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The Gut Microbiome and Atrial Arrhythmias: A Narrative Review of Emerging Mechanisms

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Abstract

Background: The gut microbiome is increasingly recognized as a key modulator of systemic physiology, including inflammation, metabolism, and autonomic function, all of which are factors implicated in the development of cardiac arrhythmias. Despite this, its specific role in arrhythmogenesis, particularly atrial arrhythmias, remains underexplored. **Purpose:** This narrative review aims to provide an update on current information about how the gut microbiome may influence cardiac electrophysiology and contribute to the onset of atrial arrhythmias, with a focus on proposed mechanisms and call for further research into potential therapeutic interventions. **Methods:** Given the emerging nature of this topic and the limited consolidated literature, a narrative review approach was adopted. Sources were identified through targeted database searches using key terms such as gut microbiome, cardiac arrhythmias, atrial arrhythmias, inflammation, and autonomic nervous system. Articles were selected based on relevance and contribution to foundational or novel insights within the field. **Results:** Key mechanisms that need to be further researched linking the gut microbiome to arrhythmogenesis include systemic inflammation, microbial metabolite production and modulation of the autonomic nervous system. Dysbiosis contributes to an altered gut microbiome environment, allowing inflammatory mediators to affect cardiac function and disrupt electrical signaling. **Conclusions:** The gut microbiome appears to play a contributory role in arrhythmogenesis through pathways involving inflammation, metabolism, and autonomic regulation. While evidence continues to emerge, further research is needed to clarify the nature of this relationship and establish its relevance to atrial arrhythmia development.

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Introduction

The gut microbiome has become an emerging area of research in healthcare. Its potential role in influencing various organ systems, contributing to disease development, and informing new treatment options is actively being explored. One area that requires further investigation is the possible link between the gut microbiome composition and the risk of atrial arrhythmias. The heart

contains an intrinsic electrical conduction system that enables it to contract rhythmically and independently of direct input from other organ systems (Bhattacharyya & Munshi, 2020). On its own, the heart's pacemaker, the sinoatrial node, typically maintains a rhythm of approximately 60 to 100 beats per minute (Bhattacharyya & Munshi, 2020). However, in the body, this rate is regulated by the autonomic nervous system, which

adjusts the heart rate in response to physiological demands (Fedele & Brand, 2020). Whether beating independently or under autonomic influence, the heart's electrical impulses follow a specific conduction pathway (Fedele & Brand, 2020). When disruptions occur along this conduction pathway, the result is a disturbance in the heart's rhythm known as an arrhythmia (Antzelevitch & Burashnikov, 2011).

Arrhythmias are disorders of the heart's electrical system, causing irregular heart rhythms that can result in significant morbidity and mortality (Dai et al., 2021). There are many different types of arrhythmias. Different factors including the origin, rate or speed, whether it is regular or irregular, and the specific mechanism all contribute towards how a presenting arrhythmia is defined (Qananwah et al., 2024). While some arrhythmias can be classified as benign other arrhythmias, such as atrial fibrillation (AF) and ventricular arrhythmias, are associated with poor prognosis, including stroke, heart failure, and sudden cardiac death (SCD) (Waldmann et al., 2020). Dai et al. (2021) highlight traditional risk factors such as structural heart disease, electrolyte imbalances, and genetic predisposition as major contributors to an individual's risk for arrhythmias. More recently, however, emerging research has proposed that the gut microbiome may also play a role in arrhythmogenesis by influencing systemic inflammation, metabolism, and even the autonomic nervous system (Fan et al., 2023).

Atrial arrhythmias are the most common sustained cardiac arrhythmia and are a major risk factor for cardiac related concerns including ischemic stroke as well as increased risk for morbidity and

mortality (Khurshid et al., 2018). Among all rhythm abnormalities reported by Khurshid et al. (2018) in a prospective cohort study of 502,627 individuals using data from the UK Biobank, atrial fibrillation was the most prevalent type of arrhythmia across all age groups and both sexes, highlighting it as one of the most common forms of cardiac arrhythmia impacting the population. Further, Kornej et al. (2020) found that in the United States alone, at least 3 to 6 million people have atrial fibrillation with numbers projected to reach 6 to 16 million by 2025. Given the increasing burden of atrial arrhythmias worldwide and the expanding recognition of the gut microbiome's role in systemic health, exploring this intersection is both timely and necessary. Understanding how the gut microbiome may influence cardiac electrophysiology is important because it introduces a potentially modifiable factor in the pathogenesis of arrhythmias. Unlike many traditional risk factors such as age or structural heart disease, the gut microbiome can be modified through diet and probiotics which are non-invasive, quickly implementable, and cost efficient when compared to a healthcare system visit. If certain microbial profiles or metabolites are shown to contribute to arrhythmogenesis, this could be a possible avenue of further research for personalized prevention and treatment strategies. As such, exploring the gut-heart axis is not only scientifically relevant but also may hold promise for advancing integrative approaches to cardiovascular care.

Methods

This paper is a narrative review aimed at exploring the emerging relationship between the gut microbiome and atrial arrhythmias. Given the novelty of this

topic and the limited volume of consolidated research, a systematic approach was not employed. Instead, relevant articles were identified through targeted searches of scientific databases such as PubMed and Google Scholar, using keywords including “gut microbiome”, “cardiac arrhythmias”, “autonomic nervous system”, and “inflammation”. This review focused on atrial arrhythmias, reflecting the emphasis of the identified literature and screening process. While studies addressing ventricular arrhythmias or other cardiovascular conditions influenced by the gut microbiome were considered during the initial search, most relevant articles pertained to atrial arrhythmias, and thus the review centers on this area. Studies published in English between 2007 and 2025 were considered to capture both early investigations and more recent advances in this developing field. Articles were identified through keyword searches using Boolean logic with “AND” and “OR” as appropriate. Studies were excluded if they were not peer-reviewed journal articles, not published in English, or did not directly address the relationship between the gut microbiome and cardiac health or electrophysiology. Additional sources were selected based on relevance to the topic and contribution to foundational or emerging concepts in the field. The decision to select this approach was chosen to allow flexibility in capturing a wide range of perspectives from the existing literature.

Results and Discussions

The Gut Microbiome- Heart Axis

The gut microbiome is a complex community of microorganisms residing in the gastrointestinal tract, critical for maintaining health (Guinane & Cotter,

2013). Dysbiosis, an imbalance in the microbial community, has been linked to a variety of diseases, ranging from inflammatory conditions to metabolic syndromes and even cardiovascular disorders (Singh et al., 2024). Evidence suggests that the gut microbiome plays a role in regulating cardiac electrophysiology through various pathways, including microbial metabolites, immune modulation, and autonomic nervous system regulation (Singh et al., 2024). However, much of the evidence remains correlational limiting the direct applicability to human arrhythmias. Further longitudinal and interventional human studies are needed to clarify causality and mechanisms. The gut microbiome could be an underexplored factor in arrhythmogenesis, with potential therapeutic implications for the prevention and treatment of arrhythmias. This narrative review aims to review and provide an update on the complex relationship between the gut microbiome and atrial arrhythmias, to offer insights into the mechanisms through which the microbiome may influence heart rhythms, and the potential of therapeutic target for arrhythmia management.

Increased blood pressure, inflammation, and atherosclerosis all contribute towards atrial arrhythmias, particularly atrial fibrillation. Aune et al. (2023) revealed in their meta-analysis of cohort studies that persons with hypertension have a 50% increase in the relative risk of developing atrial fibrillation compared to persons without hypertension. However, it should be noted that cohort studies are observational and thus cannot fully establish causality. Potential confounding factors such as medication use and lifestyle were variably

controlled across included studies, which may affect the accuracy of the relative risk estimate (Aune et al., 2023). Guo et al. (2012) found in their review that inflammation plays a role in the pathophysiology development of atrial arrhythmias. Additionally, X. Yang et al. (2023) conducted a prospective cohort study of 478,524 individuals finding that multiple systemic inflammatory indicators showed strong associations with the onset of atrial fibrillation. It is also important to consider that as with other cohort studies, this observational design limits causal inference, and potential confounding factors such as lifestyle and medication use were not fully controlled, which could influence the strength of the associations. Atherosclerosis has also been found to be a risk factor for atrial arrhythmias (Willeit & Kiechl, 2024). Studies conducted by Eryd et al. (2014), Heeringa et al. (2007), and Willeit et al. (2013) all investigating the potential of atherosclerosis as a risk predictor for atrial arrhythmias determined that there is a positive relationship between variable and outcome.

The gut microbiome is composed of trillions of bacteria and other microorganisms, predominantly residing in the large intestine (Thursby & Jude, 2017). These microbes are involved in numerous physiological processes, including nutrient absorption, metabolism, and immune function (Martinez et al., 2021; Thursby & Jude, 2017). It has been previously discovered that the gut microbiome has been shown to influence various aspects of cardiovascular health (Tang et al., 2017). For instance, it plays a role in regulating blood pressure through the production of short-chain fatty acids (SCFAs) like butyrate, acetate, and propionate, which

have been found to promote vasodilation and reduce systemic inflammation (Z. Yang et al., 2023). In addition, microbial-derived metabolites, including trimethylamine N-oxide (TMAO), have been hypothesized in the pathogenesis of atherosclerosis, a known risk factor for arrhythmias (Huang et al., 2021). The gut microbiome can supposedly influence cardiac function both directly and indirectly through these microbial metabolites. Microbial metabolites, for example, have been shown to influence the electrophysiologic properties of the heart by modulating ion channels and the autonomic nervous system (Fan et al., 2023). It should be noted that, while growing evidence suggests that gut microbial products influence physiological factors associated with atrial arrhythmias such as blood pressure regulation, systemic inflammation, and atherosclerosis direct causative links remain unclear. Much like assembling a complex puzzle, current research offers compelling pieces, but the full picture of how the gut microbiome systemically affects cardiac electrophysiology is far from complete. The magnitude, direction, and clinical relevance of these effects are still not fully understood.

Short-Chain Fatty Acids as a Mediator in Cardiovascular Function

SCFAs can bind to G protein-coupled receptors (GPCRs) such as GPR41 and GPR43, which are expressed in various tissues including vascular, immune, and renal cells (Vinolo et al., 2011). Activation of these receptors can lead to vasodilation and improved endothelial function, contributing to lower blood pressure (Vinolo et al., 2011). In terms of inflammation, SCFAs suppress pro-inflammatory pathways by inhibiting

histone deacetylases (HDACs), which leads to increased expression of anti-inflammatory genes (Vinolo et al., 2011). They also promote the development and function of regulatory T-cells (Tregs) which through HDAC inhibition enhances production and suppressive function of regulatory T cells, helping to maintain immune balance and prevent excessive inflammation (Tao et al., 2007). Although these findings provide important mechanistic insights into how SCFAs modulate inflammation and vascular function via GPCRs and HDAC inhibition, evidence derives from cellular and molecular studies. The clinical relevance of these pathways in human cardiovascular health and arrhythmia risk remains to be confirmed, especially considering interindividual differences in microbiome composition and SCFA production.

Trimethylamine N-oxide (TMAO) as a Mediator in Cardiovascular Function

Trimethylamine N-oxide (TMAO) is a metabolite produced in the liver from trimethylamine (TMA), which is generated by gut bacteria during the digestion of dietary nutrients rich in choline, phosphatidylcholine, and L-carnitine (Gatarek & Kaluzna-Czaplinska, 2021). High concentration of TMAO in the blood promotes the accumulation of cholesterol in white blood cells, specifically macrophages, leading to foam cell formation, a key step in vascular plaque development (Gatarek & Kaluzna-Czaplinska, 2021). TMAO also enhances platelet hyperreactivity and thrombosis risk, by increasing calcium release inside platelets, important for platelet activation and aggregation (Zhu et al., 2016). When TMAO is present in circulation, it amplifies the response of platelets to common agonists like ADP, collagen, and thrombin

(Zhu et al., 2016). This heightened calcium signaling accelerates the conformational changes and surface expression of receptors needed for platelet clumping and clot formation, increasing the chance of cardiovascular events like heart attacks and strokes (Zhu et al., 2016). TMAO may also trigger vascular inflammation by activating pro-inflammatory signaling pathways such as NF- κ B (Da Cruz et al., 2024). TMAO activates NF- κ B signaling pathways in various cell types, including endothelial cells and vascular smooth muscle cells (Da Cruz et al., 2024). This activation leads to the increased expression of pro-inflammatory cytokines (IL-6 and TNF- α), adhesion molecules (VCAM-1 and ICAM-1), and other inflammatory mediators that contribute to vascular inflammation and endothelial dysfunction (Da Cruz et al., 2024; Al-Obaide et al., 2017). While these findings suggest a plausible mechanistic link between TMAO and cardiovascular risk, the evidence remains largely associative, and further studies are needed to confirm causality and clinical relevance.

Microbial Metabolites and Ion Channel Regulation

Both SCFAs and TMAO have been proposed to alter ion channels related to the cardiac system. SCFAs can cross the blood-brain barrier via monocarboxylate transporters (MCTs) and influence various neurons with different receptor expressions, leading to cascading effects which include increased sympathetic outflow that raises heart rate and promotes vasoconstriction, or enhanced parasympathetic outflow (Bruning et al., 2019). This can affect the expression or function of key cardiac ion channels, such as potassium (K^+), sodium (Na^+), and calcium (Ca^{2+}) channels, altering action

potential duration and conduction velocity (Fan et al., 2023). TMAO has been shown to directly impact calcium handling in cardiomyocytes (Oakley et al., 2020). It can enhance intracellular calcium release by influencing sarcoplasmic reticulum function or modulating calcium ion channel sensitivity (Oakley et al., 2020). This may increase the likelihood of arrhythmias by disturbing the delicate balance of calcium cycling in the heart (Oakley et al., 2020; Zhang et al., 2021).

Research using human participants are beginning to explore the relationship between the gut microbiome and arrhythmias. One study found that patients with atrial fibrillation (AF) exhibited a similar microbiome composition compared to healthy controls, however they had a reduction in microbial richness (Tabata et al., 2020). While Tabata et al. (2020) provide important initial insights, the study's small sample size and cross-sectional design limit causal inference. Additionally, differences in sample collection between patients and controls, along with potential confounding factors like diet and medication, may affect the reliability and generalizability of the findings. Another study by Pai et al. (2023) found associations between conditions such as metabolic syndrome, which impact the gut microbiome, and an increased risk of arrhythmias but confounding factors and indirect measures limit the specificity of these findings. These findings suggest that microbiome composition may influence arrhythmic susceptibility in human populations, although further research is needed to determine causality and identify specific microbial species involved.

Therapeutic Implications

Given the emerging role of the gut

microbiome in arrhythmogenesis, therapeutic strategies aimed at modulating the microbiome could offer novel approaches to arrhythmia prevention and management. Probiotics and prebiotics, which aim to restore or maintain a healthy gut microbiome, have been proposed as potential therapeutic strategies. Preliminary studies suggest that certain probiotic strains may reduce inflammation and improve heart rate variability, potentially reducing the risk of arrhythmias (Wu & Chiou, 2021). However, more clinical trials are needed to evaluate the efficacy of these interventions in arrhythmic patients. Additionally, consideration for specific variations of probiotics and how to control for subjectivity difference between microbiomes in different persons should be investigated.

Dietary interventions that promote a healthy gut microbiome, such as increasing fiber intake and reducing processed foods, could also have a significant impact on cardiac health (Aziz et al., 2024). Nogal et al. (2021) proposed that diets rich in fruits, vegetables, and whole grains have been shown to increase SCFA production and promote a favorable microbiota profile, potentially reducing the risk of arrhythmias. These findings suggest that lifestyle interventions targeting the gut microbiome may offer a promising strategy for arrhythmia prevention, yet much more investigation is required to understand the long-term effects and safety of microbiome-targeted therapies.

Challenges and Future Directions

Despite the promising connections between the gut microbiome and atrial arrhythmias, there are multiple challenges and limitations in this area of research,

specifically in studying the gut microbiome. Microbiome studies are often confounded by factors such as diet, medications, and underlying comorbid conditions (Sanna et al., 2022). Additionally, the heterogeneity of microbiome profiles among individuals makes it difficult to identify definitive biomarkers for atrial arrhythmias (Sanna et al., 2022). Large-scale longitudinal studies are needed to better understand the causal relationships between the gut microbiome and atrial arrhythmias, as well as to identify specific bacteria or metabolites involved.

Future research should also focus on clinical trials evaluating the effects of microbiome modulation on arrhythmic outcomes. By identifying specific microbial species or metabolites that influence atrial arrhythmias, personalized approaches to arrhythmia management could be developed, offering more targeted and effective therapies for patients.

Conclusions

Emerging evidence suggests that the gut microbiome plays a multifaceted role in cardiac electrophysiology and may influence the development of atrial arrhythmias through mechanisms involving inflammation, microbial metabolites, and autonomic regulation. While current research is still in its early stages, the gut-heart axis presents a compelling avenue for future investigation. Interventions aimed at modulating the gut microbiome, such as dietary changes and probiotic supplementation, may offer novel strategies for arrhythmia prevention and management. Further clinical studies are needed to establish causal relationships and to translate these findings into

effective, personalized therapeutic approaches.

Author's Qualifications

The author's qualifications are as follows: Nicholas Burton BKin, MKin Student.

References

- Al-Obaide, M., Singh, R., Datta, P., Rewers-Felkins, K., Salguero, M., Al-Obaidi, I., Rao Kottapalli, K., & Vasylyeva, T. (2017). Gut microbiota-dependent trimethylamine-N-oxide and serum biomarkers in patients with T2DM and advanced CKD. *Journal of Clinical Medicine*, 6(9). <https://doi.org/10.3390/jcm6090086>
- Antzelevitch, C., & Burashnikov, A. (2011). Overview of basic mechanisms of cardiac arrhythmia. *Cardiac Electrophysiology Clinics*, 3(1), 23–45. <https://doi.org/10.1016/j.ccep.2010.10.012>
- AR Hadi, H., Alsheikh-Ali, A., Al Mahmeed, W., & Al Suwaidi, J. (2010). Inflammatory cytokines and atrial fibrillation: Current and prospective views. *Journal of Inflammation Research*, 75–97. <https://doi.org/10.2147/JIR.S10095>
- Aune, D., Yahya Mahamat-Saleh, Kobeissi, E., Feng, T., Heath, A., & Janszky, I. (2023). Blood pressure, hypertension and the risk of atrial fibrillation: A systematic review and meta-analysis of cohort studies. *European Journal of Epidemiology*, 38(2), 145–178. <https://doi.org/10.1007/s10654-022-00914-0>
- Aziz, T., Hussain, N., Hameed, Z., & Lin, L. (2024). Elucidating the role of diet in maintaining gut health to reduce the risk of obesity, cardiovascular and other age-related inflammatory diseases: Recent challenges and future recommendations. *Gut Microbes*, 16(1). <https://doi.org/10.1080/19490976.2023.2297864>
- Bhattacharyya, S., & Munshi, N. (2020). Development of the cardiac conduction system. *Cold Spring Harbor Perspectives in Biology*, 12(12). <https://doi.org/10.1101/cshperspect.a037408>

- Bi, X., Zhang, S., Jiang, H., Ma, W., Li, Y., Lu, W., Yang, F., & Wei, Z. (2022). Mechanistic insights into inflammation-induced arrhythmias: A simulation study. *Frontiers in Physiology*, 13. <https://doi.org/10.3389/fphys.2022.843292>
- Bruning, J., Chapp, A., Kaurala, G., Wang, R., Techtmann, S., & Chen, Q.-H. (2019). Gut microbiota and short chain fatty acids: Influence on the autonomic nervous system. *Neuroscience Bulletin*, 36(1), 91–95. <https://doi.org/10.1007/s12264-019-00410-8>
- Chen, X., Bing, Z., He, J., Jiang, L., Luo, X., Su, Y., Kan, B., Huang, D., & Wei, Y. (2009). Downregulation of peroxisome proliferator-activated receptor- γ expression in hypertensive atrial fibrillation. *Clinical Cardiology*, 32(6), 337–345. <https://doi.org/10.1002/clc.20566>
- Da Cruz, B., Coutinho-Wolino, K., Cardozo, L., D'Avila Pereira, A., Tinoco Mesquita, C., Stenvinkel, P., Bergman, P., Mafra, D., & Stockler-Pinto, M. (2024). Is trimethylamine N-oxide (TMAO) associated with NF- κ B mRNA expression in patients with coronary artery disease? *International Journal of Cardiovascular Sciences*. <https://doi.org/10.36660/ijcs.20230113>
- Dai, H., Zhang, Q., Much, A. A., Maor, E., Segev, A., Beinart, R., Adawi, S., Lu, Y., Bragazzi, N., & Wu, J. (2021). Global, regional, and national prevalence, incidence, mortality, and risk factors for atrial fibrillation, 1990–2017: Results from the Global Burden of Disease Study 2017. *European Heart Journal - Quality of Care & Clinical Outcomes*, 7(6), 574–582. <https://doi.org/10.1093/ehjqcco/qcaa061>
- Di Vincenzo, F., Del Gaudio, A., Petito, V., Riccardo Lopetuso, L., & Scaldaferri, F. (2023). Gut microbiota, intestinal permeability, and systemic inflammation: A narrative review. *Internal and Emergency Medicine*, 19(2), 275–293. <https://doi.org/10.1007/s11739-023-03374-w>
- Eryd, S., Ostling, G., Rosvall, M., Persson, M., Smith, J. G., Melander, O., Bedblad, B., & Engstrom, G. (2014). Carotid intima-media thickness is associated with incidence of hospitalized atrial fibrillation. *Atherosclerosis*, 233(2), 673–678. <https://doi.org/10.1016/j.atherosclerosis.2014.01.050>
- Fan, H., Liu, X., Ren, Z., Fei, X., Luo, J., Yang, X., Xue, Y., Zhang, F., & Liang, B. (2023). Gut microbiota and cardiac arrhythmia. *Frontiers in Cellular and Infection Microbiology*, 13. <https://doi.org/10.3389/fcimb.2023.1147687>
- Fedele, L., & Brand, T. (2020). The intrinsic cardiac nervous system and its role in cardiac pacemaking and conduction. *Journal of Cardiovascular Development and Disease*, 7(4). <https://doi.org/10.3390/jcdd7040054>
- Gatarek, P., & Kaluzna-Czaplinska, J. (2021). Trimethylamine N-oxide (TMAO) in human health. *Experimental and Clinical Sciences*, 20, 301–319. <https://doi.org/10.17179/excli2020-3239>
- Gawalko, M., Agbaedeng, T., Saljic, A., Muller, D., Wilck, N., Schnabel, R., Penders, J., Rienstra, M., van Gelder, I., Jespersen, T., Schotten, U., Crijns, H., Kalman, J., Sanders, P., Nattel, S., Dobrev, D., & Linz, D. (2021). Gut microbiota, dysbiosis and atrial fibrillation. Arrhythmogenic mechanisms and potential clinical implications. *Cardiovascular Research*, 118(11), 2415–2427. <https://doi.org/10.1093/cvr/cvab292>
- Guinane, C., & Cotter, P. (2013). Role of the gut microbiota in health and chronic gastrointestinal disease: Understanding a hidden metabolic organ. *Therapeutic Advances in Gastroenterology*, 6(4), 295–308. <https://doi.org/10.1177/1756283X13482996>
- Guo, Y., Lip, G., & Apostolakis, S. (2012). Inflammation in atrial fibrillation. *JACC*, 60(22), 2263–2270. <https://doi.org/10.1016/j.jacc.2012.04.063>
- Heeringa, J., van der Kuip, D., Hofman, A., Kors, J., van Rooij, F., Lip, G., & Witteman, J. (2007). Subclinical atherosclerosis and risk of atrial fibrillation The Rotterdam Study. *JAMA Internal Medicine*, 167(4), 382–387. <https://doi.org/10.1001/archinte.167.4.382>

- Huang, R., Yan, L., & Lei, Y. (2021). The Gut Microbial-derived metabolite trimethylamine N-Oxide and atrial fibrillation: Relationships, mechanisms, and therapeutic strategies. *Clinical Interventions in Aging*, 16, 1975–1986. <https://doi.org/10.2147/CIA.S339590>
- Khurshid, S., Choi, S. H., Weng, L.-C., Wang, Y., Trinquart, L., Benjamin, E., Ellinor, P., & Lubitz, S. (2018). Frequency of cardiac rhythm abnormalities in a half million adults. *Circulation: Arrhythmia and Electrophysiology*, 11(7). <https://doi.org/10.1161/CIRCEP.118.006273>
- Kornej, J., Borschel, C., Benjamin, E., & Schnabel, R. (2020). Epidemiology of atrial fibrillation in the 21st Century: Novel methods and new insights. *Circulation Research*, 127(1). <https://doi.org/10.1161/CIRCRESAHA.120.316340>
- Martinez, J., Kahana, D., Ghuman, S., Wilson, H., Wilson, J., Kim, S., Lagishetty, V., Jacobs, J., Sinha-Hikim, A., & Friedman, T. (2021). Unhealthy lifestyle and gut dysbiosis: A better understanding of the effects of poor diet and nicotine on the intestinal microbiome. *Frontiers in Endocrinology*, 12. <https://doi.org/10.3389/fendo.2021.667066>
- Nogal, A., Valdes, A., & Menni, C. (2021). The role of short-chain fatty acids in the interplay between gut microbiota and diet in cardio-metabolic health. *Gut Microbes*, 13(1). <https://doi.org/10.1080/19490976.2021.1897212>
- Oakly, C., Vallejo, J., Wang, D., Gray, M., Tiede-Lewis, L., Shawgo, T., Daon, E., Zorn, G., Stubbs, J., & Wacker, M. (2020). Trimethylamine-N-oxide acutely increases cardiac muscle contractility. *American Journal of Physiology Heart and Circulatory Physiology*, 318(5), 1272–1282. <https://doi.org/10.1152/ajpheart.00507.2019>
- Pai, U., Prabhu, M., Devasia, T., Rao, S., V, R., Samanth, J., Prabhu, S., Lolita Mathias, H., & V, C. (2023). Prevalence of metabolic syndrome and its association with atrial arrhythmias in patients with implanted permanent pacemaker for cardiac conduction abnormality. *Indian Heart Journal*, 75(6), 462–464. <https://doi.org/10.1016/j.ihj.2023.10.006>
- Park, J., Lee, E., Lee, J., Kim, W., & Kim, H. (2007). Anti-inflammatory effects of short chain fatty acids in IFN- γ -stimulated RAW 264.7 murine macrophage cells: Involvement of NF- κ B and ERK signaling pathways. *International Immunopharmacology*, 7(1), 70–77. <https://doi.org/10.1016/j.intimp.2006.08.015>
- Qanawah, Q., Ababneh, M., & Dagamseh, A. (2024). Cardiac arrhythmias classification using photoplethysmography database. *Scientific Reports*, 14. <https://doi.org/10.1038/s41598-024-53142-9>
- Sanna, S., Kurilshikov, A., van der Graaf, A., Fu, J., & Zhernakova, A. (2022). Challenges and future directions for studying effects of host genetics on the gut microbiome. *Nature Genetics*, 54, 100–106. <https://doi.org/10.1038/s41588-021-00983-z>
- Singh, P., Meenatchi, R., Ahmed, Z. H. T., Thacharodi, A., Rohinth, M., Kumar, R., Varthan M. K. H., & Hassan, S. (2024). Implications of the gut microbiome in cardiovascular diseases: Association of gut microbiome with cardiovascular diseases, therapeutic interventions and multi-omics approach for precision medicine. *Medicine in Microecology*, 19. <https://doi.org/10.1016/j.medmic.2023.100096>
- Tabata, T., Yamashita, T., Hosomi, K., Park, J., Hayashi, T., Yoshida, N., Saito, Y., Fukuzawa, K., Konishi, K., Murakami, H., Kawashima, H., Mizuguchi, K., Miyachi, M., Kunisawa, J., & Hirata, K. (2020). Gut microbial composition in patients with atrial fibrillation: Effects of diet and drugs. *Springer*, 36(1), 105–114. <https://doi.org/10.1007/s00380-020-01669-y>
- Tang, W. W., Kitai, T., & Hazen, S. (2017). Gut Microbiota in cardiovascular health and disease. *Circulation Research*, 120(7), 1183–1196. <https://doi.org/10.1161/CIRCRESAHA.117.309715>
- Tao, R., de Zoeten, E., Ozkaynak, E., Chen, C., Wang, L., Porrett, P., Li, B., Turka, L., Olson, E., Greene, M., Wells, A., & Hancock, W.

- (2007). Deacetylase inhibition promotes the generation and function of regulatory T cells. *Nature Medicine*, 13, 1299–1307. <https://doi.org/10.1038/nm1652>
- Thursby, E., & Juge, N. (2017). Introduction to the human gut microbiota. *Biochemical Journal*, 474(11), 1823–1836. <https://doi.org/10.1042/BCJ20160510>
- Vinolo, M., Rodrigues, H., Nachbar, R., & Curi, R. (2011). Regulation of inflammation by short chain fatty acids. *Nutrients*, 3(10), 858–876. <https://doi.org/10.3390/nu3100858>
- Waldmann, V., Jouven, X., Narayanan, K., Piot, O., Chugh, S., Albert, C., & Marijon, E. (2020). Association between atrial fibrillation and sudden cardiac death: Pathophysiological and epidemiological insights. *Circulation Research*, 127(2). <https://doi.org/10.1161/CIRCRESAHA.120.316756>
- Willeit, K., Pechlaner, R., Egger, G., Weger, S., Oberhollenzer, M., Willeit, J., & Kiechl, S. (2013). Carotid atherosclerosis and incident atrial fibrillation. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 33(11). <https://doi.org/10.1161/ATVBAHA.113.302272>
- Willeit, K., & Kiechl, S. (2024). Atherosclerosis and atrial fibrillation – Two closely intertwined diseases. *Atherosclerosis*, 233(2), 679–681. <https://doi.org/10.1016/j.atherosclerosis.2013.11.082>
- Wu, H., & Chiou, J. (2021). Potential benefits of probiotics and prebiotics for coronary heart disease and stroke. *Nutrients*, 13(8). <https://doi.org/10.3390/nu13082878>
- Yang, X., Zhao, S., Wang, S., Cao, X., Xu, Y., Yan, M., Pang, M., Yi, F., & Wang, H. (2023). Systemic inflammation indicators and risk of incident arrhythmias in 478,524 individuals: Evidence from the UK Biobank cohort. *BMC Medicine*, 21. <https://doi.org/10.1186/s12916-023-02770-5>
- Yang, Z., Wang, Q., Liu, Y., Wang, L., Ge, Z., & Zhenzhen, L. (2023). Gut microbiota and hypertension: Association, mechanisms and treatment. *Clinical and Experimental Hypertension*, 45(1). <https://doi.org/10.1080/10641963.2023.2195135>
- Yukino-Iwashita, M., Nagatomo, Y., Kawai, A., Taruoka, A., Yumita, Y., Kagami, K., Yasuda, R., Toya, T., Ikegami, Y., Masaki, N., Ido, Y., & Adachi, T. (2022). Short-chain fatty acids in gut–heart axis: Their role in the pathology of heart failure. *Personalized Medicine*, 12(11). <https://doi.org/10.3390/jpm12111805>
- Zhang, Y., Wang, Y., Ke, B., & Du, J. (2021). TMAO: How gut microbiota contributes to heart failure. *Translational Research*, 228, 109–125. <https://doi.org/10.1016/j.trsl.2020.08.007>
- Zhu, W., Gregory, J., Org, E., Buffa, J., Gupta, N., Wang, Z., Li, L., Fu, X., Wu, Y., Mehrabian, M., Sartor, R. B., McIntyre, T., Silverstein, R., Tang, W. W., DiDonato, J., Brown, M., Lusa, A., & Hazen, S. (2016). Gut microbial metabolite TMAO enhances platelet hyperreactivity and thrombosis risk. *Cell Press*, 165(1), 111–124. <https://doi.org/10.1016/j.cell.2016.02.011>