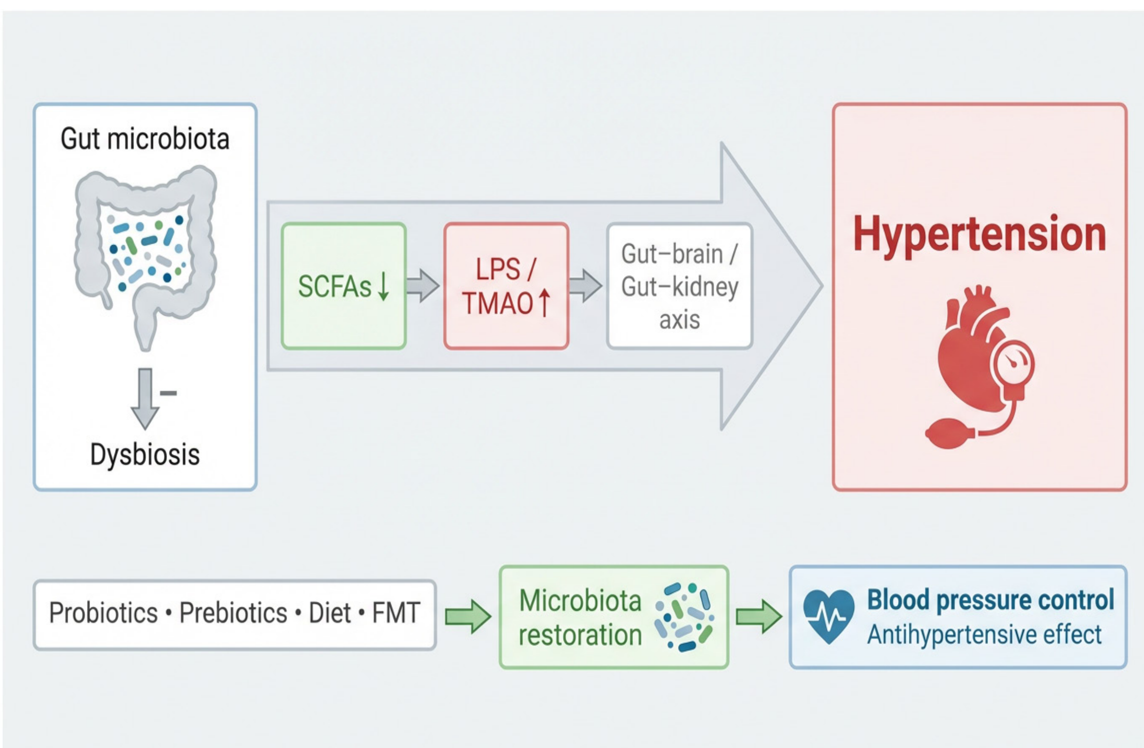
Gut Microbiota and Hypertension: From Pathogenesis to Therapeutic Potential

Authors
Haitao Yang, Jingkun Liu

Correspondence
10787149@qq.com (J. Liu)

Graphical Abstract



https://doi.org/10.71321/w9jjqk66
 L. Conflux. Vol. 2, No. 2 (2026)

Review Article

Life Conflux

Gut Microbiota and Hypertension: From Pathogenesis to Therapeutic Potential

Haitao Yang [1,2] , Jingkun Liu [3*]

Received: 2025-10-13 | Accepted: 2026-01-22 | Published online: 2026-03-07

Abstract

Hypertension is a major global health burden with high morbidity. Beyond traditional genetic and metabolic factors, increasing evidence shows that gut microbiota dysbiosis plays an important role in the development and progression of hypertension. Clinical studies have revealed that hypertensive patients display reduced microbial diversity, decreased abundance of short-chain fatty acid (SCFA)–producing bacteria, and enrichment of pro-inflammatory taxa such as Prevotella and Klebsiella. These microbial alterations are associated with endothelial dysfunction, chronic inflammation, and activation of the sympathetic nervous system through the gut–brain and gut–kidney axis. Mechanistically, microbial metabolites such as SCFAs, lipopolysaccharide (LPS), and trimethylamine-N-oxide (TMAO) participate in blood pressure regulation by influencing vascular tone, immune responses, and renal sodium handling. Loss of SCFA-producing bacteria decreases nitric oxide bioavailability and impairs vasodilation, while accumulation of LPS and TMAO promotes vascular inflammation and oxidative stress. Disruption of intestinal barrier integrity further exacerbates systemic inflammation, creating a feedback loop that sustains elevated blood pressure. Therapeutically, modulation of gut microbiota through probiotics, prebiotics, dietary interventions, and fecal microbiota transplantation (FMT) has shown promising antihypertensive effects in both animal and human studies. In addition, some antihypertensive drugs can remodel gut microbiota composition, suggesting potential synergistic benefits of combined treatment. In conclusion, the gut microbiota serves as a key and modifiable factor in hypertension pathogenesis. Understanding its mechanisms and therapeutic potential provides novel perspectives for developing microbiota-based and personalized strategies to improve blood pressure control and reduce cardiovascular risk.

Keywords: Gut microbiota; Hypertension; Microbiota-targeted therapy

Introduction

Hypertension is one of the most prevalent cardiovascular disorders worldwide, characterized by high morbidity. Hypertension is one of the most prevalent cardiovascular disorders worldwide, characterized by high morbidity, disability, and mortality. According to the World Health Organization (WHO), approximately one-third of adults globally suffer from hypertension, and this proportion continues to rise [1]. Hypertension is not only a major risk factor for myocardial infarction, stroke, and renal failure but also one of the leading causes of global disease burden. The pathogenesis of hypertension is complex and multifactorial, involving genetic predisposition, dietary habits, metabolic disturbances, and neurohumoral dysregulation. In recent years, accumulating evidence has revealed that the interaction between the host and the gut microbiota plays a crucial role in the development and progression of hypertension [2].

A growing body of basic and clinical studies demonstrate a close association between hypertension and gut microbiota dysbiosis. Alterations in gut microbial composition may serve as an important causative factor for hypertension, while the hypertensive state and its related metabolic disturbances can in turn further modify gut microbial communities, forming a bidirectional and self-perpetuating cycle. Mechanistically, gut microbiota participate in blood pressure regulation through multiple pathways, including the production of short-chain fatty acids (SCFAs), immune modulation, and the gut–brain and gut–kidney axis [3]. Conversely, hypertension-induced chronic inflammation, endothelial dysfunction, and disruption of the intestinal barrier exacerbate microbial imbalance, promoting the accumulation of pro-inflammatory metabolites such as

1 Department of Cardiology, The first Affiliated Hospital of Xinjiang Medical University, Urumqi 830011, China.

2 State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China

3 Department of Thoracic and Abdominal Radiotherapy, The Affiliated Tumor Hospital of Xinjiang Medical University, Urumqi 830011, China.

* Corresponding Author.

lipopolysaccharide (LPS) and trimethylamine-N-oxide (TMAO), which contribute to vascular injury and systemic inflammation [4-5].

Given the pivotal role of the gut microbiota in hypertension pathogenesis, targeting gut microbial homeostasis has emerged as a novel therapeutic strategy. In recent years, interventions such as probiotics, prebiotics, dietary modulation, and fecal microbiota transplantation (FMT) have shown promising antihypertensive effects and good safety profiles in both animal models and early clinical trials [6]. Compared with conventional pharmacological treatments, microbiota-targeted approaches offer multi-target regulation, metabolic and immune modulation, and the potential for long-term restoration of host homeostasis [7]. Therefore, this review systematically summarizes the relationship between gut microbiota and hypertension from three major perspectives—clinical evidence, pathogenic mechanisms, and therapeutic interventions—to provide new insights and theoretical support for future precision prevention and treatment strategies.

Clinical Studies on Gut Microbiota and Hypertension

Accumulating clinical evidence supports a strong association between gut microbiota composition and blood pressure regulation in human populations. Large-scale cohort studies and cross-sectional analyses have consistently demonstrated that patients with hypertension exhibit reduced gut microbial diversity, characterized by depletion of SCFAs–producing bacteria such as Faecalibacterium prausnitzii, Roseburia, and Akkermansia muciniphila, along with an enrichment of pro-inflammatory taxa including Prevotella, Klebsiella, and Enterobacter species [8]. These microbial alterations are associated with decreased circulating levels of SCFAs—key metabolites that exert vasodilatory, anti-inflammatory, and renoprotective effects—while pro-hypertensive metabolites such as TMAO and LPS are elevated, promoting endothelial dysfunction and systemic inflammation. However, it is important to note that while SCFAs are generally associated with blood pressure reduction, certain SCFAs, especially acetate, may increase blood pressure under specific conditions, such as through the activation of the renin-angiotensin system or sympathetic nervous system [9]. This complexity in SCFA actions reflects the nuanced role of microbial metabolites in regulating blood pressure.

Notably, emerging longitudinal evidence suggests that gut microbiota dysbiosis may precede the development of hypertension rather than merely result from it. For instance, a longitudinal study on hypertensive disorders in pregnancy conducted in a Chinese cohort analyzed gut microbiota at early, mid, and late gestational stages, revealing dynamic microbial shifts associated with blood pressure changes. The study found that alterations in specific genera, including Methanobrevibacter, correlated with the progression of gestational hypertension, suggesting a possible causal link between microbial imbalance and hypertension onset [10]. Although this investigation focused on pregnancy-related hypertension—a distinct subtype from essential hypertension—its longitudinal design provides valuable evidence that microbiota alterations may precede the clinical onset of elevated blood pressure. Moreover, functional analyses indicated that changes in microbial metabolic activity may appear earlier than compositional shifts, supporting the hypothesis that microbial metabolism may be a more sensitive indicator of early hypertensive changes. Furthermore, FMT from normotensive donors to hypertensive patients has provided direct clinical evidence for microbiota-mediated blood pressure regulation. In a recent multicenter, randomized controlled trial, oral capsule-based FMT led to a transient reduction of approximately 4 mmHg in systolic blood pressure after one week, accompanied by increased microbial richness and the restoration of beneficial taxa such as Akkermansia and Adlercreutzia [6]. While these results highlight the potential therapeutic benefits of microbiota-targeted interventions, the antihypertensive effect was not maintained over time, and the long-term sustainability and efficacy of such interventions remain uncertain. These findings underscore the safety, feasibility, and therapeutic potential of microbiota-targeted interventions, yet challenges remain regarding their consistency and long-term outcomes.

In addition to FMT, dietary and probiotic interventions targeting gut microbial composition have also demonstrated blood pressure–lowering potential. Controlled clinical trials using Lactobacillus plantarum, Bifidobacterium breve, and dietary fiber supplementation have reported modest but significant reductions in both systolic and diastolic blood pressure, particularly in patients with metabolic syndrome or mild hypertension [11-12]. However, the effects of probiotics are often strain-specific, and their colonization in the gut tends to be transient, which limits their long-term impact. Collectively, these findings underscore the clinical relevance of gut microbial dysbiosis in hypertension and highlight the potential of microbiota-targeted strategies as adjunctive or alternative therapeutic options. However, current microbiota interventions typically yield more modest blood pressure reductions compared to conventional medications, and their long-term safety, efficacy, and ethical considerations, especially in FMT, require further exploration. Future large-scale, longitudinal, and mechanistic studies are needed to establish causality, identify microbial biomarkers predictive of treatment response, and optimize personalized microbiota-based interventions for long-term blood pressure control.

Mechanistic Insights

The gut microbiota contributes to blood pressure regulation through multiple interconnected mechanisms that involve metabolic, immunological, and neurohumoral pathways. Among these, SCFAs metabolism, immune and inflammatory modulation, the gut–brain axis, and the gut–kidney axis represent the four major mechanistic routes linking intestinal microbes to hypertension pathogenesis (Figure 1).

SCFAs and Vascular Regulation

SCFAs—primarily acetate, propionate, and butyrate—are key metabolites produced by bacterial fermentation of dietary fibers. These molecules exert antihypertensive effects through several mechanisms, including activation of G-protein–coupled receptors (GPR41, GPR43, and Olfr78), enhancement of endothelial nitric oxide synthase (eNOS) activity, and suppression of systemic inflammation. SCFAs can induce vasodilation by stimulating endothelial nitric oxide (NO) production and reducing oxidative stress [13]. Clinical and experimental studies have shown that hypertensive individuals and animal models exhibit reduced fecal and plasma SCFAs levels, mainly due to decreased abundance of SCFAs-producing genera such as Roseburia, Coprococcus, and Faecalibacterium [14]. Resto-

https://doi.org/10.71321/w9jjqk66

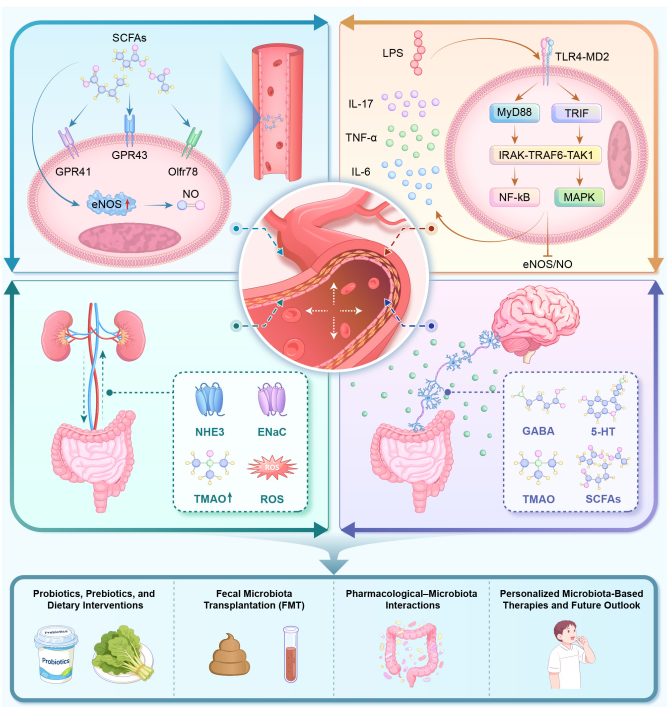


Figure 1. Gut microbiota and hypertension. Hypertension is associated with gut microbiota dysbiosis, characterized by reduced microbial diversity, depletion of short-chain fatty acid (SCFA)–producing bacteria (e.g., Faecalibacterium prausnitzii, Roseburia, Akkermansia muciniphila), and enrichment of pro-inflammatory taxa (e.g., Prevotella, Klebsiella). These alterations promote elevated levels of lipopolysaccharide (LPS) and trimethylamine-N-oxide (TMAO) and decreased SCFAs, leading to endothelial dysfunction, chronic inflammation, and sympathetic activation via the gut–brain and gut–kidney axis, thereby sustaining elevated blood pressure. Restoring microbial homeostasis through probiotics, prebiotics, dietary interventions, and fecal microbiota transplantation, alone or in combination with antihypertensive drugs, represents a promising therapeutic strategy for blood pressure control.

ration of SCFAs levels through dietary fiber supplementation or probiotic intervention has been demonstrated to lower blood pressure, underscoring the central role of microbial-derived metabolites in vascular homeostasis. However, the effects of SCFAs are context dependent and receptor specific. Although many studies report antihypertensive effects of short chain fatty acids, particularly propionate and butyrate, other evidence suggests that certain SCFAs may raise blood pressure under specific conditions. For example, acetate can activate the olfactory receptor Olfr78, promoting renin release and potentially increasing blood pressure via the renin–angiotensin system and sympathetic stimulation. This dual action highlights the nuanced regulatory role of SCFAs in cardiovascular physiology.

Immune and Inflammatory Modulation

Gut microbiota profoundly influence systemic immune tone and inflammatory status, both of which are closely associated with hypertension. Dysbiosis can promote intestinal barrier disruption and translocation of microbial components such as LPS into the circulation, activating toll-like receptor 4 (TLR4) signaling and inducing chronic low-grade inflammation. This process leads to increased production of pro-inflammatory cytokines including IL-6, TNF-α, and IL-17, which contribute to endothelial dysfunction, vascular remodeling, and elevated peripheral resistance [5]. Experimental studies in germ-free and antibiotic-treated hypertensive mice have shown that restoration of commensal bacteria attenuates inflammation and normalizes blood pressure, indicating that microbial-driven immune dysregulation is a key pathogenic mechanism in hypertension [15].

The Gut–Brain Axis

The gut–brain axis represents a bidirectional communication system between the gastrointestinal tract and central nervous system that modulates autonomic control of blood pressure. Microbial metabolites such as SCFAs, TMAO, and neurotransmitter-like molecules (e.g., γ-aminobutyric acid, serotonin) can cross the intestinal barrier and influence neuronal signaling. These signals interact with both the central and peripheral nervous systems, including pathways such as the vagus nerve, enteric nervous system, and hypothalamic-pituitary-adrenal (HPA) axis, which together regulate autonomic tone and vascular function. Dysbiosis enhances sympathetic nervous system activity via vagal afferents and hypothalamic inflammation, particularly within the paraventricular nucleus, thereby increasing vascular tone and sustaining hypertension [16]. However, the effects of microbial metabolites on blood pressure regulation are complex and receptor-specific. For instance, while some microbial metabolites such as butyrate exert antihypertensive effects, others like acetate, through activation of Olfr78, may increase blood pressure by promoting renin release and sympathetic activation. This dual action highlights the nuanced regulatory role of the gut microbiota in cardiovascular physiology. Studies have shown that antibiotic-induced modulation of gut microbiota reduces sympathetic output and lowers blood pressure, further supporting the contribution of gut–brain communication to hypertension pathophysiology [17]. Thus, while interventions targeting the gut–brain axis show potential, their long-term effectiveness and safety in humans remain unclear, and further studies are needed to elucidate the exact mechanisms and identify personalized therapeutic strategies.

The Gut–Kidney Axis and Sodium Homeostasis

The gut–kidney axis has emerged as another important pathway linking microbiota to hypertension, primarily through regulation of sodium balance, renal inflammation, and oxidative stress. Microbial metabolites can influence renal expression of sodium transporters such as NHE3 and ENaC, affecting sodium reabsorption and blood pressure. Moreover, elevated TMAO levels, commonly observed in hypertensive individuals, promote renal fibrosis and impair pressure natriuresis [18-19]. Conversely, SCFAs such as acetate and propionate enhance renal vasodilation and natriuresis via activation of GPR41/43, contributing to blood pressure reduction. These findings highlight that gut microbiota act as a metabolic–endocrine interface that modulates renal function and systemic hemodynamics.

However, evidence from human studies is still limited, and the relative contribution of gut derived metabolites to chronic kidney changes in hypertension requires further mechanistic and longitudinal investigation. In summary, the gut microbiota exerts multifaceted effects on blood pressure regulation through metabolic, immune, neurogenic, and renal pathways. Dysbiosis can disrupt this homeostatic network, leading to increased vascular resistance, inflammation, sympathetic activation, and altered sodium handling. Understanding these mechanisms provides a theoretical foundation for microbiota-targeted therapies aimed at restoring host–microbe equilibrium and achieving long-term blood pressure control, but the translation of preclinical findings to consistent clinical outcomes remains a major challenge.

Interactions Between Mechanisms

The mechanisms through which gut microbiota regulate blood pressure are highly interconnected, creating a complex network that influences cardiovascular homeostasis. SCFAs, for example, not only promote vasodilation by stimulating endothelial nitric oxide production but also modulate immune responses by reducing pro-inflammatory cytokine production. This immune modulation can affect sympathetic nervous system activity via the gut–brain axis, altering vascular tone and contributing to blood pressure regulation. Additionally, microbial metabolites like TMAO can exacerbate vascular inflammation and fibrosis, leading to increased vascular resistance and elevated blood pressure. The gut–kidney axis also plays a role, as SCFAs activate receptors such as GPR41/43 in the kidneys to enhance natriuresis and reduce sodium retention, thereby helping to lower blood pressure. These interconnected pathways highlight the multifactorial nature of hypertension, suggesting that altering one mechanism, such as increasing SCFAs, can affect multiple systems involved in blood pressure control, from the vasculature to the nervous system and kidneys. Understanding these interactions points to the need for integrated therapeutic approaches that target multiple pathways simultaneously.

Therapeutic Strategies and Future Directions

Given the multifactorial role of the gut microbiota in hypertension pathogenesis, targeting the intestinal microecosystem has emerged as a promising therapeutic approach. Current interventions focus on restoring microbial diversity, enhancing beneficial metabolites such as SCFAs, and suppressing pro-inflammatory or pro-hypertensive pathways. These strategies include probiotics and prebiotics, dietary modulation, FMT, and pharmacological–microbiota interactions, which together represent the evolving frontier of microbiota-based therapy for hypertension.

Probiotics, Prebiotics, and Dietary Interventions

Numerous clinical and experimental studies have demonstrated that probiotics can modestly but significantly reduce blood pressure, especially in patients with mild hypertension or metabolic syndrome. Supplementation with strains such as Lactobacillus plantarum, L. helveticus, and Bifidobacterium breve has been shown to improve endothelial function, enhance SCFA production, and reduce oxidative stress [20]. However, the effects of probiotics are strain-specific, and the colonization of beneficial bacteria is often transient, which limits their long-term efficacy. Moreover, the effects observed in clinical trials are often modest compared to conventional pharmacological treatments. Meta-analyses suggest that multi-strain probiotic formulations administered for more than eight weeks yield the most pronounced antihypertensive effects. Yet, there is significant variability in the outcomes, and the long-term safety of these interventions remains unclear. Prebiotics—mainly nondigestible fibers like inulin and fructooligosaccharides—promote the growth of beneficial bacteria and increase SCFA synthesis, indirectly contributing to vasodilation and improved metabolic homeostasis [12]. Although prebiotics show promise, their effects can be influenced by diet and individual microbiome composition, making the outcomes more variable. Dietary interventions emphasizing high fiber, polyphenol-rich foods (e.g., fruits, vegetables, whole grains), and reduced salt intake have similarly been associated with favorable microbial remodeling and improved blood pressure control, further supporting the role of diet–microbiota interactions in hypertension management [21]. However, these dietary interventions are not universally effective, as some individuals may not respond adequately due to differences in gut microbiome composition or metabolic factors.

FMT

FMT represents a direct and powerful method for restoring gut microbial diversity. Clinical trials and animal studies have shown that transferring microbiota from normotensive donors to hypertensive recipients can reduce both systolic and diastolic blood pressure. Mechanistically, FMT reestablishes a balanced microbial community, increases SCFA-producing taxa, and decreases pro-inflammatory species such as Eggerthella lenta and Erysipelatoclostridium ramosum [22]. However, the effects of FMT are variable, and the therapeutic benefits observed in some trials have not been consistently reproduced in others. The transient nature of its effects, as seen in the first multicenter, randomized, placebo-controlled trial of FMT capsules, suggests that FMT may not provide long-term blood pressure control, and the observed reductions in systolic blood pressure (~4 mmHg) may be modest compared to conventional antihypertensive therapies. Despite these challenges, the trial demonstrated transient reductions in systolic blood pressure and improvements in microbial diversity, supporting the concept of microbiota manipulation as a viable therapeutic strategy [6]. Nonetheless, the clinical applicability of FMT is limited by several factors, including the complexity of donor-recipient matching, the safety concerns regarding long-term use, and the potential ethical issues surrounding the procedure. Future research should focus on optimizing FMT protocols, such as donor selection, delivery route, dosing frequency, and the development of next-generation standardized microbial consortia for targeted and reproducible effects. Additionally, further studies are needed to establish the long-term safety, efficacy, and clinical relevance of FMT in diverse patient populations.

Pharmacological–Microbiota Interactions

An emerging area of research highlights the bidirectional interactions between antihypertensive drugs and gut microbiota. Several medications, including angiotensin receptor blockers (e.g., irbesartan) and calcium channel blockers, have been found to modulate microbial composition by enriching beneficial genera like Lactobacillus and Akkermansia, potentially augmenting their blood pressure–lowering effects [23]. However, the effects of antihypertensive drugs on microbiota

https://doi.org/10.71321/w9jjqk66

composition are not fully understood, and the long-term consequences of these changes remain uncertain. Additionally, while some studies suggest that these microbiota changes could amplify the blood pressure–lowering effects of medications, the overall clinical impact is still debated, as microbiota modulation could also lead to unexpected side effects. Conversely, gut microbiota can metabolize and alter the bioavailability or efficacy of certain antihypertensive drugs through enzymatic modifications. For example, certain microbial populations may enhance or reduce the absorption of specific medications, thus influencing their therapeutic outcomes. These reciprocal interactions suggest that combining pharmacological treatments with microbiota-targeted approaches may yield synergistic therapeutic outcomes [24]. Nevertheless, these interactions are highly individual, and the variability in patient responses due to differences in microbiota composition poses a challenge for the widespread clinical implementation of microbiota-targeted therapies. Understanding these interactions at the metabolic and genomic levels will be essential for developing precision medicine strategies tailored to individual microbial profiles.

Personalized Microbiota-Based Therapies and Future Outlook

The heterogeneity of gut microbiota across individuals and populations poses both challenges and opportunities for personalized hypertension management. Advances in metagenomics, metabolomics, and artificial intelligence–driven modeling now allow the identification of microbial biomarkers predictive of therapeutic response. However, the variability in microbiota profiles between individuals complicates the development of standardized interventions, and the predictive power of microbial biomarkers for treatment outcomes remains inconsistent. Integration of multi-omics data can help design individualized interventions combining probiotics, diet, and pharmacotherapy to achieve sustained blood pressure control. Moreover, sex-specific differences in microbiota composition and hormonal influences on microbial metabolism warrant further exploration to refine personalized treatment strategies. These differences could affect how individuals respond to both dietary and pharmacological interventions, highlighting the need for gender-specific therapeutic approaches. Future research should also investigate the long-term safety, efficacy, and regulatory frameworks for microbiota-based therapies, as well as addressing ethical concerns related to microbiota manipulation, such as donor-recipient matching for FMT. Ensuring their clinical translation into standardized care for hypertension will require rigorous clinical trials and evidence-based guidelines to overcome the challenges associated with individual variability and treatment consistency.

Conclusion

In conclusion, gut microbiota represent a dynamic and modifiable determinant of blood pressure regulation. Restoring microbial homeostasis through dietary, probiotic, and microbial transplantation strategies provides a novel avenue for hypertension management beyond traditional pharmacological approaches. While current evidence underscores promising short-term benefits, the long-term efficacy of these interventions remains uncertain, and significant individual variability complicates the establishment of universal treatment protocols. Long-term safety, optimal dosage, and the risk of adverse effects in different populations require further investigation. Additionally, the mechanistic complexities of how gut microbiota influence blood pressure, including their interactions with other physiological systems and the host's genetic and environmental factors, remain to be fully understood. The integration of microbiome science with precision medicine and systems biology will be instrumental in developing targeted, sustainable, and patient-specific therapeutic solutions for hypertension, ultimately contributing to improved cardiovascular outcomes and global health. However, to translate these findings into clinical practice, future research must address the gaps in our understanding of microbiota-based therapies and overcome the challenges of individual variability, therapeutic consistency, and long-term clinical validation.

Abbreviations

Fecal microbiota transplantation: FMT; Hypothalamic-pituitary-adrenal: HPA; Lipopolysaccharide: LPS; Nitric oxide: NO; Short-chain fatty acid: SCFA; Toll-like receptor 4: TLR4; Trimethylamine-N-oxide: TMAO.

Author Contributions

HaiTao Yang drafted and revised the manuscript. JingKun Liu conceived the idea, supervised the study, and provided critical revisions. All authors read and approved the final version of the manuscript.

Acknowledgements

The authors thank the Department of Cardiology, The First Affiliated Hospital of Xinjiang Medical University, and the Department of Thoracic and Abdominal Radiotherapy, The Affiliated Tumor Hospital of Xinjiang Medical University, for their support.

Funding Information

Not applicable.

Ethics Approval and Consent to Participate

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

Competing Interests

The authors declare that they have no competing interests.

Data Availability

The authors declare that they have no existing or potential commercial or financial relationships that could create a conflict of interest at the time of conducting this study.

References

[1] Mishra SR, Satheesh G, Khanal V, Nguyen TN, Picone D, Chapman N, et al. Closing the Gap in Global Disparities in Hypertension Control. Hypertension. 2025 Mar;82(3):407-410. https://doi.org/10.1161/HYPERTENSIONAHA.124.24137

[2] Marques FZ, Mackay CR, Kaye DM. Beyond gut feelings: how the gut microbiota regulates blood pressure. Nat Rev Cardiol. 2018 Jan;15(1):20-32. https://doi.org/10.1038/nrcardio.2017.120

[3] Bartolomaeus H, Balogh A, Yakoub M, Homann S, Markó L, Höges S, et al. Short-Chain Fatty Acid Propionate Protects From Hypertensive Cardiovascular Damage. Circulation. 2019 Mar 12;139(11):1407-1421. https://doi.org/10.1161/CIRCULATIONAHA.118.036652

[4] Richards EM, Li J, Stevens BR, Pepine CJ, Raizada MK. Gut Microbiome and Neuroinflammation in Hypertension. Circ Res. 2022 Feb 4;130(3):401-417. https://doi.org/10.1161/CIRCRESAHA.121.319816

[5] Yang HT, Jiang ZH, Yang Y, Wu TT, Zheng YY, Ma YT, et al. Faecalibacterium prausnitzii as a potential Antiatherosclerotic microbe. Cell Commun Signal. 2024 Jan 19;22(1):54. https://doi.org/10.1186/s12964-023-01464-y

[6] Fan L, Chen J, Zhang Q, Ren J, Chen Y, Yang J, et al. Fecal microbiota transplantation for hypertension: an exploratory, multicenter, randomized, blinded, placebo-controlled trial. Microbiome. 2025 May 23;13(1):133. https://doi.org/10.1186/s40168-025-02118-6

[7] Li J, Wang SY, Yan KX, Wang P, Jiao J, Wang YD, et al. Intestinal microbiota by angiotensin receptor blocker therapy exerts protective effects against hypertensive damages. Imeta. 2024 Jul 18;3(4):e222. https://doi.org/10.1002/imt2.222

[8] Guo Y, Li X, Wang Z, Yu B. Gut Microbiota Dysbiosis in Human Hypertension: A Systematic Review of Observational Studies. Front Cardiovasc Med. 2021 May 14;8:650227. https://doi.org/10.3389/fcvm.2021.650227

[9] Hsu CN, Yu HR, Chan JYH, Lee WC, Wu KLH, Hou CY, et al. Maternal Acetate Supplementation Reverses Blood Pressure Increase in Male Offspring Induced by Exposure to Minocycline during Pregnancy and Lactation. Int J Mol Sci. 2022 Jul 18;23(14):7924. https://doi.org/10.3390/ijms23147924

[10] Wu X, Li Q, Cai J, Huang H, Ma S, Tan H. Longitudinal change of gut microbiota in hypertensive disorders in pregnancy: a nested case-control and Mendelian randomization study. Sci Rep. 2023 Oct 9;13(1):16986. https://doi.org/10.1038/s41598-023-43780-w

[11] Lewis-Mikhael AM, Davoodvandi A, Jafarnejad S. Effect of Lactobacillusplantarum containing probiotics on blood pressure: A systematic review and meta-analysis. Pharmacol Res. 2020 Mar;153:104663. https://doi.org/10.1016/j.phrs.2020.104663

[12] Zhao TX, Zhang L, Zhou N, Sun DS, Xie JH, Xu SK. Long-term use of probiotics for the management of office and ambulatory blood pressure: A systematic review and meta-analysis of randomized, controlled trials. Food Sci Nutr. 2022 Sep 20;11(1):101-113. https://doi.org/10.1002/fsn3.3069

[13] Dardi P, Dos Santos-Eichler RA, de Oliveira S, Vinolo MAR, Câmara NOS, Rossoni LV. Reduced intestinal butyrate availability is associated with the vascular remodeling in resistance arteries of hypertensive rats. Front Physiol. 2022 Sep 29;13:998362. https://doi.org/10.3389/fphys.2022.998362

[14] Xu L, Yu Q, Ma L, Su T, Zhang D, Yao D, et al. In vitro simulated fecal fermentation of mixed grains on short-chain fatty acid generation and its metabolized mechanism. Food Res Int. 2023 Aug;170:112949. https://doi.org/10.1016/j.foodres.2023.112949

[15] Joe B, McCarthy CG, Edwards JM, Cheng X, Chakraborty S, Yang T, et al. Microbiota Introduced to Germ-Free Rats Restores Vascular Contractility and Blood Pressure. Hypertension. 2020 Dec;76(6):1847-1855. https://doi.org/10.1161/HYPERTENSIONAHA.120.15939

[16] Kwon YN, Kim YJ. Gut-Brain-Microbiota Axis and Hypertension: A Literature Review. Curr Pharm Des. 2021;27(37):3939-3946. https://doi.org/10.2174/1381612827666210706161733

[17] Yang T, Maki KA, Marques FZ, Cai J, Joe B, Pepine CJ, et al. Hypertension and the Gut Microbiome: A Science Advisory From the American Heart Association. Hypertension. 2025 Sep;82(9):e160-e170. https://doi.org/10.1161/HYP.0000000000000247

[18] Jiang S, Shui Y, Cui Y, Tang C, Wang X, Qiu X, et al. Gut microbiota dependent trimethylamine N-oxide aggravates angiotensin II-induced hypertension. Redox Biol. 2021 Oct;46:102115. https://doi.org/10.1016/j.redox.2021.102115

[19] Tanaka M, Itoh H. Hypertension as a Metabolic Disorder and the Novel Role of the Gut. Curr Hypertens Rep. 2019 Jun 24;21(8):63. https://doi.org/10.1007/s11906-019-0964-5

[20] Robles-Vera I, de la Visitación N, Toral M, Sánchez M, Romero M, Gómez-Guzmán M, et al. Probiotic Bifidobacterium breve prevents DOCA-salt hypertension. FASEB J. 2020 Oct;34(10):13626-13640. https://doi.org/10.1096/fj.202001532R

[21] Zambrano AK, Cadena-Ullauri S, Ruiz-Pozo VA, Tamayo-Trujillo R, Paz-Cruz E, Guevara-Ramírez P, et al. Impact of fundamental components of the Mediterranean diet on the microbiota composition in blood pressure regulation. J Transl Med. 2024 May 3;22(1):417. https://doi.org/10.1186/s12967-024-05175-x

[22] Fan L, Ren J, Chen Y, Wang Y, Guo Z, Bu P, et al. Effect of fecal microbiota transplantation on primary hypertension and the underlying mechanism of gut microbiome restoration: protocol of a randomized, blinded, placebo-controlled study. Trials. 2022 Feb 24;23(1):178. https://doi.org/10.1186/s13063-022-06086-2

[23] Xiong Y, He Y, Chen Z, Wu T, Xiong Y, Peng Y, et al. Lactobacillus induced by irbesartan on spontaneously hyperten-

sive rat contribute to its antihypertensive effect. J Hypertens. 2024 Mar 1;42(3):460-470. https://doi.org/10.1097/HJH.0000000000003613

[24] Kyoung J, Atluri RR, Yang T. Resistance to Antihypertensive Drugs: Is Gut Microbiota the Missing Link? Hypertension. 2022 Oct;79(10):2138-2147. https://doi.org/10.1161/HYPERTENSIONAHA.122.19826