Molecular mechanisms and therapeutic strategies of gut microbiota modulation in Sarcopenia (Review)

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Abstract. Sarcopenia is an age-related disease that is characterized by a decline in muscle mass and function with significant epidemiological and clinical implications. In recent years, gut microbiota has gained attention as an important regulatory factor in human health. To the best of our knowledge, this is the first study to introduce the definition and epidemiological background of sarcopenia and analyze the potential impact of the gut microbiota on muscle metabolism and growth, including aspects such as gut microbiota metabolites, muscle protein synthesis and energy metabolism. Additionally, this article summarizes the current research progress in gut microbiota interventions for the treatment of sarcopenia, such as probiotics, prebiotics and fecal microbiota transplantation and discusses future research directions and potential therapeutic strategies.

Contents

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1. Introduction

With the intensification of population aging, sarcopenia has emerged as a growing public health concern (1). Sarcopenia, an age-related decline in muscle mass and function, is characterized by weight loss, slow walking pace, limited mobility, reduced grip strength and frequent falls (2). It affects the quality of life of patients and is closely associated with the occurrence and development of various chronic diseases, including chronic kidney disease (3), metabolic-associated fatty liver disease (4), inflammatory bowel disease (5,6), Parkinson's disease (7,8), Alzheimer's disease and chronic obstructive pulmonary disease (9). Epidemiological data have reported an increasing incidence of sarcopenia in the elderly population, leading to a significant physical and economic burden on patients (1). Therefore, understanding the molecular mechanisms underlying sarcopenia is important for developing new therapeutic strategies (10).

In recent years, scientific research has revealed the pivotal role of the gut microbiota in human health and diseases, particularly in the pathogenesis and progression of sarcopenia (11). The gut microbiota is a complex microbial community that actively participates in several physiological and pathological processes through its metabolites and interactions with the host (Fig. 1). Research on the association between the gut microbiota and muscle health has revealed complex interactions between the microbial community and the host, which likely impact muscle metabolism, growth and atrophy through multifaceted pathways, thereby influencing muscle quality and function (12,13).

The present article aimed to provide a comprehensive understanding of sarcopenia by introducing its definition and epidemiological data, thereby offering readers valuable insights into the disease background (14). Subsequently, a detailed exploration of the definition and composition of the gut microbiota is presented. Furthermore, the complex links between gut microbiota and sarcopenia will be elucidated, unraveling the precise molecular mechanisms through which the gut microbiota influences muscle quality and function. Additionally, an overview of current research advancements in gut microbiota interventions for sarcopenia is provided, along with discussions on future research directions and potential therapeutic strategies (15). By presenting this progressive series of insights, the present study strived to construct a robust theoretical framework that delves into the specific

mechanisms through which the gut microbiota affects muscle metabolism and growth, while also laying the groundwork for discussions on research progress, challenges and future prospects regarding gut microbiota interventions for sarcopenia.

Gut microbiota refers to the microbial community present in the human gastrointestinal tract, including bacteria, fungi, viruses, and other microorganisms. Bacteria are the major components of the gut microbiota (Table I) (16). Commonly encountered bacterial taxa in the gut microbiota include, but are not limited to, the following major groups: Bacteroidetes (antagonistic group), including genera such as *Bacteroides* and *Prevotella*, which comprise antagonistic and tolerogenic bacteria, respectively; Firmicutes (dominant group), including the Clostridia class and *Bacillus* group, containing beneficial bacteria such as *Lactobacillus* and *Clostridium*; Proteobacteria (deformative group), encompassing the order Enterobacteriales and the *Vibrio cholerae* species, including *Escherichia coli*; Actinobacteria (actinobacteria group), including the Actinobacteria phylum, where *Bifidobacterium* is commonly found (17-19). In addition to these major groups, various other microbial species from different phyla such as anaerobic and *Anaerococcus* species may also inhabit the gut. Furthermore, several types of viruses such as haloviruses and bacteriophages are present in the intestinal tract. The composition of the gut microbiota can be influenced by multiple factors, including dietary habits, environmental factors, age, physiological status and genetic factors (20). Therefore, the composition of gut microbiota may vary among individuals.

2. Gut microbiota dysbiosis in sarcopenia: Evidence and characteristics

Gut microbiota features in patients with sarcopenia. Previous studies have demonstrated significant differences in gut microbiota composition between individuals with sarcopenia and their healthy counterparts (21). Dysbiosis of the gut microbiota and its metabolites may contribute to distinct clinical complexities observed in frail elderly individuals (22). Specifically, the colonization of the gut microbiota in sarcopenia patients undergoing maintenance hemodialysis (MHD) has shown a diminished abundance of *Akkermansia* in the intestines of mice, indicating a potential role of altered gut microbiota in the development of skeletal muscle disorders in MHD patients (23). Particularly, reduced diversity and altered abundance of specific bacterial taxa have been observed in the gut microbiota of patients with sarcopenia (24,25). These changes include a decrease in beneficial taxa, such as *Akkermansia* and *Lactobacillus*, which play vital roles in maintaining the gut barrier function and regulating immune responses. Harmful bacteria, including *Clostridium* and Proteobacteria, tend to be more prevalent in the gut of patients (26-28). Metabolites produced by these abnormal bacterial populations may negatively affect the muscle health. These findings suggest that dysbiosis of the gut microbiota significantly contributes to the onset and progression of sarcopenia (Fig. 2). Thus, patients with sarcopenia exhibit specific gut microbiota characteristics. Reduced diversity, decreased abundance of beneficial taxa and increased levels of harmful bacteria collectively suggest the involvement of gut microbiota dysbiosis in the pathogenesis and progression of sarcopenia.

Although the association between gut microbiota imbalance and sarcopenia has been extensively reported, further exploration is required to establish a causal relationship. Current research has provided evidence from animal models and clinical trials. For instance, transplanting gut microbiota from healthy individuals into mice with muscle wasting demonstrated significant improvements in the muscle mass and function, indicating the therapeutic potential of gut microbiota restoration for treating muscle wasting (29,30). Moreover, supplementation with specific probiotics and prebiotics was reported to enhance the muscle mass and function in patients with sarcopenia, further supporting the role of gut microbiota in sarcopenia (31,32). Nonetheless, additional longitudinal studies and randomized controlled trials are necessary to elucidate the precise mechanisms underlying the gut microbiota imbalance in sarcopenia.

3. Mechanisms of gut microbiota dysbiosis in sarcopenia: Pathophysiological insights

An imbalance in gut microbiota, also known as dysbiosis of gut microbiota, has been shown to be associated with various muscle dysfunctions (33-57). The gut microbiota influence the muscle growth and metabolic processes by regulating the host energy balance and immune response through several mechanisms (58,59).

Imbalances in gut microbiota may affect the muscle health by triggering systemic inflammatory responses (21,60,61). Research indicates that imbalanced gut microbiota can impair the intestinal barrier function, increase the intestinal permeability and facilitate the translocation of bacterial endotoxins such as lipopolysaccharides, into the bloodstream, thus eliciting systemic inflammation (62,63). This chronic low-grade inflammatory state is considered a crucial pathological mechanism of sarcopenia, as inflammatory factors like TNF-α and IL-6, activated via the NF-κB signaling pathway, inhibit muscle protein synthesis and promote muscle protein degradation (64,65).

Metabolites produced by the gut microbiota, including short-chain fatty acids (SCFAs) and branched-chain amino acids, play a pivotal role in regulating muscle metabolism and function. SCFAs, such as butyrate and propionate, possess anti-inflammatory and immunomodulatory effects, promoting the muscle protein synthesis through the activation of the AMP-activated protein kinase signaling pathway (66). Conversely, an imbalance in gut microbiota can lead to a decline in the production of these beneficial metabolites, thereby affecting muscle health. Additionally, an increase in certain detrimental metabolites, such as indole and p-cresol, has been associated with muscle atrophy (67,68).

Genetic factors also contribute to the relationship between gut microbiota imbalance and muscle atrophy (69). Certain genetic variations can influence the composition and function of the gut microbiota, indirectly affecting the muscle health. For instance, mutations in FOXO3 are associated with gut microbiota diversity and muscle mass (70,71). Moreover, gene-environment interactions may regulate the muscle metabolism and function by influencing the gut microbiota, offering new insights for future personalized treatment strategies (72). Thus, dysbiosis of the gut microbiota affects muscle

Table I. Gut microbiota and sarcopenia.

A, Probiotics	
Classification/type of gut microbiota	Functions of gut microbiota in sarcopenia
Verrucomicrobia	
Akkermansia	d-Pinitol demonstrates potential in alleviating diabetic sarcopenia by increasing the abundance of *Akkermansia* and modulating metabolic pathways including nucleotide metabolism, β-alanine metabolism, histidine metabolism and calcium signaling pathway in the gastrocnemius muscle, as revealed by high-throughput analyses in a Streptozotocin-induced SAMP8 mouse model (33). Thus, the decrease in abundance may be related to muscle dysfunction, which helps maintain intestinal barrier and anti-inflammatory effects (33,34).
Firmicutes	
Lactobacillus	Probiotics *Lactobacillus paracasei* P62 and *Bifidobacterium bifidum* P61, alone or in combination, effectively mitigate sarcopenia and cognitive decline in aged mice by modulating gut microbiota and key signaling pathways, such as AKT, NF-κB and/or FOXO3a signaling pathways, resulting in increased muscle mass and improved functionality (35). Thus, *lactobacillus* reduces inflammatory response and may slow down muscle atrophy by enhancing intestinal barrier function and regulating immune response (35-37).
Roseburia	A lower abundance of *Roseburia* in the gut microbiota of elderly patients is negatively associated with interleukin-6 levels (36). Moreover, Roseburia produces butyrate, which helps maintain intestinal health and may have a positive effect on slowing down muscle atrophy.
Faecalibacterium	*Faecalibacterium*, a butyrate-producing bacterium, is causally linked to increased skeletal muscle mass through its role in gut microbial synthesis of butyrate, potentially leading to novel interventions for muscle mass maintenance (41). Thus, Faecalibactrium produces anti-inflammatory SCFAs that help maintain intestinal barriers and muscle health (42-44).
Actinobacteria	
Bifidobacterium	Actinobacteria include various bacteria that produce beneficial metabolites, which may contribute to anti-inflammatory and immune regulation (38,39). For example, the depletion of Actinobacteria in the gastrointestinal tract following FMT from autistic children is associated with increased pro-inflammatory factors and intestinal inflammation (36). *Bifidobacterium bifidum* plays a pivotal role in mitigating sarcopenia by enhancing gut health, which subsequently impacts key signaling cascades like AKT, NF-κB and FOXO3a, thereby improving muscle strength and cognitive function in aging mice (35). Additionally, bifidobacterium produces beneficial metabolites such as SCFAs, which contribute to muscle health and immune function (35,40).
Bacteroidetes	
Bacteroides	Bacteroides ferment dietary fiber to produce SCFAs, which may have a positive impact on muscle metabolism and function (45,46).
Prevotella	A lower abundance of *Prevotella* in the gut microbiota may be associated with the onset and development of sarcopenia in older adults (47). Mechanically, Prevotella may slow down muscle atrophy by producing beneficial metabolites and regulating host immune responses (47-49).
B, Pathogenic bacteria	
Classification/type of gut microbiota	Functions of gut microbiota in sarcopenia
Firmicutes	
Staphylococcus	Panton-Valentine Leukocidin expressed by *Staphylococcus aureus* contributes to muscle damage in myositis associated with CA-MRSA infections through the induction of pro-inflammatory chemokines and neutrophil recruitment, rather than direct cytolytic activity (50). *Staphylococcus* may induce inflammation on the surface of the skin and mucous membranes, affecting muscle health (51).
Clostridium	*Clostridium* species, including *Clostridium symbiosum* and *Clostridium citroniae*, are associated with increased relative abundance in individuals with sarcopenia, suggesting a potential role in the pathogenesis of the condition (44). Some *Clostridium* species may be associated with inflammation and muscle loss in patients with muscular atrophy (53).

Table I. Continued.

B, Pathogenic bacteria	
Classification/type of gut microbiota	Functions of gut microbiota in sarcopenia
Proteobacteria	
Escherichia coli	*Escherichia coli* may cause intestinal inflammation and muscle loss under certain conditions (52). A systematic review suggests that alterations in gut microbiota, including an increase in Enterobacteriaceae like *Escherichia coli*, are associated with sarcopenia, indicating a potential role for these bacteria in the pathogenesis of age-related muscle function decline (41).
Enterobacteriaceae	The overgrowth of Proteobacteria in the gut due to age-related changes and reduced bacterial diversity contributes to sarcopenia by enhancing inflammatory markers, generating ROS and inducing the destruction of free radical macromolecules, thereby modulating the host's metabolism and promoting muscle degradation (54). The overabundance of *Enterobacteriaceae*, particularly *Escherichia-Shigella* and *Klebsiella*, in the gut microbiota of patients with sarcopenia is associated with impaired protein processing and amino acid synthesis pathways, contributing to muscle mass loss and function (21,55). *Enterobacteriaceae* is associated with inflammation and decreased intestinal barrier function related to muscle atrophy (41,56).

SAMP8, senescence accelerated mouse-prone 8; AKT, AKT serine/threonine kinase 1; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; FOXO3a, forkhead box O3; FMT, fecal microbiota transplantation; CA-MRSA, community-acquired- methicillin-resistant *Staphylococcus aureus*; ROS, reactive oxygen species; SCFA, short-chain fatty acids.

health through various mechanisms, including modulation of inflammatory responses, alterations in metabolite production and interaction with genetic factors. Elucidating these mechanisms is crucial for developing targeted interventions to mitigate muscle dysfunction associated with gut microbiota imbalance.

4. Role of epigenetics in the relationship between gut microbiota and sarcopenia

Impact of gut microbiota on muscle health via epigenetic mechanisms. Gut microbiota can modulate the epigenetic status of the host either directly or indirectly through the production of various metabolites, including SCFAs (73,74). These metabolites can enter the bloodstream and affect distant tissues, including muscle cells (75). Fecal butyrate levels have been reported in older individuals with low muscle mass, suggesting a potential role for altered gut microbiota in the development of sarcopenia. These findings highlight the potential of gut microbial features and fecal butyrate as biomarkers for the early detection of sarcopenia (76), making them valuable diagnostic and intervention strategies. For instance, butyric acid, an SCFA, inhibits histone deacetylases, leading to increased histone acetylation and subsequent alterations in gene expression (77). Epigenetic regulation can influence the differentiation and regeneration capacity of muscle cells, thereby affecting the muscle health and function (78).

Furthermore, the gut microbiota modulates host gene expression by regulating the expression of microRNAs (miRNAs). miRNAs are a class of non-coding RNA molecules that regulate gene expression by inhibiting translation or promoting the degradation of specific mRNA targets (79). Studies have indicated that changes in the gut microbiota composition are associated with altered expression patterns of specific miRNAs, which may be involved in regulating muscle metabolism and processes associated with muscle atrophy (Fig. 3; Table II) (80-95). Circulating miRNAs (c-miRNAs), including miR-21, miR-126, miR-146a and miR-222, have been identified as potential biomarkers for sarcopenia (81). The upregulation of miR-141-3p in ovariectomized mice contributes to mitochondrial dysfunction by inhibiting FKBP prolyl isomerase 5 and Fibin, indicating that targeting miR-141-3p may be a promising therapeutic strategy for mitigating obesogenic sarcopenia (82). The expression profiles of miR-1, miR-133a/b, miR-206, miR-208b and miR-499 in 109 non-sarcopenic and 109 sarcopenic individuals were analyzed. These results revealed that sarcopenia and malnutrition frequently coexist in elderly individuals, suggesting that lower levels of miR-133b and miR-206 are associated with sarcopenia. The relationship between miR-133b and sarcopenia is mediated by the nutritional status, indicating the potential role of nutrition in modulating age-related muscle decline (83). The downregulation of miR-532-3p, which is associated with inflammation, regulates the apoptotic pathway during the development of sarcopenia by targeting BCL2 antagonist/killer 1 (84). Acupuncture has the potential to alleviate sarcopenia by regulating mitochondrial function and suppressing chronic inflammation through the miR-146a/interleukin 1 receptor associated kinase 1/TNF receptor associated factor 6/NF-kB signaling pathway, thus potentially decreasing the muscle wastage (85). Severe malnutrition and sarcopenia are strongly associated with poor surgical and oncological outcomes in patients with cancer. Decreased psoas muscle mass index (PMI) is an independent prognostic factor for overall survival, disease-free survival and metastasis in patients with colorectal

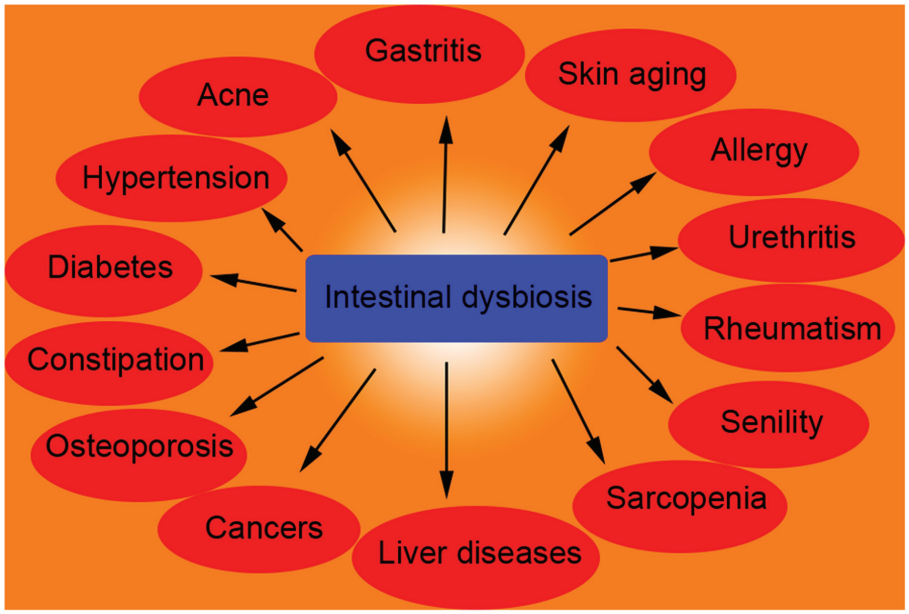

Figure 1. Gut microbiota actively participates in various physiological and pathological processes through its metabolites and interactions with the host.

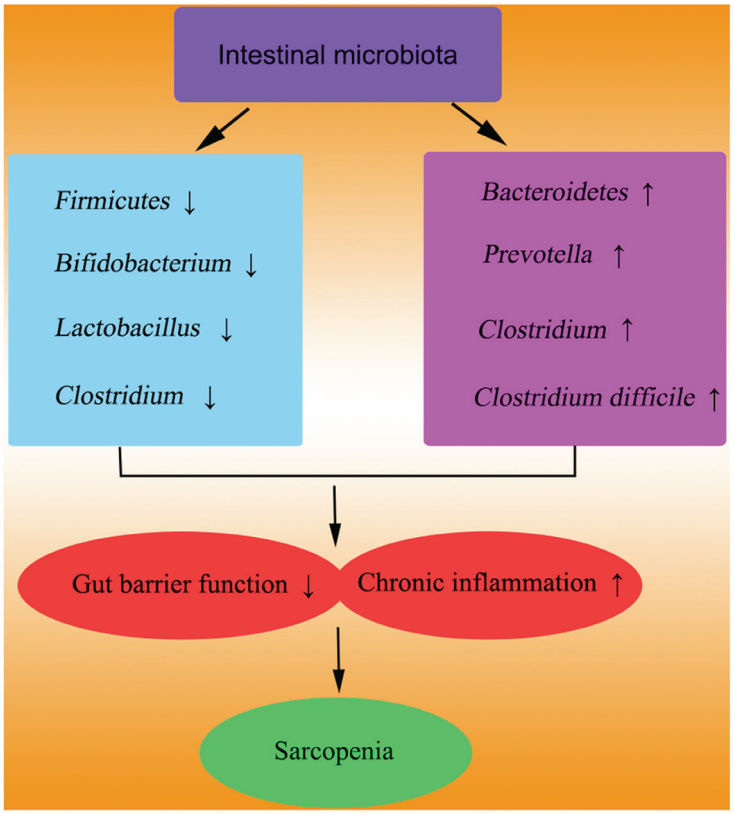

Figure 2. Patients with sarcopenia exhibit specific characteristics in their gut microbiota composition, including reduced diversity, decreased abundance of beneficial taxa and increased levels of harmful bacteria.

cancer (CRC). Serum miR-21 expression, which is associated with PMI, may serve as a potential biomarker of sarcopenia in patients with CRC (86). miR-33a serves as a clinical prognostic marker for sarcopenia and glioma by targeting FOS-like 1, AP-1 transcription factor subunit and engrailed homeobox 2 (87). The plasma levels of miR-29b, miR-181a and miR-494 were detected in a cohort of 93 individuals with sarcopenia. The results revealed a significant downregulation of plasma miR-29b in elderly individuals with sarcopenia and cardiovascular risk factors, including diabetes, hypertension and dyslipidemia (88).

Role of epigenetics in sarcopenia pathogenesis. Epigenetics serve a pivotal role in the development of sarcopenia, with

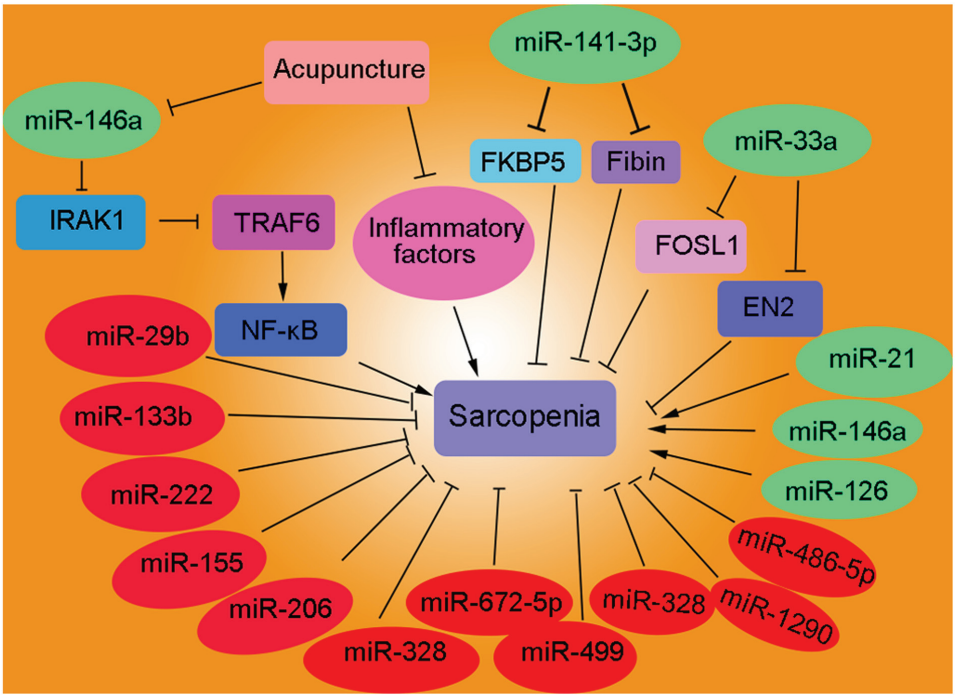

Figure 3. Gut microbiota modulates host gene expression by regulating the expression of miRNAs. FKBP5, FKBP prolyl isomerase 5; FOSL1, FOS like 1, AP-1 transcription factor subunit; EN2, engrailed homeobox 2; TRAF6, TNF receptor associated factor 6; IRAK1, interleukin-1 receptor-associated kinase 1; miRNAs/miRs, microRNAs.

DNA methylation, histone modifications and non-coding RNA regulation being the most extensively studied. Alterations in DNA methylation patterns in patients with sarcopenia can lead to the dysregulation of gene expression associated with muscle growth and repair (96). For instance, genes such as myogenic differentiation 1 and myocyte enhancer factor 2, which are crucial for muscle development, have promoter regions susceptible to changes in the methylation status that can affect their activity (97). Histone modifications also serve a critical role in sarcopenia, particularly in the imbalance between histone acetylation and deacetylation, which affects the muscle fiber-type conversion and energy metabolism (98). Non-coding RNAs, particularly miRNAs and long non-coding RNAs (lncRNAs), have emerged as key regulators of muscle atrophy and regeneration. These molecules modulate the muscle mass and function by targeting multiple signaling pathways, such as insulin-like growth factor 1/AKT/mTOR and TGF-β/SMAD pathways (99,100).

5. Diagnosis and monitoring of gut microbiota dysbiosis

Limitations of current diagnostic techniques. Currently, the diagnosis of gut microbiota relies heavily on high-throughput sequencing technologies, such as 16S ribosomal RNA gene sequencing and metagenomic analysis (101). Although these methods offer detailed information about the diversity and abundance of the gut microbiota, they have few limitations. Firstly, they often require expensive equipment and specialized knowledge, which limits their widespread application in clinical practice (102). Secondly, data interpretation can be complex and influenced by sample processing and analysis platforms (103). Furthermore, these techniques do not provide information on the microbial activity and function, which is crucial for understanding the relationship between gut microbiota dysbiosis and sarcopenia.

Prospects of emerging technologies. To overcome the limitations of the current diagnostic techniques, researchers are exploring new approaches for monitoring and diagnosing gut microbiota dysbiosis. One promising method is metabolomic analysis, which assesses microbial activity by detecting small molecular metabolites in blood, urine or fecal samples (102,104). Metabolomics not only reflects the functional state of the microbial community, but also reveals interactions between the host and microbiota (105). Moreover, the development of bioinformatics tools in recent years has enabled improved interpretation of complex datasets and the identification of disease-related biomarkers (106). Another emerging field is microbiome editing technologies, such as the CRISPR-Cas system, which provide a potential means of modulating specific microbial members to correct dysbiosis (107,108). Finally, portable devices and rapid testing platforms are under development, potentially allowing gut microbiota monitoring in the home or primary healthcare settings in the future (109).

6. Treatment strategies for sarcopenia targeting gut microbiota

Application of probiotics and prebiotics in treatment. The application of probiotics and prebiotics has emerged as an important strategy for modulating gut microbiota balance and impacting host health. In the context of sarcopenia treatment, probiotics can positively influence muscle metabolism by improving gut microbiota composition, enhancing intestinal barrier function and attenuating inflammatory responses (110).

Table II. Circulating microRNAs identified as biomarkers for sarcopenia.

miRNAs	Direction of deregulation	Related molecular mechanism of miRNAs	(Refs.)
miR-21	Upregulation	Plasma levels of Dkk-3, CAF22 and specific miRNAs including miR-21 and miR-206 serve as valuable indicators for evaluating accelerated sarcopenia in elderly individuals with respiratory conditions.	(89)
miR-126	Upregulation	Hsa-miR-126-5p exhibits the highest area under the curve value of 0.914.	(90)
miR-146a	Upregulation	miR-146a is involved in sarcopenia by mediating the IRAK1/TRAF6/NF-κB signaling pathway in rats.	(85)
miR-29b	Downregulation	A significant decrease in plasma levels of miR-29b is found in response to sarcopenia in elderly individuals with cardiovascular risk factors.	(88)
miR-33a	Upregulation	It has been found that hsa-mir-33a, which targeted both FOSL1 and EN2, exhibits promising predictive value for both glioblastoma and the reduction of skeletal muscle mass.	(87)
miR-141-3p	Upregulation	The increased levels of miR-141-3p lead to mitochondrial dysfunction by inhibiting Fkbp5 and Fibin, indicating that targeting miR-141-3p could be a potential therapeutic strategy for mitigating obesogenic sarcopenia.	(82)
miR-133b, miR-206	Downregulation	Decreased levels of miR-133b and miR-206 were found to be associated with a deteriorated nutritional status.	(83)
miR-155, miR-208b, miR-222, miR-210, miR-328, and miR-499	Downregulation	Plasma levels of miR-155, miR-208b, miR-222, miR-210, miR-328 and miR-499 are found to be significantly decreased in individuals with sarcopenia compared with those without sarcopenia.	(91)
miR-206	Downregulation	In both osteoporosis and sarcopenia, miR-155, miR-206 and miR-328 exhibit consistent dysregulation in terms of down-regulation.	(92)
miR-486-5p	Downregulation	BMSC-derived exosomes inhibit dexamethasone-induced muscle atrophy via miR486-5p/Foxo1 Axis.	(93)
miR-532-3p	Downregulation	Inflammation-driven reduction of miR-532-3p serves a role in the development of sarcopenia by modulating BAK1 expression.	(84)
miR-1290	Downregulation	miR-1290 promotes myoblast differentiation and prevents myotube atrophy by activating the Akt/p70/FoxO3 signaling pathway. These findings suggest that miR-1290 holds promise as a potential therapeutic target for the treatment of sarcopenia.	(94)
miR-672-5p	Downregulation	The expression of miR-672-5p is found to alleviate sarcopenia.	(95)

miR/miRNA, microRNA; Dkk-3, dickkopf-related protein 3; CAF22, plasma C-terminal agrin-fragment-22; IRAK1, interleukin-1 receptor-associated kinase 1; TRAF6, TNF receptor associated factor 6; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; FOSL1, FOS like 1, AP-1 transcription factor subunit; EN2, engrailed homeobox 2; Fkbp5, FKBP prolyl isomerase 5; BMSC, bone marrow mesenchymal stromal cells; Foxo1, forkhead box protein O1; BAK1, BCL2 antagonist/killer 2; Akt, AKT serine/threonine kinase.

For instance, specific strains of lactic acid bacteria have been shown to increase the production of SCFAs in the gut, which are vital for maintaining the muscle function and promoting muscle synthesis (111). Furthermore, prebiotics, as non-digestible food ingredients, promote the growth of beneficial bacterial communities such as *Bifidobacteria* and *Lactobacilli*, which indirectly affect muscle health through the production of metabolites such as SCFAs (112). However, the clinical application of probiotics and prebiotics requires further randomized controlled trials to validate their efficacy and safety.

Drug development targeting gut microbiota. The development of drugs targeting gut microbiota represents a promising therapeutic strategy to address the connection between gut microbiota dysbiosis and sarcopenia. These drugs regulate specific microbial communities or their metabolites to restore the gut microbiota balance and improve muscle function (113). For example, the administration of antibiotics or specific antimicrobial peptides can inhibit detrimental bacterial communities and alleviate their detrimental effects on host health (114). Additionally, research is exploring the utilization of prebiotics, invertase inhibitors and other approaches to modulate the activity and metabolic pathways of specific bacterial communities. Although these methods have potential, precise targeting and dose control are required to avoid adverse effects on microbial communities.

Fecal microbiota transplantation (FMT) and sarcopenia. FMT is a method for restoring the gut microbiota balance in the recipient's intestines by transplanting the gut microbiota of healthy donors. Although research on the use of FMT for the treatment of sarcopenia is still in its early stages, some encouraging findings have been reported. An animal study demonstrated that FMT transplantation of the gut microbiota of a healthy donor significantly improved the muscle atrophy caused by gut microbiota dysbiosis (115). Additionally, FMT positively affects muscle health by restoring gut microbiota diversity, enhancing intestinal barrier function and reducing inflammation (116). Despite the potential of FMT, further verification of its safety, efficacy and long-term effects in clinical applications is required.

Lifestyle interventions and gut microbiota modulation. In addition to direct interventions using probiotics, prebiotics or medications, lifestyle modifications are effective approaches for modulating the gut microbiota and treating sarcopenia. Dietary habits have a significant impact on gut microbial diversity and function. Consumption of a high-fiber diet promotes the growth of beneficial bacterial communities and increases the production of SCFAs, which are advantageous for maintaining muscle health. Moreover, moderate exercise has been shown to improve gut microbiota composition and enhance beneficial functions for overall health (117). Therefore, combining dietary adjustments with appropriate physical activity may represent a comprehensive and sustainable strategy for improving gut health and preventing or treating sarcopenia.

7. Conclusions and perspective

The present review article discusses the complex relationship between the gut microbiota and sarcopenia, emphasizing the important role of the gut microbiota in muscle health. By analyzing the mechanisms by which the gut microbiota influence muscle metabolism and growth, the present study provides a novel perspective for the prevention and treatment of sarcopenia. Until now, to the best of our knowledge, there have been no existing reports directly associating the specific types of bacteria discussed in the present study with the regulation of specific miRNAs in the context of sarcopenia, such as the *Akkermansia*, *Lactobacillus*, *Faecalibacterium*, *Prevotella*, Proteobacteria. This highlights miRNAs as a novel research direction and starting points in the current understanding of the molecular mechanisms involved.

In terms of treatment, the research progress on gut microbiota interventions for sarcopenia is promising. Intervention strategies such as probiotics, prebiotics and FMT have the potential to improve gut microbiota balance and muscle health. However, the safety and efficacy of these interventions requires further validation. Additionally, the development of personalized treatment strategies is essential, as there may be significant variations in the gut microbiota composition and response among individuals. Future research should also investigate the specific mechanisms through which the gut microbiota influences sarcopenia and address the limitations of existing technologies and methods. Firstly, an in-depth exploration of the complex relationship between gut microbiota and muscle metabolism, inflammatory responses and immune regulation is crucial for understanding the underlying mechanisms. Secondly, the development of more precise and efficient gut microbiota modulation technologies, such as gene editing technologies based on CRISPR-Cas9, will enable the precise control of specific microbial communities. Additionally, large-scale, long-term clinical studies evaluating the long-term effects and safety of different intervention methods are essential for establishing the clinical value of these interventions (118). Finally, interdisciplinary collaborations combining bioinformatics, systems biology and artificial intelligence technologies will help uncover the complex network relationships between gut microbiota and sarcopenia, providing a theoretical basis and technical support for the development of new treatment strategies.

Notably, Das *et al* (119) recently reviewed therapeutic approaches for sarcopenia by modulating the gut microbial health. The article by Das *et al* (119) and the present article focused on the relationship between the gut microbiota and muscular atrophy, and both studies considered the balance of the gut microbiota as a potential therapeutic strategy for sarcopenia. However, there are several differences between the two. Specifically, Das *et al* (119) focused on practical applications and discussed the management of sarcopenia by modulating the gut microbiota. The present study provided a comprehensive theoretical framework delving into the molecular mechanisms by which the gut microbiota is associated with sarcopenia. Moreover, Das *et al* (119) focused on translating the current research progress into practical treatment strategies; however, the present study emphasized a deep understanding of the mechanisms by which the gut microbiota influences muscle metabolism and growth. In summary, Das *et al* (119) provided practical treatment and management methods suitable for clinical doctors and patients seeking solutions. However, the present study provided an in-depth analysis of the relationship between muscular atrophy and the gut microbiota, which is suitable for readers interested in the molecular mechanism of the disease.

There were several studies on gut microbiota and sarcopenia; however, each study focused on different aspects. For example, Li *et al* (120) primarily focused on exercise as an intervention method, exploring how physical activity can impact muscle health by altering the gut microbiota and how it can prevent sarcopenia through modifications to the gut microbial community. Moreover, the study by Liu *et al* (16) included a total of 26 preclinical studies and 10 clinical studies, systematically reviewing the association between the gut microbiota and sarcopenia and investigating the relationship between changes in the gut microbiota and muscle/physical performance. Zhang *et al* (121) investigated the correlation between the gut microbiota and sarcopenia by analyzing data from human and animal studies, as well as the potential biological mechanisms through which the gut microbiota may affect muscle health, including protein synthesis, mitochondrial function, chronic inflammation and immune response. The novelty of this review lies in elucidating the molecular mechanisms between the gut microbiota and muscle atrophy, as well as mediating the progression of sarcopenia. Moreover, the present study also explored the

potential strategies for treating muscle atrophy by regulating the gut microbiota.

In conclusion, this review discusses the association between the gut microbiota and sarcopenia and elucidates the molecular mechanisms through which the gut microbial community affects the muscle metabolism and function. Furthermore, it summarizes the current research progress on the relationship between gut microbiota imbalance and sarcopenia, and proposes potential therapeutic strategies based on signaling pathways. Overall, gut microbiota plays an important role in the onset and development of sarcopenia. By investigating the mechanisms and intervention strategies in depth, the present study hopes to provide novel solutions for the prevention and treatment of sarcopenia, thereby improving the quality of life of patients.

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Author's contributions

CY designed the concept of the study, wrote and reviewed the manuscript and read and confirmed the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declares that they have no competing interests.

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