OPEN ACCESS

ISSN: 2835-9496

Frasier K, et al. (2024): 451
DOI: 10.47991/2835-9496/AJCMR-134

Research Article

American Journal of Clinical and Medical Research

The Role of Skin Microbiota in Cardiovascular Health: Exploring the Gut-Skin-Heart Axis

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Citation: Frasier K, Li V, Hassan M, Lohana S, Vinagolu-Baur J, et al. (2024) The Role of Skin Microbiota in Cardiovascular Health: Exploring the Gut-Skin-Heart Axis. Ameri J Clin Med Re: AJCMR-134.

Received Date: 19 May, 2024; **Accepted Date:** 27 May, 2024; **Published Date:** 31 May, 2024

Abstract

This study investigates the intricate relationships among skin microbiota, gut microbiota, and cardiovascular health, framed within the emerging concept of the gut-skin-heart axis. While extensive research has highlighted the role of gut microbiota in cardiovascular diseases, the impact of skin microbiota remains less explored, necessitating a comprehensive examination. A literature search utilizing PubMed, Embase, and Web of Science databases was conducted, focusing on peer-reviewed articles discussing the relationship between alterations in skin microbiota and its cardiovascular effects. The paper identifies gaps in knowledge regarding skin microbiota's role in cardiovascular pathophysiology. Studies suggest that skin microbiota dysbiosis is linked with cardiovascular health issues. Findings also associate certain skin conditions, such as psoriasis and atopic dermatitis, with increased cardiovascular risks. Additionally, emerging insights into how skin microbiota may affect cardiovascular functions through immune-mediated pathways are explored. The gut-skin-heart axis presents a novel and significant area for cardiovascular research, underscoring the need for further exploration of skin microbiota's role. Future research should aim at uncovering specific microbial signatures linked to cardiovascular risks and developing therapeutic strategies targeting the skin microbiome to prevent and manage cardiovascular diseases, emphasizing the potential for innovative diagnostic and therapeutic approaches that could lead to personalized cardiovascular care.

Keywords: *atherosclerosis; cardiovascular health; skin microbiota; dysbiosis; gut-skin-heart axis.*

Introduction

The human microbiome, comprising diverse microbial communities inhabiting various body sites, is pivotal in maintaining physiological homeostasis and modulating disease susceptibility. The skin and gut microbiota have garnered significant attention among these microbial ecosystems due to their potential implications in numerous health conditions, including cardiovascular diseases (CVD). The concept of the gut-skin-heart axis has recently emerged, highlighting the intricate interplay between gut microbiota, skin microbiota, and cardiovascular health. While considerable research has focused on recognizing the role of gut microbiota in cardiovascular health, the contribution of skin microbiota to cardiovascular pathophysiology still needs to be explored.

The skin microbiota, consisting of diverse microbial communities on the skin's surface, is increasingly recognized for its role in local and systemic health. Recent studies have highlighted the dynamic nature of the skin microbiota and its influence on various physiological processes, including immune function and inflammatory responses. For example, research demonstrates that alterations in skin microbiota composition can impact immune cell activation and cytokine production, suggesting a potential link between skin microbiota dysbiosis and inflammatory diseases, including those affecting the cardiovascular system [1]. Furthermore, advances in sequencing technologies have enabled comprehensive characterization of the skin microbiome, revealing complex microbial interactions and their potential implications for host health [2].

While the gut microbiota has been extensively studied in the context of cardiovascular health, emerging evidence suggests that the skin microbiota may also play a significant role in cardiovascular pathophysiology. Studies have indicated that skin microbiota dysbiosis is associated with various dermatological conditions characterized by chronic inflammation, such as psoriasis and atopic dermatitis, which are also recognized risk factors for CVDs [3,4]. Moreover, recent research has proposed potential mechanisms through which alterations in skin microbiota composition may influence systemic inflammation and endothelial dysfunction, thereby contributing to the development and progression of cardiovascular disorders [5].

Given the increasing body of evidence linking skin microbiota to cardiovascular health, further investigation into the mechanisms underlying the gut-skin-heart axis is warranted. This paper aims to provide an in-depth review of the current literature on the role of skin microbiota in cardiovascular health, exploring potential mechanisms underlying the gut-skin-heart axis and identifying areas for future research to advance our

understanding of this groundbreaking topic. By studying the complex interactions between gut microbiota, skin microbiota, and cardiovascular physiology, future research will identify novel therapeutic targets and interventions for preventing and managing CVDs. Additionally, exploring the potential of targeting the skin microbiota as a therapeutic strategy holds promise for personalized approaches to cardiovascular health management, paving the way for precision medicine in the field of cardio-dermatology [6].

Materials and Methods

This systematic literature review was designed to explore the relationships between skin microbiota, gut microbiota, and cardiovascular health, specifically focusing on the emerging concept of the gut-skin-heart axis. A detailed search strategy was developed to retrieve relevant studies from electronic databases including PubMed, Embase, and Web of Science. The search was conducted using a combination of keywords related to "skin microbiota," "gut microbiota," "cardiovascular health," "cardiovascular diseases," and "gut-skin-heart axis." The search strategy was adjusted for each database to optimize the retrieval process. Studies were screened by two independent researchers, ensuring a broad analysis of the impact of skin microbiota alterations on cardiovascular health and the interactions within the gut-skin-heart axis. The articles included underwent qualitative analysis of their key points for further discussion.

Results

Skin Microbiota and Cardiovascular Health: Current Evidence

The skin, the body's largest organ, serves as a crucial barrier against environmental pathogens and provides a habitat for a myriad of microbial species collectively known as the skin microbiota. Extensive research has demonstrated a complex interplay between skin microbiota and cardiovascular health. Studies like those conducted by Smith et al. and Johnson et al. have identified associations between skin microbiota dysbiosis and increased cardiovascular risks, particularly in patients with chronic inflammatory conditions such as psoriasis and coronary artery disease [7,8]. These studies report significant alterations in skin microbiota composition correlated with an elevated risk of cardiovascular events. For instance, Johnson et al. observed decreased diversity in skin microbiota among patients with coronary artery disease compared to healthy individuals, suggesting a link between skin microbial imbalance and cardiovascular health.

Further elucidating the impact of skin microbiota, a study by Mei et al. revealed sex-specific differences in microbiota composition that were directly associated with variations in blood pressure, indicating a potential mechanistic pathway through which skin microbiota could influence cardiovascular physiology [9]. This study underscores the need for additional research to fully understand how alterations in skin microbiota contribute to CVD mechanisms.

Systemic infections stemming from skin flora, particularly involving coagulase-negative *Staphylococci* (CoNS) such as *Staphylococcus haemolyticus* (*S. haemolyticus*) and *Staphylococcus lugdunensis* (*S. lugdunensis*), highlight the clinical relevance of skin microbiota. *S. haemolyticus* is known to cause a range of nosocomial infections, including infective endocarditis (IE), bacteremia, septicemia, and catheter-associated infections through biofilm formation, all of which have significant cardiovascular implications [10]. *S. lugdunensis*, often found in lower body skin regions such as the inguinal fold and perineum, has been associated with severe infections such as destructive IE, resulting from a left-sided infection that causes vegetation [11]. This often requires surgical interventions and frequently leads to bacteremia and septic complications.

In addition to these findings, research highlights the extensive diversity within the skin microbiota across different body regions, with variations in microbial communities like *Corynebacterium striatum* (*C. striatum*), *Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes, and Proteobacteria* [12,13]. These variations are influenced by the specific chemical and anatomical environments of the skin, which can affect the overall health and disease susceptibility of an individual.

Moreover, the connection between dental health and cardiovascular risk is also evident, with oral and gut microbiota being associated with atherosclerosis and increased mortality [13]. Studies have shown that poor oral hygiene leading to gum disease results in biofilm formation, which can introduce bacteria into the bloodstream, elevating C-reactive protein (CRP) levels—a known marker of inflammation linked to increased cardiovascular risk [14]. A meta-analysis by Leng et al. reinforces the link between periodontal disease and cardiovascular events, advocating for preventative dental care as a means to mitigate cardiovascular risk [15]. These findings collectively highlight the significant role of skin and oral microbiota in influencing cardiovascular health, demonstrating the interconnectedness of microbial health across different body systems and its impact on overall CVD risk.

Discussion

Mechanisms of the Gut-Skin-Heart Axis

The mechanisms underlying the gut-skin-heart axis involve intricate interactions between gut microbiota, skin microbiota, and host physiology, ultimately influencing cardiovascular health. This axis demonstrates how crosstalk between gut and skin microbiota and their systemic inflammatory effects can impact vascular functions and contribute to the atherogenesis. Microbial metabolites and immune mediators derived from the gut microbiota have been documented to influence these cardiovascular mechanisms profoundly. As disturbances in gut microbiota composition and intestinal permeability can lead to systemic inflammation that adversely affect the skin barrier function, this modulates the skin microbiota composition, which can exert direct effects on cardiovascular physiology through metabolites and immune signals that enter the systemic circulation. These interactions may affect endothelial function, alter vascular tone, and potentially enhance the risk of thrombosis, underscoring the integrated nature of microbiota across body systems and their impact on cardiovascular health.

The role of diet in shaping the microbiome is increasingly recognized, extending its influence beyond the gut to affect the skin's microbial community. This relationship suggests that dietary interventions could significantly impact the microbiome's configuration, thereby influencing systemic health outcomes related to cardiovascular health. Diets high in saturated fats and processed foods, for example, are known to alter the skin's microbial balance, increase sebum production, and exacerbate conditions such as acne and dermatitis, which contribute to systemic inflammation—a key factor in CVD

pathogenesis [16,17,18,19]. Further, systemic inflammation is central to the pathogenesis of atherosclerosis through mechanisms that affect endothelial function and arterial plaque formation [19]. Research by Moitinho-Silva et al. supports the direct impact of dietary patterns on the skin microbiome, demonstrating significant correlations between total energy and macronutrient intake and the abundance of bacterial amplicon sequence variants (ASVs) within the genera *Propionibacterium*, *Corynebacterium*, and *Staphylococcus* [20]. This relationship highlights the potential of dietary interventions to modify skin microbiota in ways that might mitigate cardiovascular risks. Moreover, preclinical research by Moestrup et al. has shown that a high-fat diet can alter skin lipid composition and increase levels of specific bacteria like *Corynebacterium*, which are implicated in both skin disorders and systemic inflammatory processes [21].

The impact of dietary patterns on cardiovascular health is mediated through both direct and indirect mechanisms. Dietary components modulate immune responses and produce metabolites via the gut microbiota that impact the skin, affecting overall health [22,23]. Lifestyle choices such as smoking pose risks for atherosclerotic CVD in addition to altering both gut and skin microbiota, contributing to a systemic inflammatory state [24,25,26]. Thus, by influencing the composition of the skin microbiota, dietary patterns not only impact local cutaneous conditions but could also contribute to the broader systemic inflammatory environment associated with the development of CVDs. These interactions highlight the need for a holistic approach to diet and lifestyle modifications as part of CVD prevention and management strategies, recognizing the crucial role of microbiota across different body systems.

Future directions

The current understanding of the role of skin microbiota in cardiovascular health, while promising, highlights significant gaps in our knowledge that need to be addressed through future research. There is a growing consensus that specific microbial signatures in the skin may be linked to cardiovascular risk factors and outcomes, necessitating a focused exploration into these relationships. Identifying these signatures through longitudinal studies would provide insights into the dynamics of skin microbiota changes and their correlation with the progression and treatment responses of CVDs.

A deeper mechanistic understanding is crucial for developing targeted interventions. Studies investigating the immunological and metabolic pathways by which skin microbiota dysbiosis influences cardiovascular pathophysiology could reveal new therapeutic targets. For example, understanding how specific bacterial strains influence inflammatory pathways could guide the creation of interventions aimed at modulating these microorganisms to mitigate their adverse effects. Such research could lead to the development of innovative diagnostic tools and therapeutic strategies, potentially transforming the prevention and management of CVDs by targeting the skin microbiome. This approach promises to shift the paradigm from reactive to preventive cardiovascular medicine, making early intervention a feasible and effective strategy.

The intertwining of skin and gut microbiota with cardiovascular health is another area to explore. The impact of diet on these microbiota communities and their subsequent effect on systemic inflammation and cardiovascular health requires comprehensive investigation. Studies should explore how dietary components such as fats, proteins, and carbohydrates influence the composition and function of these microbiomes and identify potential dietary interventions. Additionally, the role of the immune system in mediating these effects offers another layer of complexity and opportunity for discovery. This research could lead to holistic dietary guidelines that not only promote general health but also specifically support cardiovascular and microbiome health.

The influence of stress, particularly through elevated cortisol levels, on the gut microbiota composition, skin health, and overall cardiovascular wellness is a critical area of research. Understanding how stress intersects with microbial health could unlock new strategies for managing cardiovascular risk. Elevated stress levels have been shown to disrupt both gut and skin microbiota, which may, in turn, exacerbate inflammation and contribute to the progression of CVDs. Investigating these relationships could lead to stress management becoming an integral part of CVD prevention and treatment protocols. Moreover, such studies could elucidate the pathways through which psychological well-being impacts physical health, particularly cardiovascular health through microbiota interactions.

There is also a pressing need to understand how commonly used medications, such as antibiotics, proton pump inhibitors, and nonsteroidal anti-inflammatory drugs (NSAIDs), influence the microbiome balance and contribute to cardiovascular risks. These medications are widely prescribed, and their impact on microbiota could have far-reaching implications for cardiovascular health, potentially disrupting microbial communities and promoting inflammatory processes. Furthermore, environmental factors such as pollution, toxins, and ultraviolet radiation play a significant role in skin health and its microbiota, which in turn can affect cardiovascular health. Systematic reviews or meta-analyses could be instrumental in synthesizing existing data and identifying patterns or causal links within the gut-skin-heart axis. By addressing these diverse but interconnected areas, future research can provide a more holistic understanding of the relationships between microbiota, environment, and cardiovascular health, thereby advancing our ability to treat and prevent CVDs in a more personalized and effective manner.

Conclusion

In conclusion, the gut-skin-heart axis represents an emerging novel topic in cardiovascular research, emphasizing the intricate interplay between gut microbiota, skin microbiota, and cardiovascular health. While the role of gut microbiota in cardiovascular diseases has been extensively studied, the contribution of skin microbiota still needs to be explored. However, it holds significant promise for advancing our understanding of cardiovascular pathophysiology. By further understanding the mechanisms underlying the gut-skin-heart axis and identifying potential therapeutic targets, future research endeavors may lead to innovative preventive and therapeutic strategies for cardiovascular diseases. Ultimately, unraveling the complexities of the gut-skin-heart axis may pave the way for personalized approaches to cardiovascular diagnosis, treatment, and management.

Funding: This research received no external funding.

Conflicts of Interest: The authors have no conflicts of interest to disclose.

Data Availability Statement: No underlying data was collected or produced in this study.

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