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REVIEW

Combined Nutrition with Exercise: Fueling the Fight Against Sarcopenia Through a Bibliometric Analysis and Review

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Objective: This bibliometric analysis and review aimed to examine the current research status and trends in the combination of nutrition and exercise training for sarcopenia. Additionally, it sought to provide researchers with future research directions in this field.
Methods: Relevant publications were obtained from the Web of Science Core Collection (WoSCC) database, covering the period from January 1995 to October 2023. The collected publications were analyzed using CiteSpace, VOSviewer, Bibliometrix, and Review Manager.
Results: Out of the 2528 retrieved publications, the United States emerged as the leading contributor in terms of publication volume. The University of Texas System was identified as the most productive institution. Luc J C van Loon emerged as the most published author in this field. Analysis of keywords revealed recent hot topics and emerging areas of interest, such as "gut microbiota" and "mechanisms". Upon further evaluation, resistance training (RT) and protein supplementation were identified as the most commonly employed and effective methods.
Conclusion: RT and protein supplementation are widely recognized as effective strategies. Future research should focus on investigating the molecular aspects of sarcopenia. Moreover, the potential therapeutic role of gut microbiota in sarcopenia requires further comprehensive investigation in human subjects to establish its correlation.
Keywords: sarcopenia, nutrition, exercise, bibliometric analysis, review

Introduction

Sarcopenia, a muscle disease characterized by reduced muscle strength, muscle mass, and/or physical performance,[1,2] is influenced by various factors such as physical inactivity, malnutrition, smoking, sleep deficiency, and diabetes.[3–6] The development of sarcopenia in elderly individuals can be attributed to these factors. Chronic inflammation, heightened oxidative stress, and mitochondrial dysfunction are potential contributors to the pathogenesis of sarcopenia.[7,8] The prevalence of sarcopenia among older individuals globally varies depending on the diagnostic criteria used. Estimates range from 5% according to the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) to 17% according to the International Working Group on Sarcopenia (IWGS).[9,10]

Sarcopenia has significant detrimental effects on older adults, including an increased risk of osteoporosis, falls, fractures, and mortality.[4] The number of studies focusing on the treatment of sarcopenia has increased in recent years. Previous research has suggested that combining exercise with nutrition yields similar efficacy to exercise alone.[11] However, a more recent study has indicated that a combination of nutrition and exercise is the most effective strategy

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for improving sarcopenia.[12] The varying outcomes of these studies indicate that the effectiveness of combining nutrition and exercise in the treatment of sarcopenia requires further investigation.[13]

Bibliometric analysis is a quantitative research technique that visually represents scientific literature, providing insights into research trends and hotspots in various fields.[14] It is a valuable tool for researchers to stay updated with the current state of research. While separate bibliometric analyses have been conducted on nutrition and exercise separately in the context of sarcopenia, there is a lack of published bibliometric analysis on the impact of combining nutrition and exercise training for sarcopenia. Conducting such an analysis is crucial for obtaining an accurate understanding of the current research landscape in this field.

In this study, the researchers utilized the RoB (Risk of Bias) tool in Review Manager software to assess the quality of recent articles, in addition to bibliometric analysis. Previous studies have proposed that combining nutritional intervention with physical exercise is a complementary approach that improves muscle health.[15] Notably, prompt protein supplementation after exercise has been shown to reverse negative muscle protein balance and synergistically enhance muscle protein synthesis (MPS), potentially leading to improvements in sarcopenia. These findings support the notion that the combination of exercise and nutrition may be more effective for treating sarcopenia, as suggested by previous research studies.[12,16,17]

Utilizing appropriate scientometric techniques to uncover the current state, frontiers, and potential research directions in a particular area is important. Therefore, this study employed a bibliometric analysis and review of the literature published between January 1995 and October 2023. To facilitate this analysis, software such as CiteSpace and Review Manager were utilized. The primary objective of this study was to investigate research trends and hotspots in the field and provide valuable references for future studies.

Materials and Methods

Data Collection and Search Strategy

Web of Science (WoS) is widely acknowledged as being amongst the most widely used academic databases.[18,19] For this study, the relevant literature was researched and exported via the Web of Science Core Collection (WoSCC) database on October 31, 2023, using the search terms provided below: topic =("nutrition intake" or "dietary supplements" or "diet" or "diets" or "dietary" or "nutrition" or "supplementation" or "protein") and ("sarcopenia" or "sarcopenic") and ("exercise" or "training" or "sport" or "movement" or "motion" or "physical activity" or "exercise therapy") and ("older" or "elderly" or "aging"), index = Science Citation Index Expanded (SCI-EXPANDED), and time span = 1995–2023. The flow chart of the retrieval strategy was shown in Figure 1.

Eligibility Criteria for Literature

The types of documents are mainly "article" and "review", including early access.

Withdrawal Criteria for Literature

(1) Meeting abstract; (2) Letter; (3) Editorial material; (4) Proceeding paper; (5) Correction; (6) Note; (7) Book chapters; (8) Reprint news item; (9) Retracted publications and (10) Non-English publications.

Analysis Tools

The bibliometric analysis in this research involved the use of multiple software tools for different purposes. Here is a breakdown of the software used and their specific functionalities:

GraphPad Prism 9: GraphPad Prism 9 was utilized to create the search flowchart. This software is known for its capabilities in graphing, statistical analysis, and data visualization.

Bibliometrix 4.1: Bibliometrix, developed by Massimo Aria and Corrado Cuccurullo, is a programming language specifically designed for conducting detailed bibliometric analyses. It follows the Science Mapping Workflow and provides various analytical features.

VOSviewer 1.6.19: VOSviewer is a bibliometric software developed by Nees Jan van Eck at Leiden University.[20] It was used in this study to analyze the co-authorship map of countries, authors, and institutions. VOSviewer excels in graphical display, allowing for clear visualization of cooperative relationships between projects.[21]

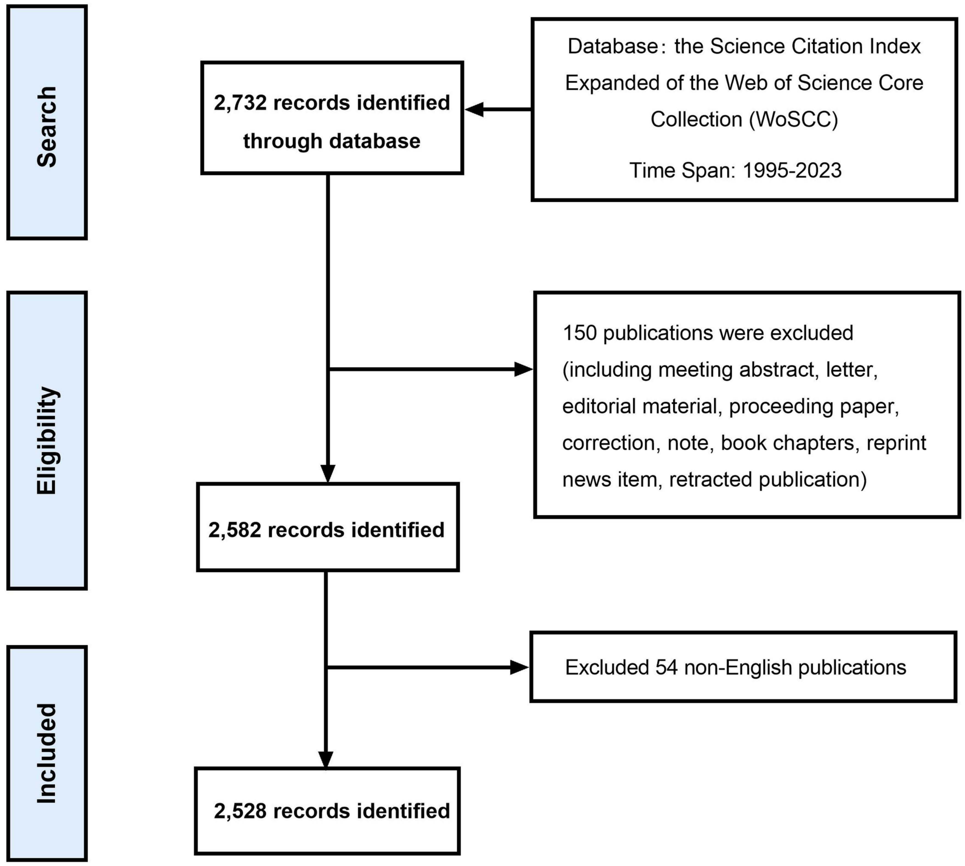

Figure 1 Flow chart of the retrieval strategy.

CiteSpace 6.2. R3: CiteSpace, created by Professor Chaomei Chen of Drexel University, is a Java-based software tool focused on visualizing bibliometric networks.[22] It analyzes data on institutions, authors, and keywords to reveal co-occurrence links. CiteSpace also features burst analysis and timeline visualization, highlighting trends and shifts in research hotspots.[23]

Review Manager 5.3: Review Manager is a software commonly used for assessing bias in systematic reviews and meta-analyses. In this study, Review Manager was used to evaluate the risk of bias in eligible randomized controlled trials (RCTs) from the past five years. The RoB tool was employed to assess various domains, such as random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other biases. The domains were categorized as having a "low risk of bias", "some concerns", or "high risk of bias".

Results

The Most Productive Countries Analysis

A total of 2528 publications on the topic of nutrition combined with exercise training for sarcopenia were produced by 63 countries between 1995 and 2023. Figure 2A illustrates the distribution of publications by country, represented by a color bar, while the collaboration between countries is depicted by colored links. Thicker lines indicate a higher level of collaboration between countries.

The top 10 countries in terms of the number of published articles are the ones whose names are highlighted. Among these countries, the United States ranked first with 662 publications, accounting for 26.18% of the total. The United Kingdom followed closely with 291 publications (11.51%), while China had 288 publications (11.39%). Japan contributed 269 publications (10.64%), and Italy had 249 publications (9.85%).

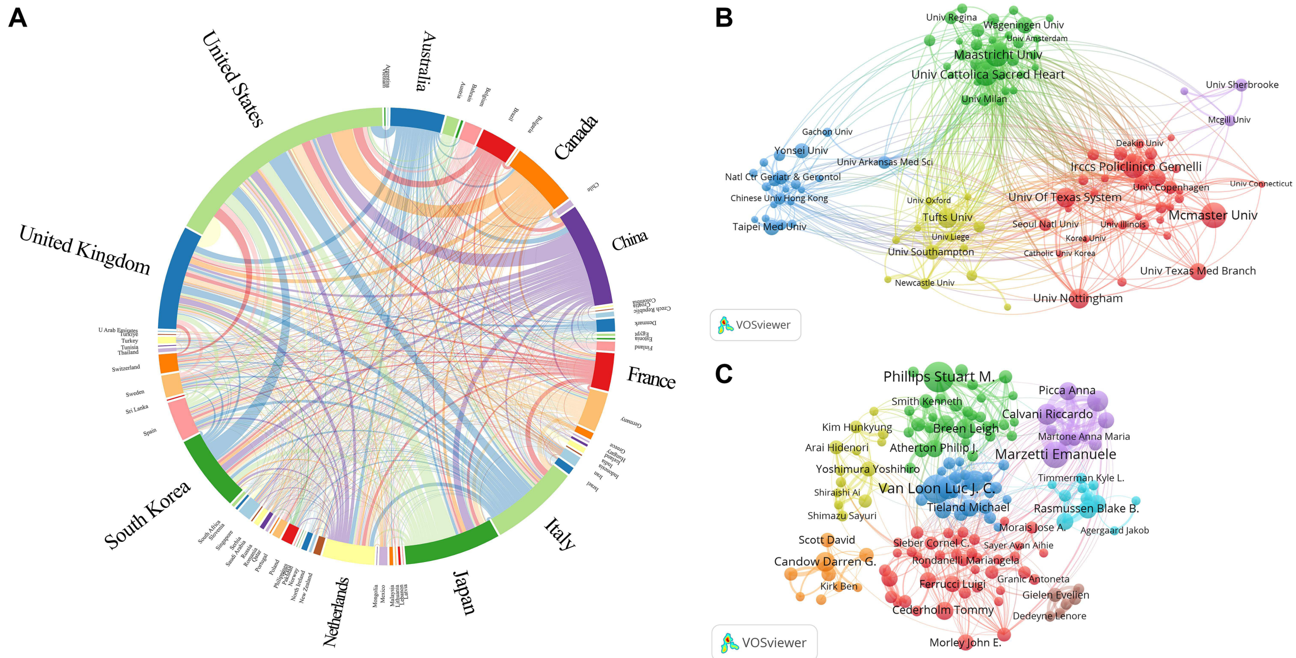

Figure 2 Analysis of contribution and cooperation. (**A**) Chord diagram of the national publications and cooperation; (**B**) Cooperation network map between institutions; (**C**) Cooperation network map between authors.

The Most Productive Institution Analysis

A total of 2528 publications on the topic of nutrition combined with exercise training for sarcopenia were produced by 2626 institutions between 1995 and 2023. Figure 2B displays a map illustrating the cooperation network between these institutions.

In the map, nodes represent institutions, and links between nodes represent collaborative relationships. The size of the nodes is directly proportional to the number of publications attributed to each institution. The color intensity of the lines between the nodes indicates the level of cooperation between institutions.

Among the institutions with more than 10 publications in the field, the University of Texas System ranked first with 64 publications. The Catholic University of the Sacred Heart followed closely with 60 publications, while Maastricht University had 59 publications. McMaster University and IRCCS Policlinico Gemelli were also prominent contributors with 57 and 56 publications, respectively.

The Most Influential Authors Analysis

A total of 2528 publications on the topic of nutrition combined with exercise training for sarcopenia involved contributions from 9781 authors. Figure 2C presents a cooperation network map among these authors.

The cooperation network map illustrates that authors collaborate closely with each other and form groups, often led by highly prolific authors. This visual representation provides insights into the collaborative relationships and patterns of authorship in the field.

Table 1 highlights the most prolific authors in terms of the number of published articles and their respective H-index values. Luc J C van Loon emerges as the most prolific author with 45 articles and an H-index of 89. Stuart Phillips closely follows with 44 articles and an H-index of 95. Emanuele Marzetti has contributed 37 articles with an H-index of 66, while Landi Francesco has published 31 articles with an H-index of 88. Riccardo Calvani rounds up the list with 26 articles and an H-index of 51.

Keywords Analysis

Keywords with Co-Occurrences and Clusters Analysis

Keywords indeed play a crucial role in summarizing research topics and identifying research hotspots.[24] In the analysis conducted using the bibliometrix package, a total of 3612 keywords were included in the study on nutrition combined with exercise training for sarcopenia. The top 50 keywords are visually represented in Figure 3A through a word cloud.

Table 1 Top 5 Authors on Nutrition Combined Exercise Training Research for Sarcopenia in Terms of the Number of Published Articles

Rank	Author	Publications	H index	Country	TC
1	Luc J C van Loon	45	89	Netherlands	27,835
2	Stuart Phillips	44	95	Canada	31,971
3	Emanuele Marzetti	37	66	Italy	15,452
4	Landi Francesco	31	88	Italy	42,497
5	Riccardo Calvani	26	51	Roma	8965

Abbreviations: H-index, Hirsch index; TC, Total Citations.

The word cloud provides a clear visualization of the most frequently occurring keywords. The font size of each keyword in the word cloud is proportional to its frequency of occurrence in the analyzed publications. Therefore, keywords that appear more frequently will have a larger font size in the word cloud, indicating their prominence and significance in the research landscape.

The co-occurrence relationships between keywords and clusters can provide valuable insights into internal connections and historical trends within research fields.[22] In this study, CiteSpace was employed to analyze the co-occurrence of keywords and clusters.

By selecting the keyword node type and utilizing pathfinder, pruning sliced networks, and pruning the merged network techniques, the analysis of keyword co-occurrence was conducted. The Log-likelihood ratio (LLR) was used for clustering analysis of keywords, resulting in the identification of 10 clusters. The landscape view of keywords and clusters is depicted in Figure 3B.

Furthermore, timeline analysis of the clusters can help identify the historical span of the literature within each cluster and highlight hot trends in research fields.[22] Figure 3C presents the clusters along horizontal timelines, arranging the keywords chronologically. Each keyword is represented as a node, with its size indicating its frequency of occurrence.

Based on the content and intrinsic relationships among the clusters identified in the analysis, they can be classified into three categories: (#0) muscle mass is the first category, mainly involving diagnosis and functional assessment; (#1) anabolic resistance, (#2) mitochondria, (#4) satellite cells, (#5) oxidative stress, (#6) sarcopenic obesity, and (#7) sex hormone are the second category, primarily focusing on risk factors and pathogenesis; (#3) vitamin D, (#8) protein intake, and (#9) strength training are the third category, mostly concentrating on the management.

Category 1: Sarcopenia is characterized by a decrease in skeletal muscle mass, which is influenced by both MPS and muscle protein breakdown (MPB). Exercise and nutrition are recognized as effective interventions for sarcopenia. However, a meta-analysis conducted in 2021 that evaluated the impact of exercise-alone, nutrition-alone, and combined exercise and nutrition interventions on sarcopenia found no significant differences in terms of muscle mass among the three approaches.[11]

The lack of significant differences in muscle mass outcomes may be attributed to several factors, including inconsistencies in evaluation tools and outcome measurements used across studies. Different studies might have employed different methods to assess muscle mass, leading to variations in the results obtained.

Bioelectrical impedance analysis (BIA) is a commonly used technique to determine the skeletal muscle mass index (SMI) for diagnosing sarcopenia. However, it is worth noting that the cutoff point for SMI varies between nations. This discrepancy in cutoff points can impact the precision of sarcopenia diagnosis and potentially lead to inconsistencies in identifying individuals with sarcopenia.[25]

Category 2: Anabolic resistance refers to a reduction in MPS rates following common anabolic stimuli in skeletal muscle.[26] In individuals with sarcopenia, anabolic resistance is primarily observed as a weakened response to MPS stimulation induced by strength exercise training and protein intake.[27]

The mechanisms underlying the synthetic metabolism associated with aging and anabolic resistance include several factors. Firstly, there is diminished activity in anabolic molecular signaling pathways, leading to a decreased ability to

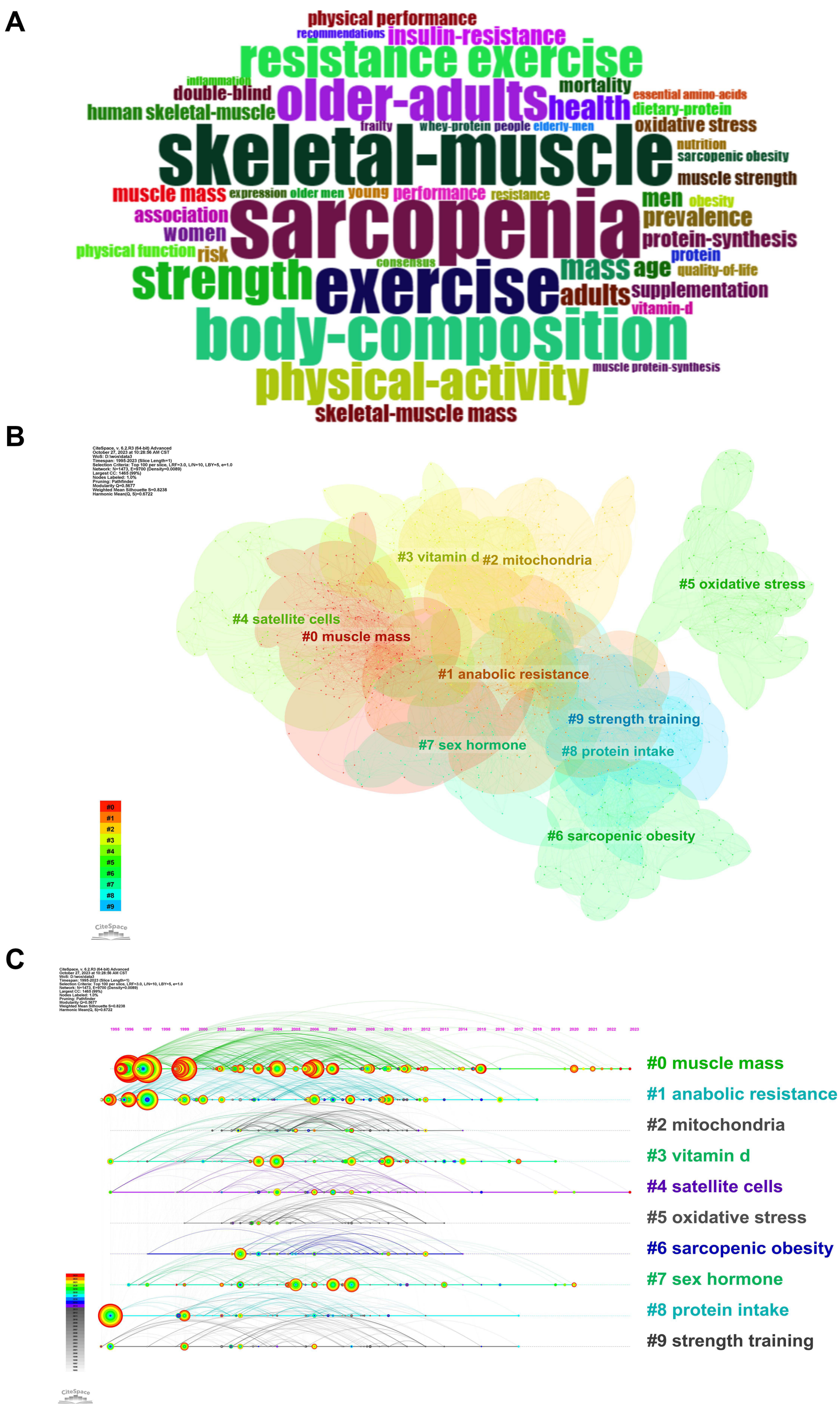

Figure 3 Analysis of keywords on nutrition combined exercise training for sarcopenia. (**A**) The word cloud of top 50 keyword; (**B**) Network visualization of keywords and clusters; (**C**) Timeline visualization of keywords and clusters.

stimulate protein synthesis. Additionally, there is reduced recruitment of insulin to the capillaries and increased retention of amino acids in the splanchnic area, further contributing to anabolic resistance.[28]

Mitochondrial dysfunction and oxidative stress also play a role in sarcopenia. Mitochondria, the powerhouse of cells, experience oxidative stress and reduced antioxidant defense mechanisms with age. This creates a harmful cycle that results in worsened mitochondrial separation, hindered fusion of mitochondria, suppressed electron transport chain function, decreased ATP production, increased mitochondrial DNA (mtDNA) damage, and impaired mitochondrial biogenesis. These mitochondrial abnormalities contribute to the development and progression of sarcopenia.[29]

However, engaging in moderate-intensity exercise for over four weeks has been shown to reduce sarcopenia by improving mitochondrial dysfunction. Exercise can help restore mitochondrial function and enhance mitochondrial biogenesis, leading to improved muscle health.[30]

Sex hormones, such as 17β-estradiol and testosterone, play a significant role in the health of skeletal muscle and are implicated in the pathophysiology and mechanisms of sarcopenia. These hormones can impact mitochondrial function through various pathways, including promoting mitochondrial biogenesis, mitophagy (the removal of damaged mitochondria), and ATP production within the mitochondria.[31] Low levels of free testosterone have been associated with reduced muscle strength in women and decreased physical performance in men over a two-year period.[32]

Satellite cells, which are skeletal muscle-specific somatic stem cells, have a crucial role in maintaining muscle trophism and regenerating muscle tissue.[33–35] While satellite cells are typically in a dormant state, they can be stimulated through activation, proliferation, differentiation, and fusion with existing muscle fibers.[36–38] Chronic exercise has been shown to activate and recruit satellite cells persistently.[39] Recent research, including animal experiments and human studies, has suggested that stem cell transplantation and tissue engineering could be potential treatments for sarcopenia in the future.[40]

Oxidative stress is a significant contributor to the occurrence and progression of sarcopenia. With age, the antioxidant capacity of cells decreases, and the activation, proliferation, and differentiation of skeletal muscle satellite cells are greatly inhibited due to the synergistic effects of oxidative stress and inflammation. This leads to the loss of muscle mass and strength.[41] Oxidative stress also activates p38 mitogen-activated protein kinase (MAPK) and stimulates forkhead box O3 (FoxO3), which inhibits mammalian target of rapamycin (mTOR) and contributes to protein breakdown rather than synthesis.[42,43] Microalgae, due to their composition, are believed to have potential antioxidant effects on mitochondrial function and oxidative stress. They are expected to become a treatment option for improving sarcopenia in the future.[44]

Sarcopenic obesity (SO) is characterized by the combination of obesity with low skeletal muscle mass and function (sarcopenia).[45] The prevalence of SO is around 0.9% in males and 1.4% in females.[46] SO is associated with multiple detrimental biological mechanisms.[47] Behavioral factors in older individuals, such as physical inactivity and inadequate nutrition intake, can also contribute to SO.[48–50] Interestingly, recent studies have found that older adults with longer sleep durations are more prone to SO.[51] Lifestyle modifications, including dietary management and exercise, are considered the most appropriate approach to improve SO.[47]

Category 3: Vitamin D and its receptor play a crucial role in regulating the activity of satellite cells, MPS, mitochondrial metabolism, and energy generation through various protein pathways, thereby maintaining the mass and function of skeletal muscle.[52,53]

In the elderly, the synthesis of vitamin D is hindered due to factors such as intestinal malabsorption, inadequate sun exposure, and impaired hydroxylation metabolism in the liver and kidneys. This can potentially contribute to the onset of sarcopenia.[54–56] Increasing serum vitamin D levels have been associated with an increase in irisin in women diagnosed with sarcopenia. Irisin is a myokine that is believed to have a positive effect on muscle health.[57] Past research has indicated that a reduction in irisin levels can contribute to a higher prevalence of sarcopenia.[58,59]

In 2011, researchers recommended a daily intake of 800 IU of vitamin D for the elderly, with the objective of increasing vitamin D levels in the blood to >50 nmol/L.[60] However, the correlation between the dose of vitamin D and improvements in muscle strength or mass has not been fully confirmed yet.[61]

Keywords with Citation Burst Analysis

Burst detection analysis can provide insights into the historical evolution and emerging trends in research fields by identifying keywords with significant citation bursts.[22] In the context of sarcopenia research, Figure 4 illustrates the top 20 keywords with the strongest citation bursts lasting for at least 2 years.

The top five keywords with the highest strength burst were "growth factor i" (13.62), "older men" (10.23), "necrosis factor alpha" (9.2), "essential amino acids" (9.14), "gait speed" (8.57). The analysis of keyword citation bursts can be split into two stages:

During the first stage of analysis (2002–2017), almost half of the burst keywords focused on the molecular level. These keywords included "growth factor i", "messenger RNA", "growth hormone", "gene expression", "necrosis factor alpha", and "interleukin 6". This suggests that research during this period was primarily focused on understanding the molecular mechanisms and pathways involved in sarcopenia.

In the second stage (2018–2023), the highest strength burst keywords were "gait speed" and "questionnaire". These keywords highlight the importance of assessment and timely evaluation in identifying individuals at risk of sarcopenia or those already diagnosed with sarcopenia. With increasing life expectancy and a growing geriatric population worldwide, the pressures posed by an aging society are mounting.[62] As sarcopenia has negative implications for musculoskeletal health, prevention and management strategies are becoming increasingly important.

Previous research has emphasized the importance of questionnaires and gait speed in the early diagnosis of sarcopenia. Questionnaires can be a cost-effective tool to identify adults with impaired mobility and help healthcare professionals and patients recognize sarcopenia based on its characteristic features.[1]

Gait speed, on the other hand, is a simple and accessible screening test. It can serve as an indicator of effectiveness during interventions and post-intervention periods. A two-stage algorithm suggests that individuals with poor gait speed, with or without poor grip strength, should be considered "at risk of sarcopenia".[63]

The performance of various screening tools for sarcopenia has been assessed using data from the SarcoPhAge cohort.[64] The method developed by Ishii et al demonstrated superior mathematical properties in distinguishing individuals at risk of sarcopenia from those without the condition.[65] These screening methods can be valuable in clinical practice to identify individuals who do not have sarcopenia.

Further research should focus on developing targeted and specific instruments to achieve more accurate diagnostic outcomes in sarcopenia. By refining and improving the existing screening tools, healthcare professionals will be better equipped to identify individuals at risk or affected by sarcopenia, leading to more effective management and interventions.

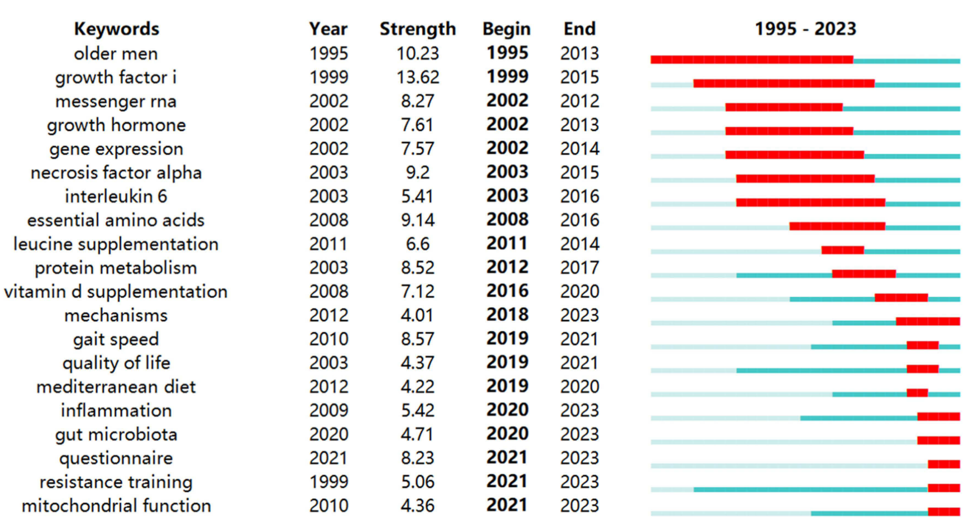

Figure 4 Top 20 keywords with the strongest citation bursts on nutrition combined exercise training research works on sarcopenia.
Notes: The bar graph displays commonly cited keywords in red and less frequently cited keywords in green. A greater strength represents a higher frequency of citation.

Interventions to combat sarcopenia are crucial for improving individuals' quality of life and reducing the risk of adverse outcomes. One intervention that has received considerable attention from researchers between 2019 and 2020 is the Mediterranean diet (MED). The MED has the potential to protect muscles by enhancing antioxidant and anti-inflammatory capabilities, thereby reducing the risk of age-related diseases associated with sarcopenia.[66–68]

During this period, the keyword "mechanisms" had the longest duration of citation burst, indicating significant attention to understanding the underlying mechanisms involved in sarcopenia. Current understanding suggests that the occurrence and progression of sarcopenia are related to increased levels of inflammation,[8] mitochondrial dysfunction,[7] and other factors.

The composition and diversity of gut microbiota are among the various potential factors that can impact the immune system and help prevent age-related diseases.[69,70] Exploring the role of nutrition and exercise training in improving sarcopenia, this article will delve into the mechanisms by which these interventions can be beneficial.h nutrition combined with exercise training can improve sarcopenia.

Secondary Screening of Randomized Controlled Trails

In order to assess the implementation and efficacy of interventions combining exercise and nutrition for sarcopenia, a secondary screening was conducted on the previously mentioned 2528 articles. The screening was based on the PICOS principle, which outlines the inclusion criteria as follows: (1) participants meeting the characteristics of sarcopenia, (2) interventions involving exercise combined with nutrition, (3) comparison groups receiving health education or no change in their original lifestyle (including meeting basic daily protein requirements), (4) main outcomes focused on muscle mass, muscle strength, or muscle function assessed through various tests such as gait speed, timed up and go test, chair-stand test, and the short physical performance battery (SPPB), and (5) RCTs. The publication timeframe was limited to articles published between 2019 and 2023. Ultimately, 9 articles met these criteria.

The 9 RCTs identified underwent quality assessment using the RoBtool in Review Manager software. The results of the evaluation are presented in Figure 5. Out of the analyzed studies, 8 reported random sequence generation, and 4 reported allocation concealment. Achieving double-blinding in exercise-related trials was challenging due to the non-pharmacological nature of exercise interventions. Three studies were single-blinded, meaning that the allocation was unknown or unclear to the outcome assessor. The outcome data was complete in 3 studies, and no selective reporting was found in any of the studies. The risk of other biases was unknown in 7 studies.

Table 2 provides an overview of the basic characteristics of the 9 RCTs included in the analysis. Here are some key findings:

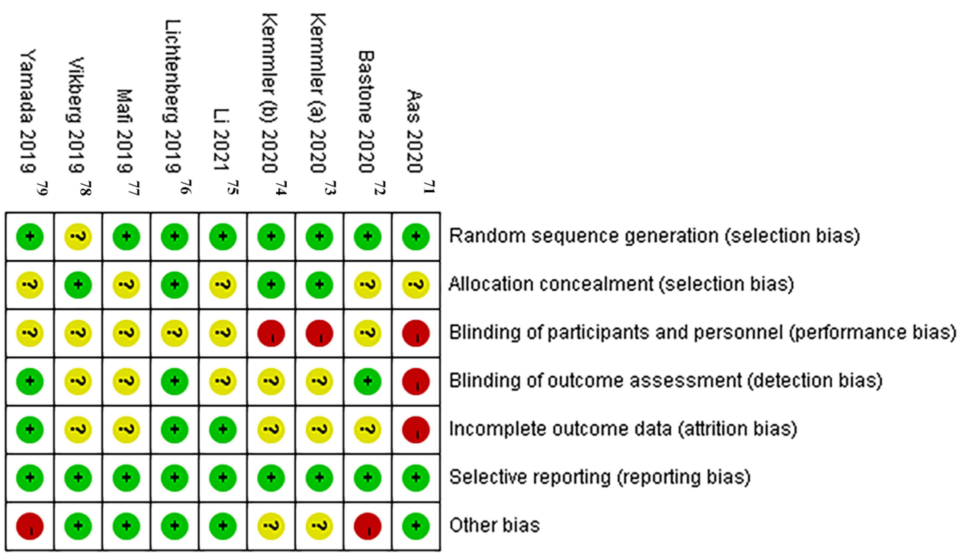

Figure 5 Risk of bias summary displaying the evaluations of each item for 9 RCTs included.

Table 2 Basic Characteristics of RCTs on Exercise Combined with Nutrition in Population with Features of Sarcopenia in Recent Years

Author	Population	Intervention	Duration	Main Outcomes		
				Muscle Mass	Muscle Strength	Muscle Function
Aas[71]	Mobility-limited older people	HI-RT plus protein	10 weeks	+	+	+
Bastone[72]	Older people with low handgrip strength	RT plus protein	12 weeks	-	+	+
Kemmler(a)[73]	Osteosarcopenia	HI-RT plus protein	72 weeks	+	+	-
Kemmler(b)[74]	Osteosarcopenia	HI-RT plus protein	12 months	+	+	NR
Li[75]	Sarcopenia	RT plus whey protein, vitamin D3, etc.	12 weeks	+	+	NR
Lichtenberg[76]	Osteosarcopenia	HI-RT plus protein	28 weeks	+	+	NR
Mafi[77]	Sarcopenia	RT plus epicatechin	8 weeks	+	NR	+
Vikberg[78]	Pre-sarcopenia	RT plus protein, etc.	10 weeks	NR	NR	+
Yamada[79]	Sarcopenia	RT plus whey protein and vitamin D	12 weeks	+	+	+

Notes: The symbols "+" and "-" respectively indicate a significant improvement or no significant change in outcome compared to the control group (P<0.05). The abbreviation "NR" indicates that the outcome was not referred in the study, while "HI" and "RT" refer to high intensity and resistance training, respectively.

Participants: Two articles focused on individuals at risk of sarcopenia or showing some characteristics of sarcopenia, while the remaining seven articles specifically targeted individuals with sarcopenia.

Exercise Interventions: All nine studies implemented resistance training (RT) as part of the intervention. Four of these studies employed high-intensity RT.

Nutritional Interventions: Six studies incorporated protein supplementation as part of the intervention. Two studies focused on a combination of protein and vitamin D supplementation. One study investigated the effects of epicatechin supplementation.

Efficacy: In terms of efficacy, exercise combined with nutritional interventions in the nine RCTs resulted in statistically significant improvements in the main outcome indicators compared to the control group. However, it should be noted that muscle mass did not show significant improvement in the Bastone article, and muscle function did not significantly improve in the Kemmler (a) article.

Taking these findings into consideration, it can be tentatively suggested that exercise combined with nutrition is an effective intervention for sarcopenia. RT and protein supplementation emerged as the most commonly employed methods in recent years. These findings highlight the potential benefits of incorporating exercise and nutritional strategies in the management and treatment of sarcopenia.

Discussion

As individuals age, muscle strength tends to decline at a faster rate than skeletal muscle mass, and this decline is strongly associated with dysfunction, the development of sarcopenia, and increased mortality risk. Interventions that focus on promoting muscle strength, either alone or in conjunction with enhancing muscle mass, are likely to have significant benefits for overall health and quality of life.[80]

Strength training, particularly RT, is recommended as an effective approach to combat sarcopenia, given that sarcopenia is characterized by both reduced muscle mass and strength. RT can produce positive effects on sarcopenia through various physiological mechanisms. For instance, it can stimulate the activation and proliferation of satellite cells, enhance MPS, and inhibit MPB, thereby increasing both muscle mass and strength.[81]

RT also activates the mTORC-1 signaling pathway, leading to the phosphorylation and activation of downstream proteins such as ribosomal protein s6 (rps6) and eukaryotic initiation factor 4E binding protein 1 (4E-BP1). These molecular events ultimately contribute to an increase in MPS, further supporting the positive effects of RT on sarcopenia.[82,83]

To address sarcopenia comprehensively, it is recommended to include exercises that target large muscle groups throughout the body. Additionally, while low-intensity RT (≤50% of one-repetition maximum, 1RM) has been shown to promote increases in muscle strength, some studies suggest that high-intensity RT (80% 1RM) may yield greater gains in maximum strength. Other RT protocols, such as mixed-mode exercise combined with aerobic training (AT) and blood flow restriction training, are also being investigated for their potential benefits in sarcopenia management.[84]

Indeed, the findings regarding the effects of RT on sarcopenia have been somewhat inconsistent. A meta-analysis conducted in 2021 reported positive improvements in knee extension strength, timed up and go (TUG) test, and gait speed with RT, but no significant effects on the chair-stand test.[85] However, a subsequent meta-analysis in 2023 suggested that RT may be more effective in improving chair-stand test results compared to alternative training programs. These discrepancies could be attributed to variations in participant characteristics and the specific RT protocols employed across different studies.

In recent years, there has been a growing interest in investigating intervention strategies for sarcopenia at the omics level. Research has shown that regular exercise has a profound impact on the skeletal muscle proteome and the composition of muscle fibers.[86,87] For instance, RT can lead to significant alterations in the expression pattern of myosin heavy chain (MyHC) subtypes. These changes may include decreased levels of MyHC-1 (Myosin-7) and increased levels of MyHC-2x (Myosin-1), which could contribute to improvements in muscle function and performance.[88]

Furthermore, the content of mitochondrial proteins in the muscles of untrained elderly individuals tends to decrease, resulting in decreased oxidative capacity. However, after undergoing RT, there is an observed increase in the content of mitochondrial proteins, such as cytochrome c (CYCS) and malate dehydrogenase 2 (MDH2), within the muscles. This suggests that RT can have a positive impact on mitochondrial function and enhance the oxidative capacity of skeletal muscles.[89]

In fact, various forms of exercise, such as AT, have been shown to have significant benefits for patients with sarcopenia.[90]

AT can have a positive impact on mitochondrial efficiency by increasing mitochondrial density and activity. It also promotes insulin sensitivity, reduces fat deposition in muscles, and enhances muscle function. Additionally, there is evidence suggesting a relationship between sleep quality and the prevalence of sarcopenia, with insufficient sleep potentially contributing to its development.[91] Sleep deprivation can lead to elevated cortisol levels and reduced insulin-like growth factor 1 (IGF-1) levels, which can contribute to muscle degeneration.[92,93] Prolonged AT has been shown to inhibit myonuclear apoptosis and increase IGF-1 levels, potentially mitigating muscle aging.[94] Furthermore, exercise training programs like AT may improve sleep quality in older adults with sleep problems.[95] While the indirect effects of AT on mitigating sarcopenia through improved sleep quality are promising, further research is needed to confirm and explore this relationship.

In addition to exercise, nutritional supplementation plays a crucial role in combating sarcopenia. Malnourished aged skeletal muscle often exhibits dysregulated expression of various proteins.[96] For example, slow-twitch soleus muscles may show irregular expression of proteins like ELAVL1 and RRAS2. ELAVL1 has been associated with skeletal muscle atrophy,[97] while RRAS2 is linked to the MAPK signaling pathway, which can affect skeletal muscle hypertrophy. Amino acids and proteins are commonly used as nutritional supplements to combat sarcopenia. Protein supplementation has been found to downregulate the Ubiquitin-proteasome pathway (UPP), reduce oxidative stress, inhibit autophagy, downregulate certain microRNAs (miRNAs), and improve the abundance of gut microbiota, all of which can be beneficial in treating sarcopenia.[98]

It is important to note that an increase in skeletal muscle mass and strength is typically not observed solely with protein or amino acid supplementation without exercise training.[99] Research has shown that protein supplementation, when combined with RT, yields greater improvements in muscle mass and strength among elderly individuals compared to RT alone.[100] This can be explained by the dynamic balance between MPS and MPB. After RT, both MPS and MPB increase, but timely protein intake, such as through supplementation, can cause a synergistic increase in MPS, resulting in a positive muscle protein balance. When RT is combined with adequate nutritional supplements, it maximizes the stimulation of MPS, ultimately leading to an increase in muscle mass.

In summary, exercise, particularly AT, along with nutritional supplementation, including protein intake, are important strategies in the fight against sarcopenia. These interventions have the potential to improve muscle function, prevent muscle degeneration, and promote muscle protein synthesis, ultimately enhancing muscle mass and strength in individuals with sarcopenia.

In recent years, the study of sarcopenia has led to increased attention on the role of gut microbiota, as evident from the citation burst. Research has revealed a potential relationship between gut microbiota and muscle mass, muscle function, and physical performance. Certain gut microbiota have been found to enhance amino acid availability, stimulate insulin secretion and responsiveness, thereby promoting protein anabolism.[101] Moreover, specific gut microbiota can reduce inflammation through the production of short-chain fatty acids, contribute to the maintenance of skeletal muscle quality, and improve skeletal muscle function.[102,103] The composition of gut microbiota has been shown to differ among young mice, aged mice, and aged mice with sarcopenia, suggesting a potential link to the pathogenesis of sarcopenia.[104] Furthermore, a Mendelian randomized study has indicated a causal relationship between specific gut microbiota and low grip strength and appendicular lean mass.[105] However, further scientific evidence is required to establish the relationship between gut microbiota and sarcopenia as potential therapeutic targets.[106]

The ongoing research on the effectiveness of exercise training combined with protein supplementation for sarcopenia is influenced by various factors, including participant profiles (age, gender, health status), diversity of protein supplements (type, quantity, duration), exercise training protocols (type, intensity, frequency), and assessment tools.[107] These factors can contribute to differences in research outcomes and highlight the need for further investigation. Additionally, advancements in omics technology are expected to play a vital role in identifying key signaling pathways associated with sarcopenia and developing personalized treatment options for sarcopenia patients.

It is worth noting that this study appears to be the first bibliometric analysis of the effects of exercise and nutrition on sarcopenia. The analysis includes relevant literature published since the establishment of the WoS database and aims to present the current research status, identify hotspots in the field, clarify the mechanisms underlying the combination of exercise and nutrition for improving sarcopenia, and provide insights into future research directions.

There are limitations in this study. The search was conducted solely in the WoS database, and the inclusion of articles was limited to those published in English, potentially excluding relevant studies published in other languages. To obtain a comprehensive understanding of the topic, it may be necessary to consider literature from additional databases and include studies published in other languages as well.

Conclusion

This study employed bibliometric analysis and review techniques to explore the field of nutrition combined with exercise training for sarcopenia. The analysis encompassed a substantial number of publications, spanning from January 1995 to October 2023, and highlighted the United States as the leading country in terms of publications. The study also identified prominent authors and institutions contributing to this field.

The analysis of keywords revealed ongoing interest in topics such as inflammation, mitochondrial function, mechanisms, and gut microbiota, indicating their significance in sarcopenia research. Following a secondary screening, nine RCTs met the eligibility criteria, although none of them were double-blinded for participants and personnel.

RT and protein supplementation emerged as common approaches in the selected RCTs, suggesting their effectiveness in addressing sarcopenia. The study also indicated that the link between gut microbiota and sarcopenia requires further validation, and the application of omics methods could provide detailed insights for the development of superior therapies for sarcopenia patients.

In summary, this research tries to provide a comprehensive overview of the field of nutrition combined with exercise training for sarcopenia. By analyzing the extensive literature and identifying key trends, the study aims to offer researchers a broader perspective on the potential of this field of study.

Abbreviations

WoS, Web of Science; CC, core collection; RCT, randomized controlled trail; RoB, Risk of Bias; EWGSOP2, European Working Group on Sarcopenia in Older People 2; IWGS, International Working Group on Sarcopenia; MPS, muscle protein synthesis; H-index, Hirsch index; TC, total citations; LLR, log-likelihood ratio; MPB, muscle protein breakdown; BIA, bioelectrical impedance analysis; SMI, skeletal muscle mass index; mtDNA, mitochondrial DNA; MAPK, mitogen-activated protein kinase; FoxO3, forkhead box O3; mTOR, mammalian target of rapamycin; SO, sarcopenic obesity; MED, Mediterranean diet; SPPB, short physical performance battery; RT, resistance training; NR, not referred; HI, high intensity; rps6, ribosomal protein s6; 4E-BP1, 4E binding protein 1; AT, aerobic training; TUG, timed up and go; MyHC, myosin heavy chain; CYCS, cytochrome c; MDH2, malate dehydrogenase 2; UPP, Ubiquitin-proteasome pathway; 1RM, one-repetition maximum.

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Disclosure

The authors report no conflicts of interest in this work.

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