UNIVERSA MEDICINA

pISSN: 1907-3062 / eISSN: 2407-2230

Univ Med 2026;45:88-98

DOI: https://doi.org/10.18051/UnivMed.2026.v45.88-98

REVIEW ARTICLE

Myosin heavy chain as biomarker in the prevention of sarcopenia

Desy Nofita Sari[1,2*], Roman Ardian Goenarjo[2], Imelda Rosalyn Sianipar[3,4], and Chin Leong Lim[5,6]

[1]Master's Programme in Biomedical Sciences, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia
[2]Department of Medical Physiology, Faculty of Medicine, Universitas Andalas, Padang, Indonesia
[3]Department of Medical Physiology and Biophysics, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia
[4]Metabolic Disorder, Cardiovascular, and Aging Research Cluster, The Indonesian Medical Educational and Research Institute, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia
[5]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
[6]College of Health Science, Vin University, Hanoi, Vietnam

*** Correspondence Author:**
desynofitasari@med.unand.ac.id

Cite this article as: Sari DN, Goenarjo RA, Sianipar IR, Lim CL. Myosin heavy chain as biomarker in the prevention of sarcopenia. Univ Med 2026;45:88-98

Date of first submission, December 11, 2025
Date of final revised submission, February 12, 2026
Date of acceptance, February 23, 2026

ABSTRACT

Sarcopenia, or the age-related loss of skeletal muscle mass and function, can reduce total muscle contractile capacity and increase the likelihood of physical disability in older adults. The loss of muscle mass and contractile performance is generally thought to be multifactorial, with as possible contributing factor an age-related shift in the expressed amounts of myosin heavy chain (MyHC) isoforms. The composition of adult human skeletal muscle consists of a mixture of three distinct MyHC isoforms (I, IIA, and IIX). This literature review aimed to explore studies focused on the signs of sarcopenia, the early detection of initial symptoms, and awareness among the aging population. We aimed to understand the molecular changes in muscle fibers as people age and to help inform the early intervention approach to prevent sarcopenia. The literature search was conducted in several databases between 2020 to 2025, including PubMed, ScienceDirect, and SpringerLink. The search terms consisted of "sarcopenia", "muscle mass", "early detection", and "myosin heavy chain". Inclusion criteria included original full-text English-language studies on the cellular and molecular physiology of sarcopenia. Molecular changes in myosin heavy chain vary across different age groups, suggesting the potential for early detection of muscle aging. The review is limited by the variability in the definition and measurement of sarcopenia across different studies, which may affect the generalizability of the findings. This review highlights the potential significance of identification and sarcopenia management in elderly individuals. The findings would be helpful for clinicians, researchers, and policymakers to improve elderly care and quality of life.

Keywords: Early detection, muscle aging, myosin heavy chain, sarcopenia

Abbreviations

Akt	: Activasion of Protein Kinase B
ATP	: Adenosine triphosphate

DALYs	: Disability Life Years
EWGSOP2	: The European Working Group on Sarcopenia in People (EWGSOP2)
MAPK	: Mitogen Activated Protein Kinase
mTOR	: Mammalian Target of Rapamycin
MyHC	: Myosin Heavy Chain
MYH9	: Myosin heavy chain 9 gene
SCM	: Sternocleidomastoid muscle
TMG	: Tensiomyographic

INTRODUCTION

The increasing population trend has received global attention. A recent study showed that there are already one billion individuals aged 60 years and above worldwide.[1] Forecasts predicted that this number would double by 2050. Regions such as East and Southeast Asia, including Indonesia, are reportedly at the forefront of this demographic shift due to the high growth rates in their elderly populations.[2] Recent data from the Indonesian Health Survey 2023 revealed 28.96 million elderly individuals in Indonesia, accounting for 10.1% of the total population. Margareth projected that this figure could rise significantly to about 28.68% by 2050.[3]

According to the 2021 Global Burden of Disease study, the increasing global aging population poses public health challenges. The rise in Disability Life Years (DALYs), a result of both the aging demographics and the shift towards noncommunicable diseases along with restricted healthcare access, has been highlighted as a critical factor. Underdeveloped nations such as Indonesia typically experience a burden of DALYs among their population compared to more developed countries.[4]

As people age naturally, their bodies change to maintain balance and organ function as well as possible.[5] However, aging also increases susceptibility to diseases affecting various organ systems, including the musculoskeletal system. The deterioration of musculoskeletal health with aging directly affects the human capability to function optimally. Musculoskeletal conditions that often affect the elderly population include tendinopathy, sarcopenia, osteoarthritis, and osteoporosis.[6]

Sarcopenia has been associated with a decrease in muscle mass, which may lead to impairment in older people.[7] According to a study looking at sarcopenia classification methods, prevalence rates range from 10% to 27%, showing the variability in the diagnosis.[8] Another study has shown that sarcopenia has been associated with an increased risk of complications, such as infections, fractures, complications following surgery, prolonged hospital stays, metabolic syndrome, and depression.[9]

This review aims to compile information regarding sarcopenia, emphasizing its onset and the significance of early detection in the aged population to mitigate its impact. This review will address the changes in muscle fiber composition during aging and related metabolic conditions. Improving our understanding of the underlying causes of these conditions and raising awareness can lead to better preventive measures and outcomes.

In this review, we searched the literature for article on myosin heavy chain marker and sarcopenia published in English or Indonesian between 2020 to 2025. Relevant articles were retrieved from databases PubMed, ScienceDirect, and SpringerLink. We used particular inclusion and exclusion criteria to screen out irrelevant studies, ensuring that only those relevant to our research focus were included for further evaluation. We employed specific MeSH keywords, such as “sarcopenia," “muscle mass,” and “myosin heavy chain”. The selected studies were then thoroughly evaluated for quality and relevance before the way for a thorough and rigorous overview of existing knowledge on sarcopenia. Responsible authors performed a literature review and compiled the results into a report.

METHODS

In this review, a total of 944 articles published in English within the last five years were identified through searches conducted in databases PubMed, ScienceDirect, and SpringerLink. The search was restricted to studies examining sarcopenia from a molecular

physiology perspective, using combinations of keywords, such as “sarcopenia," “muscle mass,” and “myosin heavy chain”. Initially, 36 articles met the preliminary inclusion criteria; however, a number of articles were later excluded due to duplication, limited access to full text, or failure to meet the predefined scope of the review. The final selection of studies and the screening process are summarized in **Figure 1**.

Several findings describing the molecular associations underlying sarcopenia are outlined in **Table 1**, which presents the characteristics of the included studies. Multiple studies have explored myosin heavy chain (MyHC) as a biomarker in sarcopenia. A particular study discovered that MyHC expression could be influenced by averting muscle loss and the balance between muscle protein synthesis and breakdown, according to Takahashi et al.[10] during the aging process, the composition of MyHC makeup changes, which could impact muscle function and lead to loss of muscle force, velocity, and power in cases of sarcopenia.

Pathophysiology of muscle aging and sarcopenia

Sarcopenia is one of the disorders that grows increasingly prevalent as people age; prevalence rates vary based on the population and the diagnostic criteria used. At the same time, higher rates are observed in clinical settings, particularly in patients undergoing hospital treatment or living in long-term care institutions. According to research studies, the prevalence can reach 30% or even higher for those with diseases or disabilities.[8,11]

One of the most immediate consequences of sarcopenia is the onset of physical disability. Sarcopenia decreases muscle mass and grip strength.[11] This condition also reduces the ability to generate force rapidly and perform tasks involving muscle contractions. Patients with sarcopenia tend to score low on independence tests due to their diminished ability to carry out daily activities effectively. [12]

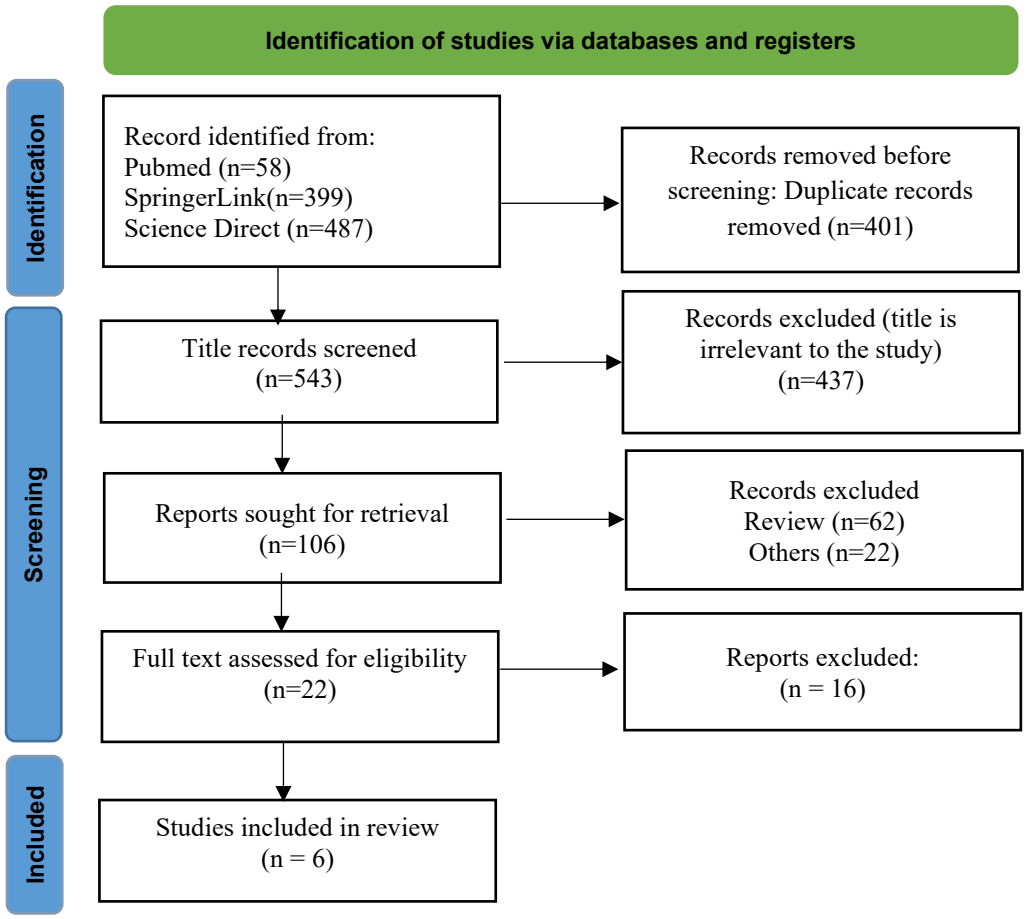

Figure 1. Article selection based on PRISMA flow

Table 1. Study characteristics

Authors	Study design	Number of subjects	Methods	Summary of results
Sharlo et al.[26]	Animal experimental	64 male rats (2.5 month-old)	Divided into four groups (control, 7-days hindlimb suspended (HS) model, 7-days HS+Arginin, and 7-days HS+A+L-NAME	MyHC-I dominance in young rats. Nitric oxide in muscles decreases when induced by HS, impairing MyHC change. Arginin treatment prevented NO content, and myHC-I decreased.
Lagou et al.[40]	Animal Cross-sectional study	24 male rats (4-week-old-group and 26-week-old-group)	Compared at two different ages corresponding to youth and young adulthood	RNA expression of specific MyHC isoforms increases with age in various muscle groups, particularly in adult rats, and muscle fiber size also increases in the gastrocnemius/soleus muscles.
Cobley et al.[41]	Human Cross-sectional study	24 males (younger <30-year-old group and older >55-year-old group)	Compared at two different ages corresponding to young and elderly, that trained and completed >3 exercise sessions per week and untrained as baseline	MyHC-II is lower in old trained compared to young trained. MyHC II was lost with age. The trained group has greater MyHC-I compared to the untrained.
Vann et al.[54]	Human Cross-sectional study	18 males (six young trained, six young untrained, and six old untrained)	Analyze the MyHC composition and compare each group	Training leads to the YT participants' greatest MyHC and actin protein abundances. Sarcoplasmic protein concentrations were not different in each group
Krakova et al.[42]	Human experimental	48 males (20-year-old group and 70-year-old group)	Twelve weeks of resistance training (old only). The young and old groups before training as a baseline.	No correlation exists between muscle fiber grouping and lower body strength or muscle mass in healthy older men. Twelve weeks of resistance exercise training increased MyHC-II fiber size but did not alter the arrangement of muscle fiber types.
Messa et al.[51]	Human Longitudinal study	34 male master sprinters (40–85 years old at start)	Following over ten years (2002-2012), the athletes who continued sprint run training	Sprint performance declined with age, but there were no significant changes in muscle fiber composition or structure

Several studies have linked sarcopenia to the aging of muscles.[13,14] Other than lifestyle modifications that may cause premature aging, factors including chronic inflammation and free radicals can accelerate aging.[15] It has been suggested that consuming too much fat and sugary meals may cause metabolic problems as one ages, reducing muscle tissue's ability to regenerate. Sarcopenia is a multifactorial condition,[16] driven by intrinsic aging processes and external factors such as physical inactivity and nutrition imbalance. Muscle fibers undergo significant changes with aging, including decreases in size and number, particularly in type II fibers, which are responsible for rapid and robust movements.[17] The interaction among muscle mass, strength levels, and functional capabilities underscores the importance of identifying and implementing intervention methods.

Myosin heavy chain expression in skeletal muscle

Myosin heavy chains (MyHC) are crucial motor proteins critical in muscle contraction and various cellular processes. They are part of the myosin superfamily, characterized by their ability to interact with actin filaments and convert chemical energy from adenosine triphosphate (ATP) hydrolysis into mechanical work. Myosin heavy chains are large polypeptides, typically around 230 kDa in size, and comprise several distinct domains.[18]

Myosin heavy chains play an important role in the muscular performance mechanism, allowing both smooth and striated muscles to work correctly. The sliding filament theory explains how muscles contract by focusing on the interaction of myosin and actin filaments. When calcium ions are present in muscle cells, myosin heads bind to actin filaments, leading to a shift powered by ATP breakdown and resulting in actin filaments moving inward and muscular contraction.[19] The MyHC molecule involves muscle contraction and motility. Research using *Dictyostelium* as a model organism has shown that altering the MyHC gene affects muscle contraction and cell motility, as evidenced in studies on muscle MyHC encoded by the myosin heavy chain 9 (MYH9) gene.[18] During mitosis and cell division, MyHC assists in forming contractile rings, facilitating cell division. They also help generate forces that allow cells to slide along surfaces while interacting with the actin cytoskeleton to maintain cell stability. Additionally, they influence various cellular functions in response to external signals.[20,21]

The activity of MyHC is highly controlled by phosphorylation and other post-translational modifications. For example, phosphorylation of specific serine residues might influence myosin filament dissociation, altering their activity in response to physiological signals.[18] The changes in MyHC isoform expression with age are thought to be regulated at the transcriptional level.[22] According to previous study, the decline in MyHC production could be attributed to a slower rate of mRNA translation or decreased translational efficiency in aged muscle. Furthermore, denervation and changes in brain activity can modify MyHC isoform composition, shifting toward slower-contracting muscle fibers.[21] Myosin heavy chains structure and function research is a priority for understanding their implications in muscle biology, disease processes, and treatment strategies.

Shifting in myosin heavy chain isoforms during aging

Several alterations occur in the expression and distribution of MyHC isoforms in the aging process. With advancing age, there is generally a shift towards a higher proportion of slower MyHC isoforms, particularly type-I. There is typically a reduction in the presence of the faster Type IIa and IIx isoforms that occurs alongside this shift.[20] Changes in muscles vary depending on the muscle group involved. Limb muscles, for example, show a significant shift toward slow isoforms.[23] Understanding this relationship is effectively exercising and rehabilitation techniques targeting different MyHC isoforms that could significantly enhance muscle hypertrophy and strength development.[24,25]

Multiple factors influence changes in MyHC isoforms. Besides aging, other conditions, such as chronic inflammation, physical inactivity, and nutrition, can induce changes in MyHC expression.[26] The molecular mechanisms underlying these changes involve various signaling pathways, including the Akt/ mammalian target of Rapamycin (mTOR) and mitogen activated protein kinase (MAPK) pathways.[27] A more comprehensive understanding of the regulation of MyHC expression has significant implications for developing therapies for muscle atrophy, such as sarcopenia.[13,28,29]

There seems to be a change in how the fast twitch muscle fibers behave and show traits such as slow twitch fibers – a phenomenon known as the shifting from fast to slow muscle fiber characteristics.[24] This transformation in muscle fiber type can happen because of a process where RNA from myonuclear changes from type IIA IIx to type I mRNA and is influenced by the regeneration mechanism linked to the MyH8 protein.[30] Fast and slow twitch muscle fibers (MyHC II and MyHC I) varied significantly in old and young sternocleidomastoid (SCM) muscle.[31] The elderly group showed a lower percentage of fast-twitch MyHC II than younger adults.[23] A recent study indicates that changes in the MyHC through translational modifications can notably impact muscle function by influencing the protein's structure and functioning, which could affect muscle contraction and movement.[32]

Sarcopenia associated with age

Sarcopenia is associated with poor outcomes, including falls and mortality, and is becoming more well-recognized in the elderly population.[33] The binary classification of sarcopenia that is currently in use complicates the identification of those who are at risk before they have considerable muscle loss.[34] Muscle strength is now emphasized as the significant indicator of sarcopenia in the new guidelines from the European Working Group on Sarcopenia in People (EWGSOP2).[34,35] For effective intervention strategies to be successful, it is necessary to emphasize low muscle strength as a critical indicator for early detection stages. The diagnosis is confirmed based on the quality or quantity of muscles and poor physical performance.[36] Once thought to be exclusively associated with age, sarcopenia is now understood to be a disorder that can start earlier in life and be impacted by various factors. This changing viewpoint emphasizes how crucial it is to start treatments early to prevent or delay the onset of sarcopenia. Sarcopenia's classification and understanding have undergone a paradigm shift with its redefinition as a muscle-related condition. Furthermore, reduced muscle mass is less important in detecting sarcopenia during medical examinations than low muscle strength.

Although muscle quantity and quality are valuable markers in research and help assess health status precisely, some challenges prohibit their widespread application in clinical practice. Because sarcopenia is frequently missed, it can be challenging for medical practitioners to identify and treat it successfully. Sarcopenia is partial because diagnostic criteria and cutoff points are inconsistent.[34] Intervention can be crucial during the early stages of sarcopenia. It is possible to delay or even prevent the development of sarcopenia by investigating the metabolic changes.

Myosin heavy chains changes in sarcopenia

Several general trends regarding MyHC changes can be inferred from **Table 2**. A common trend observed across studies is a shift from fast to slow muscle fibers with advancing age. This is evidenced by an increase in type I (slow) MyHC and a decrease in type II (fast) MyHC in older individuals.[31,37] Interventions such as diet modification, supplementation, or exercise training have been shown to influence MyHC composition. For instance, arginine supplementation has been observed to prevent the decline in type I MyHC in younger individuals.[38] The specific changes in MyHC composition also depend on the examined muscle type. Different muscles have distinct functions and characteristics, leading to varying responses to aging or interventions.[39,40] Molecular and cellular changes in aging affect muscular atrophy and are associated with fiber-type MyHC shifting. Studies with senescent animal models and older humans have confirmed fiber-type shifting.[41,42] Skeletal muscle aging was associated with a tendency of MyHC-II to MyHC-I transition, and increased oxidative stress and myofibrotic change.[31] Further research is needed to identify specific proteomic assessments for detecting muscle fiber change in sarcopenia.

Mechanism of muscle fiber changes

Muscle fibers, composed of contractile units called sarcomeres, generate force through ATP-driven interactions between myosin and actin filaments.[43] Myosin, consisting of six polypeptides, determines muscle fiber types based on different MyHC isoforms. [44]Adult human muscle fibers are classified as type I (slow-twitch) or IIA, IIB, and IIX (fast-twitch) based on their MyHC isoform expression and energy production pathways.[45] Aging induces a shift from fast-twitch to slow-twitch fibers, characterized by a decline in type II fibers and an increase in fibers co-expressing multiple MyHC isoforms.[21,45] This transition reflects a shift from glycolytic to oxidative metabolism, suggesting an increased

need for functional mitochondria in aging skeletal muscle.[46]

Several mechanisms contribute to the alterations in MyHC composition that occur with aging and sarcopenia.[47,48] For example, satellite cells are responsible for muscle regeneration. Aging leads to a decline in the number and functionality of these cells, resulting in impaired muscle repair and regeneration, particularly affecting type II fibers more severely than type I fibers. A recent study has identified specific mechanisms involved in the degradation of MyHC. The E3 ubiquitin ligase protein component was shown to target MyHC IIb and IIx for degradation, which may contribute to cancer-induced muscle shrinkage or cancer cachexia, and potentially play a role in age-related muscle loss.[49]

Myosin heavy chain synthesis decreased with fractional synthesis rates of MyHC, which were measured, and a significant decline in synthesis rates from young to old age was found, correlated with reduced muscle strength and mass.[37] This decline suggests that older adults have a reduced capacity to remodel muscle tissue, contributing to sarcopenia.[37] Aging is associated with a change in muscle fiber composition, particularly a reduction in Type II fibers primarily composed of fast-twitch MyHC.[31] This shift results in a relative increase in Type I fibers, decreasing muscle strength and contractile function. The loss of Type II fibers is particularly detrimental because these fibers are essential for explosive movements and overall muscle strength. [47,50]

The transition in MyHC expression might be a muscle fiber composition marker and correlate with older adults' overall muscle health and performance.[51] Studies suggested that measuring the levels of specific MyHC isoforms can provide insights into the muscle's functional capacity and its adaptation to aging or muscle-wasting conditions.[52,53] Changes in MyHC isoform expression can contribute to decreased muscle quality associated with sarcopenia, impairing muscle function and performance. The shift in MyHC isoform expression towards slower isoforms is linked to reduced muscle strength and performance, as slow fibers have lower contractile force than fast-twitch fibers. This functional decline contributes to the physical limitations and decreased mobility observed in individuals with sarcopenia.

Table 2. Study results of MyHC changes

Authors	Study Design	Specimen	Bioanalytical approach	MyHC Change
Sharlo et al.[26]	Animal, experimental	Soleus muscle (control versus HS-induced NO versus added arginine in youngest)	PAGE analysis of MyHC isoforms	Prevent MyHC-I decrease and MHC-II increase in the youngest by arginine
Lagou et al.[40]	Animal Cross-sectional study	Masseter, digastric, and gastrocnemius muscles (youngest versus adult)	q-rt PCR and **i**mmunofluorescence	MyHC-II increase in in masseter and limb muscle of adults
Cobley et al.[41]	Human Cross-sectional study	Vastus lateralis (younger versus older; trained and untrained)	PAGE analysis of MyHC isoforms	Increase in MyHC-I; decrease in MyHC-II
Vann et al.[54]	Human Cross-sectional study	Vastus lateralis (younger versus older)	PAGE analysis of MyHC isoforms	Decrease in myosin-binding protein MYBP-H in older persons
Krakova et al.[42]	Human experimental	Vastus lateralis (younger versus older; trained old only)	Immunohistochemistry	MyHC-II hypertrophy **in** trained older does not affect fiber grouping
Messa et al.[51]	Human Longitudinal study	Vastus lateralis (past versus present)	Immunohistochemistry	No significant changes in muscle fiber composition or structure

Muscle aging prevention

The therapy should target type II muscle fiber atrophy to prevent decreased muscle strength in aging or sarcopenia. Our study indicates that the age-related loss of muscle mass is primarily due to the atrophy of these specific fibers rather than a decrease in muscle fiber numbers. Effective intervention strategies, such as regular aerobic and resistance exercise training, have been shown to increase type II muscle fiber size, which is crucial for preventing or reversing muscle loss with aging.[54] The findings emphasize the importance of developing exercise, nutritional, or pharmacological interventions that specifically promote the hypertrophy of type II muscle fibers to combat sarcopenia and maintain muscle function in older adults. Adequate dietary protein is crucial to prevent muscle loss in older adults, as insufficient intake can lead to lower muscle protein synthesis. Managing inflammatory cytokines and vitamin D deficiency is essential to mitigate muscle aging.[55,56] Early identification and correction of malnutrition are crucial to preventing and managing sarcopenia. The most effective strategies to contrast sarcopenia rely on adopting healthier lifestyle behaviors, including adherence to high-quality diets and regular physical activity.

Myosin heavy chain applicable assessment for sarcopenia

Analyzing MyHC isoform distribution can provide insights into muscle performance. Higher proportions of fast-twitch fibers may indicate a more significant potential for explosive movements and strength. Myosin heavy chain isoforms correlate with muscle fiber metabolic profiles, influencing energy utilization during activity. The myosin heavy chain composition can shift in response to training, indicating muscle plasticity and adaptation potential.[57]

The study by Šimunic et al. identified the composition of muscle fiber types in the vastus lateralis muscle by using a tensiomyographic (TMG) assessment.[58] The study approaches to determine a correlation between muscle twitches' delay time, contraction time, and half relaxation time to predict the percentage of MyHC I. A recent review stated that TMG could be a non-invasive, reliable method for detecting and monitoring functional muscle.[59] However, it cannot provide the level of detail muscle biopsy offers. A biopsy allows for a direct assessment of muscle fiber type composition, which is essential for understanding the underlying mechanisms of muscle function and disease.

CONCLUSION

Sarcopenia is a major public health concern, particularly with the current trend of the world population ages. The evidence reported in this review underlines the relevance of early detection and intervention in reducing the effects of sarcopenia in older populations.

The potential for using MyHC as a biomarker consists of fiber-type shifting, sensitivity to muscle changes, and proteomic profiling. This review consolidates recent findings on the molecular and cellular mechanisms underlying sarcopenia, focusing on crucial markers of MyHC isoforms. These markers show promise for assessing skeletal muscle mass and function in aging, offering insights into the underlying pathology of sarcopenia. However, the variability in study methodologies and assessing different muscle types highlight the need for standardized study and clinical practice approaches.

Continued study into the molecular mechanisms underlying these alterations will be critical to creating effective sarcopenia treatment strategies and improving the quality of life for older populations. One important limitation in this investigation is the lack of methods for assessing MyHC. The variability in how different studies quantify the presence of MyHC causes direct comparison of data difficult, limiting the capacity to determine how useful MyHC is as a biomarker for preventing sarcopenia.

Conflict of Interest

The authors declare that there is no conflict of interest.

Acknowledgment

This review was supported by the Directorate of Study and Development, Universitas Indonesia, under PUTI 2024 Grant (No. NKB-650/UN2.RST/HKP.05.00/2024).

Author Contributions

DNS, RAG, and IRS were responsible for the conception and design of the study. DNS was involved in the analysis and interpretation of data as well as drafting the article. RAG and IRS made critical revisions of the article. All authors have read and approved the final manuscript.

Data Availability Statement

There were no new data generated, and data sharing is not appliable.

Declaration of the AI Usage in Scientific Writing

Nothing to declare.

References

1. Rudnicka E, Napierała P, Podfigurna A, et al. The World Health Organization approach to healthy ageing. Maturitas 2020;139:6–11. doi: 10.1016/j.maturitas.2020.05.018.
2. Statista Research Department. World Population by Age and Region. 2023.
3. Kementrian Kesehatan Republik Indonesia [Ministry of Health, Republic of Indonesia]. Profil statistik kesehatan 2023. [2023 Health statistics profile]. Jakarta: Badan Pusat Statistik; 2023. Indonesian.
4. Ferrari AJ, Santomauro DF, Aali A, et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2024;403:2133–61. doi: 10.1016/S0140-6736(24)00757-8.
5. Guo J, Huang X, Dou L, et al. Aging and aging-related diseases: from molecular mechanisms to interventions and treatments. Signal Transduct Target Ther 2022;7:391; doi: 10.1038/s41392-022-01251-0.
6. Grote C, Reinhardt D, Zhang M, et al. Regulatory mechanisms and clinical manifestations of musculoskeletal aging. J Orthop Res 2019;37:1475–88; doi: 10.1002/jor.24292.
7. Coletta G, Phillips SM. An elusive consensus definition of sarcopenia impedes research and clinical treatment: a narrative review. Ageing Res Rev 2023;86:1568–637; doi: 10.1016/j.arr.2023.101883.
8. Petermann-Rocha F, Balntzi V, Gray SR, et al. Global prevalence of sarcopenia and severe sarcopenia: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle 2022;13:86–99; doi: 10.1002/jcsm.12783.
9. Bruyère O, Beaudart C, Ethgen O, et al. The health economics burden of sarcopenia: a systematic review. Maturitas 2019;119:61–69; doi: 10.1016/j.maturitas.2018.11.003.
10. Takahashi L, Ishigami T, Tomiyama H, et al. Increased plasma levels of myosin heavy chain 11 is associated with atherosclerosis. J Clin Med 2021;10:3155; doi: 10.3390/jcm10143155.
11. Yuan S, Larsson SC. Epidemiology of sarcopenia: prevalence, risk factors, and consequences. Metabolism 2023;144:155533; doi: 10.1016/j.metabol.2023.155533.
12. Bertschi D, Kiss CM, Beerli N, et al. Impact of sarcopenia on daily functioning: a cross-sectional study among older inpatients. Aging Clin Exp Res 2022;34:2041–6; doi: 10.1007/s40520-022-02175-z.
13. Pascual-Fernández J, Fernández-Montero A, Córdova-Martínez A, et al. Sarcopenia: molecular pathways and potential targets for intervention. Int J Mol Sci 2020;21:8844; doi: 10.3390/ijms21228844.
14. Granic A, Suetterlin K, Shavlakadze T, et al. Hallmarks of ageing in human skeletal muscle and implications for understanding the pathophysiology of sarcopenia in women and men. Clin Sci 2023;137:1721–51; doi: 10.1042/CS20230319.
15. Cai Y, Song W, Li J, et al. The landscape of aging. Sci China Life Sci 2022;65:2354–454; doi: 10.1007/s11427-022-2161-3.
16. Mellen RH, Girotto OS, Marques EB, et al. Insights into pathogenesis, nutritional and drug approach in sarcopenia: a systematic review. Biomedicines 2023;11:136; doi: 10.3390/biomedicines11010136.
17. Lee EJ, Ahmad SS, Lim JH, et al. Interaction of fibromodulin and myostatin to regulate skeletal muscle aging: An opposite regulation in muscle aging, diabetes, and intracellular lipid accumulation. Cells 2021;10:2083. doi: 10.3390/cells10082083.
18. Pecci A, Ma X, Savoia A, et al. MYH9: Structure, functions and role of non-muscle myosin IIA in human disease. Gene 2018;664:152–67. doi: 10.1016/j.gene.2018.04.048.
19. Zhang N, Zhang Y, Xu J, et al. Alpha-myosin heavy chain lactylation maintains sarcomeric structure and function and alleviates the development of heart failure. Cell Res 2023;33:679–98. doi: 10.1038/s41422-023-00844-w.
20. Wu X, Zhou X, Ding X, et al. Reference gene selection and myosin heavy chain (MyHC) isoform expression in muscle tissues of domestic yak *(Bos grunniens)*. PLoS One 2020;15:8493. doi: 10.1371/journal.pone.0228493.
21. Lee C, Woods PC, Paluch AE, et al. Effects of age on human skeletal muscle: a systematic review and meta-analysis of myosin heavy chain isoform protein expression, fiber size, and distribution. Am J Physiol Cell Physiol 2024;327:1400–15. doi: 10.1152/ajpcell.00347.2024.
22. Dou M, Yao Y, Ma L, et al. The long noncoding RNA MyHC IIA/X-AS contributes to skeletal muscle myogenesis and maintains the fast fiber

phenotype. J Biol Chem 2020;295:4937–49. doi: 10.1074/jbc.RA119.010498.
23. Meznaric M, Eržen I, Karen P, et al. Effect of ageing on the myosin heavy chain composition of the human sternocleidomastoid muscle. Ann Anat 2018;216:95–9. doi: 10.1016/j.aanat.2017.12.001.
24. Moreillon M, Conde Alonso S, Broskey NT, et al. Hybrid fiber alterations in exercising seniors suggest contribution to fast-to-slow muscle fiber shift. J Cachexia Sarcopenia Muscle 2019;10: 687-95. doi: 10.1002/jcsm.12410.
25. Rogeri PS, Zanella R, Martins GL, et al. Strategies to prevent sarcopenia in the aging process: role of protein intake and exercise. Nutrients 2022;14:55–9. doi: 10.3390/nu14010052.
26. Sharlo K, Tyganov SA, Tomilovskaya E, et al. Effects of various muscle disuse states and countermeasures on muscle molecular signaling. Int J Mol Sci 2022;23:468. doi: 10.3390/ijms23010468.
27. Panwar V, Singh A, Bhatt M., et al. Multifaceted role of mTOR (mammalian target of rapamycin) signaling pathway in human health and disease. Sig Transduct Target Ther 2023;8:375. https://doi.org/10.1038/s41392-023-01608-z
28. Tu S, Hao X, Xu S, et al. Sarcopenia: current insights into molecular mechanisms, diagnostics, and emerging interventional approaches. Int J Mol Sci 2025;26:6740. doi: 10.3390/ijms26146740.
29. Börsch A, Ham DJ, Mittal N, et al. Molecular and phenotypic analysis of rodent models reveals conserved and species-specific modulators of human sarcopenia. Commun Biol 2021;4:1723. doi: 10.1038/s42003-021-01723-z.
30. Kedlian VR, Wang Y, Liu T, et al. Human skeletal muscle aging atlas. Nat Aging 2024;4:727–44. doi: 10.1038/s43587-024-00613-3.
31. Dowling P, Gargan S, Swandulla D, Ohlendieck K. Fiber-type shifting in sarcopenia of old age: proteomic profiling of the contractile apparatus of skeletal muscles. Int J Mol Sci 2023;24:2415. doi: 10.3390/ijms24032415.
32. Gonzalez-Martinez D, Johnston JR, Landim-Vieira M, et al. Structural and functional impact of troponin C-mediated Ca^{2+} sensitization on myofilament lattice spacing and cross-bridge mechanics in mouse cardiac muscle. J Mol Cell Cardiol 2018;123:26–37. doi: 10.1016/j.yjmcc.2018.08.015.
33. Sánchez Tocino ML, Cigarrán S, Ureña P, et al. Definition and evolution of the concept of sarcopenia. Nefrologia 2024;44:323–30. doi: 10.1016/j.nefro.2023.08.001.
34. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16–31. doi: 10.1093/ageing/afy169.
35. Sayer AA, Cruz-Jentoft A. Sarcopenia definition, diagnosis and treatment: consensus is growing. Age Ageing 2022;51:220. doi: 10.1093/ageing/afac220.
36. Ooi H, Welch C. Obstacles to the early diagnosis and management of sarcopenia: current perspectives. Clin Interv Aging 2024;19:323–32. doi: 10.2147/CIA.S438144.
37. Horwath O, Moberg M, Edman S, Philp A, Apró W. Ageing leads to selective type II myofibre deterioration and denervation independent of reinnervative capacity in human skeletal muscle. Exp Physiol 2025;110:277–92. doi: 10.1113/EP092222.
38. Sharlo KA, Paramonova II, Lvova ID, et al. NO-dependent mechanisms of myosin heavy chain transcription regulation in rat soleus muscle after 7-days hindlimb unloading. Front Physiol 2020;11:814. doi: 10.3389/fphys.2020.00814.
39. Oliveira JRS, Mohamed JS, Myers MJ, Brooks MJ, Alway SE Effects of hindlimb suspension and reloading on gastrocnemius and soleus muscle mass and function in geriatric mice. Exp Gerontol 2019;115:11–8. doi: 10.1016/j.exger.2018.11.011.
40. Lagou A, Schaub L, Ait-Lounis A, Denes BJ, Kiliaridis S, Antonarakis GS. Myosin heavy-chain messenger ribonucleic acid (mRNA) expression and fibre cross-sectional area in masseter, digastric, gastrocnemius and soleus muscles of young and adult rats. Biology (Basel) 2023;12:842. doi: 10.3390/biology12060842.
41. Cobley JN, Malik ZA, Morton JP, Close GL, Edwards BJ, Burniston JG. Age- and activity-related differences in the abundance of myosin essential and regulatory light chains in human muscle. Proteomes 2016;4:15. doi: 10.3390/proteomes4020015.
42. Kraková D, Holwerda AM, Betz MW, et al. Muscle fiber type grouping does not change in response to prolonged resistance exercise training in healthy older men. Exp Gerontol 2023;173:112083. doi: 10.1016/j.exger.2023.112083.
43. Wang L, Geist J, Grogan A, Hu LR, Kontrogianni-Konstantopoulos A. Thick filament protein network, functions, and disease association. Compr Physiol 2018;8:631–709. doi: 10.1002/cphy.c170023.
44. Zhao J, Du X, Fang W, Zhu H, Yue B. Architecture and molecular machinery of skeletal myofibers: a systematic review of the structure–function relationships. Front Cell Dev Biol 2025;13:2607. doi: 10.3389/fcell.2025.1602607.
45. Stuart CA, Stone WL, Howell MEA, et al. Myosin content of individual human muscle fibers isolated by laser capture microdissection. Am J

Physiol Cell Physiol 2016;310:381–9. doi: 10.1152/ajpcell.00317.2015.-Muscle.
46. Dao T, Green AE, Kim YA, et al. Sarcopenia and muscle aging: A brief overview. Endocrinol Metab (Seoul) 2020;35:716–32. doi: 10.3803/ENM.2020.405.
47. Yang Q, Chan P. Skeletal muscle metabolic alternation develops sarcopenia. Aging Dis 2022;13:801–84. doi: 10.14336/AD.2021.1107.
48. Wiedmer P, Jung T, Castro JP, et al. Sarcopenia – molecular mechanisms and open questions. Ageing Res Rev 2021;65:101200. doi: 10.1016/j.arr.2020.101200.
49. Cardaci TD, Machek SB, Wilburn DT, Hwang PS, Willoughby DS. Ubiquitin proteasome system activity is suppressed by curcumin following exercise-induced muscle damage in human skeletal muscle. J Am Coll Nutr 2021;40:401–11. doi: 10.1080/07315724.2020.1783721.
50. Bagley JR, McLeland KA, Arevalo JA, Brown LE, Coburn JW, Galpin AJ. aSkeletal muscle fatigability and myosin heavy chain fiber type in resistance trained men. J Strength Cond Res 2017;31:727–35. doi: 10.1519/JSC.0000000000001759.
51. Messa GAM, Korhonen MT, Degens H. No ageing-related increase in fibre type grouping in sprint-trained masters runners: A 10-year follow-up study. J Cachexia Sarcopenia Muscle 2024;15:334–45. doi: 10.1002/jcsm.13416.
52. Lim JY, Frontera WR. Skeletal muscle aging and sarcopenia: perspectives from mechanical studies of single permeabilized muscle fibers. J Biomech 2023;152:110423. doi: 10.1016/j.jbiomech.2023.111559.
53. Lin S, Ling M, Chen C, Cai X, Yang F, Fan Y. Screening potential diagnostic biomarkers for age-related sarcopenia in the elderly population by WGCNA and LASSO. Biomed Res Int 2022;2022:3911. doi: 10.1155/2022/7483911.
54. Vann CG, Roberson PA, Osburn SC, et al. Skeletal muscle myofibrillar protein abundance is higher in resistance-trained men, and aging in the absence of training may have an opposite effect. Sports 2020;8:1–9. doi: 10.3390/sports8010007.
55. Rogeri PS, Zanella R, Martins GL, et al. Strategies to prevent sarcopenia in the aging process: Role of protein intake and exercise. Nutrients 2022;14:52. doi: 10.3390/nu14010052.
56. Calvani R, Picca A, Coelho-Júnior HJ, Tosato M, Marzetti E, Landi F. Diet for the prevention and management of sarcopenia. Metabolism 2023; 146:155637. doi: 10.1016/j.metabol.2023.155637.
57. Privett GE, Ricci AW, Ortiz-Delatorre J, Callahan DM. Predicting myosin heavy chain isoform from postdissection fiber length in human skeletal muscle fibers. Am J Physiol Cell Physiol 2024;326:C749–C55. doi: 10.1152/ajpcell.00700.2023.
58. Šimunič B, Pišot R, Rittweger J, Degens H. Age-related slowing of contractile properties differs between power, endurance, and non-athletes: A tensiomyographic assessment. J Gerontol A Biol Sci Med Sci 2018;73:1602–8. doi: 10.1093/gerona/gly069.
59. Pus K, Paravlic AH, Šimunič B. The use of tensiomyography in older adults: a systematic review. Front Physiol 2023;14:1213993. doi: 10.3389/fphys.2023.1213993.