

The association between sarcopenia and the physical function of patients with stroke: A systematic review and meta-analysis

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Article Info

Article Notes

Received: April 09, 2021

Accepted: April 27, 2021

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Keywords:

sarcopenia
physical function; stroke
systematic review
meta-analysis

Abstract

Objectives: The purpose of this study is to identify whether there is an association between sarcopenia and physical function outcomes of patients with stroke.

Methods: A systematic search of Pubmed, Web of Science, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang database was conducted to identify studies in Chinese and English from inception of the database to March 2021. Documents were checked for relevancy. Articles exploring the association between sarcopenia and physical function of patients with stroke were included. Quality of the literature was evaluated using the Newcastle-Ottawa scale tool. Stata 15.0 software was used to conduct meta-analysis.

Results: Eight studies met the criteria for inclusion. A meta-analysis of four studies showed that sarcopenia was related to an increased risk of poor physical function of patients with stroke (total OR=3.11, 95% CI: 2.22-4.34, $P<0.0001$). Descriptive analysis was performed in the rest of studies. Overall, a correlation between the two factors was found in patients with stroke. Some studies suggested a difference based on gender and severity of the disease condition. The studies included in this review were of high methodological quality. The Egger's test ($P=0.217$) showed no publication bias.

Conclusions: This review concludes that sarcopenia is an independent predictive factor of physical function of patients with stroke. Clinicians should pay attention to gender differences and severity of disease condition. Therefore, screening, diagnosis, treatment, and prevention of sarcopenia should be part of the routine clinical practice when providing care to stroke patients.

Introduction

Sarcopenia is an under-evaluated and under-treated condition in patients with stroke. A systematic review reported that only 7 trials specifically assessed the prevalence of sarcopenia in stroke patients, with a pooled prevalence estimate of 42%¹. In addition, Recent clinical studies have shown that sarcopenia was observed in 53.6% of stroke patients². Sarcopenia is defined as "progressive and systemic skeletal muscle disease related to increased occurrence of adverse health outcome"³. Causes of sarcopenia in patients with stroke, such as denervation, muscle mass loss, systemic catabolic activation, and muscle fiber displacement, can overlap. The occurrence of the problems can be complex and multi-factorial⁴. Currently, sarcopenia is frequently observed among the elderly population, leading to complications such as falls, disability, loss of independence, hospitalization, cognitive and mobility impairments, and mortality^{3,5-7}. Therefore, early identification, diagnosis and treatment of sarcopenia are of great significance.

Stroke is now the second leading cause of death and the primary cause of disability around the globe, and the burden of disease has increased dramatically^{8,9}. In the early stages of stroke disease, predictors of long-term functional outcomes can identify which patients would benefit from specific rehabilitation services, facilitate early rehabilitation goals and discharge planning decisions, and promote care and rehabilitation services. Recently, some studies have indicated that sarcopenia among elderly patients is widely believed to be associated with functional outcomes^{10,11} and it is also correlated with a worse recovery of physical function and swallowing difficulties among hospitalized adults in rehabilitation^{2,12}. Of note, in addition to the degree of neurological deficit assessed by the National Institutes of Health Stroke Scale¹³, assessment of sarcopenia may be a quantitative predictor of the functional prognosis in patients with stroke. To our knowledge, there has been no previous systematic review on the relationship between sarcopenia and physical function of patients with stroke. In this study, physical function was defined as ability regarding basic physical and cognitive activities such as walking or reaching, as well as the routine activities of daily living, including eating, bathing, dressing, transferring, and toileting. The purpose of this systematic review is to identify whether there is an association between sarcopenia and physical function outcomes of this patient population.

Methods

Search strategy

The following database were searched for relevant studies published in the English and Chinese languages: Pubmed, Web of science, Cochrane Library, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang from inception of the database to March 2021. The search strategy included MeSH terms and their associated free words. Keywords are as follows: "Sarcopenia", "Muscular atrophy", "Muscle loss", and "Muscle weakness"; "Recovery of function", "Activities of daily living", "Functional status", "Physical fitness", and "Physical functional performance"; "Stroke", "Cerebrovascular accident", "Apoplexy", "Cerebral hemorrhage", and "Brain Vascular Accident", etc. References of the studies were checked to find other relevant studies.

Eligibility criteria and selection of studies

Inclusion criteria:

1. Confirmed stroke diagnosis on computed tomography or magnetic resonance imaging scan
2. Studies that explored the association between sarcopenia and physical function among patients with stroke
3. Prospective or retrospective observational studies meeting the above criteria.

Exclusion criteria:

1. Unpublished or duplicate studies, conference abstracts.
2. Randomized controlled trials (RCTs).
3. Studies with low methodological quality.

Two investigators independently conducted literature screening based on the data extraction and inclusion criteria. In case of disagreement or discrepancy, there would be a discussion to negotiate a solution until an agreement was reached.

Quality assessment

Two investigators independently assessed the methodological quality of each study, using the Newcastle-Ottawa Scale¹⁴. The scale assigned 2 points for assessment of group selection, 4 points for comparability, and 3 points for exposure/outcome. Quality scores ranged from 0 to 9, with 7 to 9 indicating high quality, 4 to 6 indicating moderate quality, and 0 to 3 indicating low quality.

Statistical analysis

The odds ratio (OR) was the risk estimation measure with a corresponding 95% confidence interval (CI). Statistical heterogeneity was assessed by employing the Q statistic and the I² statistic. The Q statistic was considered statistically significant at $p < 0.1$. When I² values was 25%, 50% and 75%, it indicated the threshold of low, medium, or high heterogeneity, respectively¹⁵. The tests were considered statistically significant at $p < 0.05$. Publication bias was determined using Egger's regression test at $p < 0.05$ ¹⁶. All analyses were conducted using Stata (version 15.0). In addition, some studies used descriptive analyses due to differences in the definitions, measurements, and outcomes of both dependent and independent variables.

Results

Study selection

5165 articles were identified. Duplicate articles were excluded (n=1502). After the initial screening, another 3663 articles were excluded because they did not meet the inclusion criteria based on the abstract or title. After full-text review of the remaining 19 studies, a total of 8 studies were selected in strict adherence to the inclusion and exclusion criteria. Review of the references of the included studies added no additional articles. All included studies used a cohort study design and involved a total of 1310 patients. The PRISMA flow chart is shown in Figure 1¹⁷.

Methodological quality

Details of the quality assessment of all included articles are shown in Table 1. The mean quality assessment score

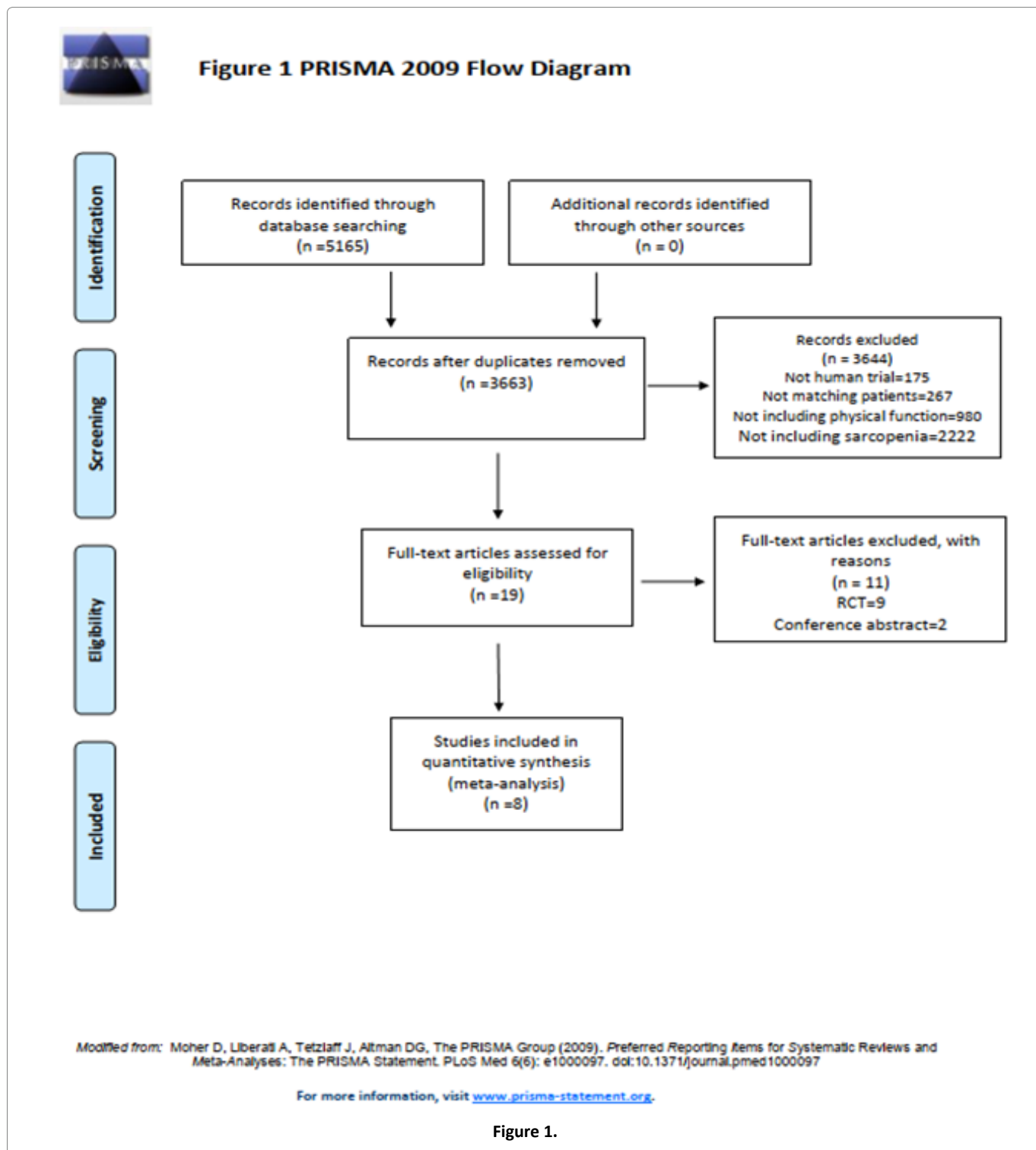


Figure 1.

was 7.5, indicating overall high quality of all studies. No studies were excluded due to low quality.

Characteristics of the studies

The 8 studies¹⁸⁻²⁵ were published between 2017²² and 2020^{19-21,23,24}, and their characteristics are shown in Table 2. They all demonstrated an association between sarcopenia and poorer physical function outcome. The included studies

used different measures to assess sarcopenia and physical function outcomes of patients with stroke. Among these studies, the outcome measures used were the modified Rankin scale (mRS)¹⁸⁻²¹, Modified Barthel Index (MBI)²², and the Functional Independence Measure motor domain score (FIM-M)²³⁻²⁵. Four of these studies used the FIM or MBI to assess the activities of daily living (ADLs) status. Moreover, the diagnosis measure of sarcopenia differed in

Table 1. Quality assessment of the included studies

Study	Selection of participants (0-4)	Comparability of participants (0-2)	Assessment of outcomes (0-3)	Evaluate and control confounding factors	Total score (0-9)
Masafumi Nozoe,2019	3	2	3	Yes	8
Takafumi Abe,2020	4	2	2	Yes	8
Youbin Yi,2017	3	2	2	Yes	7
Yongjun Jang,2019	4	2	3	Yes	9
Ken Ohyama,2019	3	2	2	Yes	7
Tatsuya Matsushita,2019	3	2	2	Yes	7
Hiroshi Irisawa,2020	3	2	2	Yes	7
Fumihiko Nagano,2020	3	2	2	Yes	7

Table 2. Characteristics of the included studies

Study, Year	Country	Setting	No. of participants	No. of female	Mean age±SD in years at baseline	Sarcopenia diagnostic criteria	Physical function outcome
Masafumi Nozoe, 2019	Japan	acute phase hospital	152	71	76±11	SARC-F Scale score ≥4	mRS
TakafumiAbe, 2020	Japan	acute phase hospital	107	36	76±10.4	SMI SMI: male <7.0 kg/m ² , female <5.7kg/m ²	mRS
Youbin Yi, 2017	South Korea	the rehabilitation unit	127	63	68.6±14.9	Grip strength male <26kg, female <18kg	MBI
Yongjun Jang, 2019	Korea	department of rehabilitation	194	79	64.3±13	Grip strength male <26kg, female <18kg	mRS
Ken Ohyama, 2019	Japan	acute care hospital	164	56	57.4±15.2	Grip strength and SMI grip strength: male <26kg, female <18kg and SMI male<7.0kg/m ² , female<5.7kg/m ²	mRS
Tatsuya Matsushit, 2019	Japan	convalescent rehabilitation wards	267	117	72.5±13.2	Grip strength and SMI grip strength: male <26kg, female <18kg and SMI male<7.0kg/m ² , female<5.7kg/m ²	FIM
Hiroshi Irisawa, 2020	Japan	stroke rehabilitation unit	179	90	79.7±11.5	Body muscle percentage (skeletal muscle mass/ body weight %): males≤30%, female≤25%	FIM
Fumihiko Nagano, 2020	Japan	rehabilitation hospital	120	70	79.3±9.9	Grip strength and SMI grip strength: male <28kg, female <18kg and SMI male<7.0kg/m ² , female<5.7kg/m ²	FIM

these studies. Some studies used skeletal muscle quantity measured by bioelectrical impedance analysis (BIA)^{20,23} or the SARC-F scale¹⁸, whereas others employed either grip strength^{21,22} or grip strength + skeletal muscle index (SMI) by BIA^{19,24,25}.

Association of sarcopenia with physical function

Modified Rankin Scale (mRS)

The relationship between sarcopenia and mRS was assessed in four studies¹⁸⁻²¹. No obvious heterogeneity was present in these studies. Therefore, we chose a fixed-effects model to report physical function comparing the sarcopenia and non-sarcopenia groups(I²=29.5%). A meta-

analysis of these studies showed that sarcopenia was related to an increased risk of poor physical function (total OR=3.11, 95% CI: 2.22-4.34, P<0.0001) as displayed in Figure 2. In addition, A study by Takafumi Abe^[20] indicated severity of the disease might be a confounding factor.

Modified Barthel Index (MBI)

The association between sarcopenia and MBI was evaluated in 1 study²². dMBI was the change in MBI score between admission and discharge. Grip strength on the unaffected side (uGS) was positively associated with improvement in MBI at discharge (P=0.019). In addition, using multiple linear regression analysis, uGS was a significant independent predictor of the amount

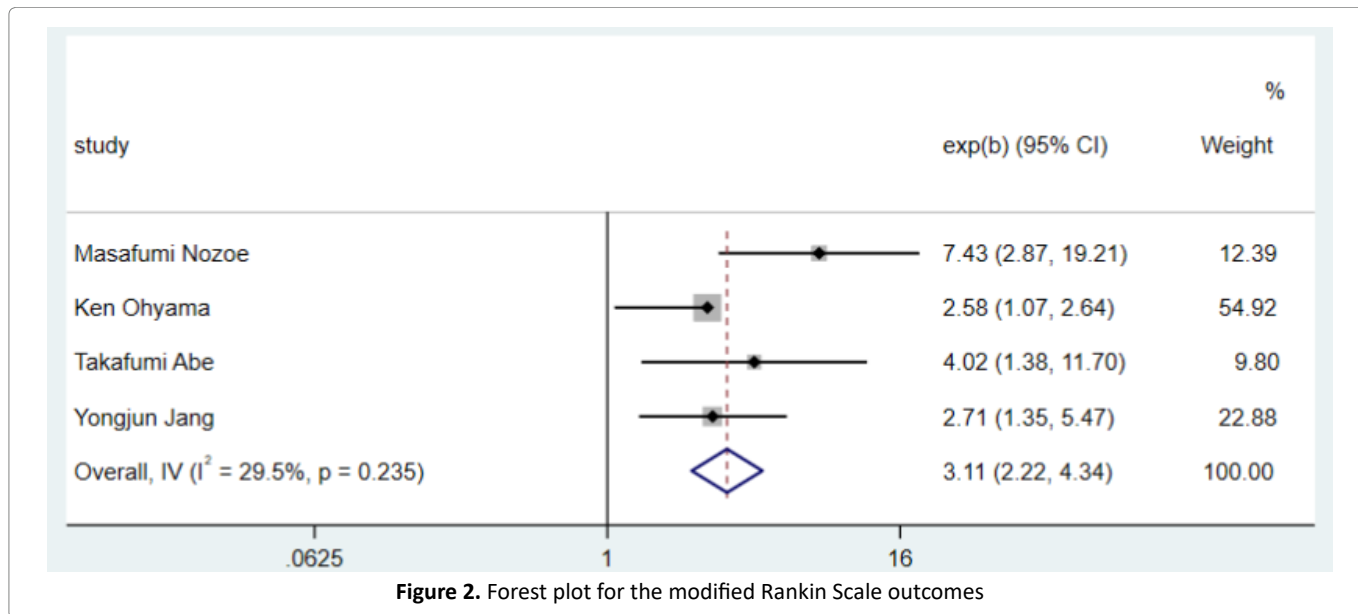


Figure 2. Forest plot for the modified Rankin Scale outcomes

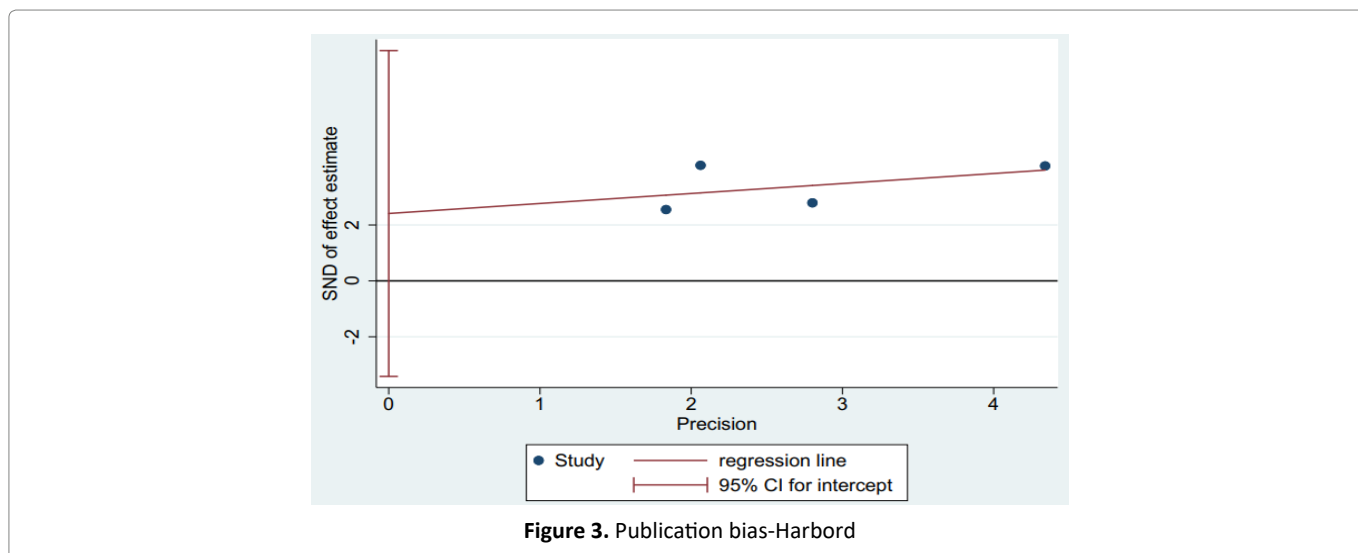


Figure 3. Publication bias-Harbord

of functional change after stroke. After adjusting for covariates, uGS was positively associated with dMBI ($P < 0.001$).

Functional Independence Measure - Motor domain (FIM-M)

Three studies²³⁻²⁵ evaluated the relationship between sarcopenia and FIM-M. One of these studies²³ showed that high muscle rate (skeletal muscle mass/body weight) (OR 2.42, 95% CI 1.05-5.59; $P = 0.03$) was significantly associated with a four-week FIM-M program among male and female patients. However, a study by Matsushita et al.²⁵ reported that a diagnosis of sarcopenia independently predicted FIM-M score ($B -4.957$, 95% CI -9.902 – -0.012) at discharge in men, but not in women. Another study²⁴ showed that changes in SMI were significantly associated with FIM-M at discharge ($\beta 0.175$, $P = 0.003$).

Publication bias

There was no publication bias in the meta-analysis after using the Egger’s test ($p = 0.217$) as displayed in Figure 3.

Discussion

A wide variety of tests and tools for the assessment of sarcopenia are currently available^{26,27}. To date, the revised guideline published by the European Working Group on Sarcopenia in Older People (EWGSOP2) propose new insights that muscle strength is the principal determinant of sarcopenia as opposed to muscle mass³. The assessment of skeletal muscle strength includes grip strength and chair stand test. Muscle strength is better than muscle mass in predicting poor clinical outcomes in patients²⁸⁻³⁰. In our study, five of the eight included studies used grip strength measurement. Moreover, one of the studies used the SARC-F to assess sarcopenia. Researchers have

reported that the scale has low to moderate sensitivity and high specificity in predicting low muscle strength³¹. The SARC-F is a self-reported questionnaire by patients that contains five areas of strength, assistance in walking, rising from a chair, climbing stairs, and falls³². Finally, two studies used bioelectrical impedance analysis (BIA) to assess skeletal muscle mass in consideration of the level of disability, consciousness, or cognitive impairment of the stroke patients. The method was chosen also due to the convenience, inexpensiveness, and accessibility. In short, the manner, in which sarcopenia was assessed by the eight studies was reasonable. The appropriate assessment method was selected based on the patient's disability or mobility, the resources available in the medical setting, or the purpose of the test as well.

We were interested in finding out whether sarcopenia occurred prior to stroke or post stroke. However, only one study¹⁸ explicitly stated that the condition existed pre-stroke in relation to functional outcome. The rest of the literature assessed sarcopenia within seven days after admission to the hospital without delineation of the specific time when it happened. Nevertheless, all studies showed that sarcopenia was related to physical function of patients with stroke. It is worth noting that gender differences and stroke severity should be considered when predicting physical function in patients with stroke. As mentioned previously, one study²⁵ only identified this correlation in the male gender. In contrast, another study²¹ concluded that women presenting with sarcopenia within 2 weeks of a stroke had a higher risk for poor prognosis than men. This discrepancy might be due to different methods used in the studies to assess sarcopenia and physical function, different follow-up times, and the presence of confounding factors such as disease severity, nutrition, etc. Moreover, the examination by Abe et al.²⁰ on the effect of skeletal muscle mass on walking function indicated that it could vary by disease severity. Physical function was worse in the mild and moderate groups with lower skeletal muscle mass, but no such relationship was found in the severe group. A possible reason for this was that the severity of stroke had a greater impact on walking function than sarcopenia in the severe group.

Stroke and sarcopenia are two different chronically disabling diseases affecting each other. Skeletal muscle is the main effector organ causing disability due to immobility after stroke. Decreased skeletal muscle mass eventually results in impaired mobility and decreased physical performance³³. This study found that sarcopenia was also related to an increased risk of poor physical function as assessed by mRS in patients with stroke (OR=3.11, 95% CI: 2.22-4.34, P<0.0001). Currently, several factors in research reports were used to predict the prognosis of stroke. Malnutrition, a cause of sarcopenia, also might

be a predictor of poor functional outcome of stroke³⁴⁻³⁶. This indirectly supported our findings that sarcopenia was an independent factor predicting physical function outcome of patients with stroke. Recent studies¹² reported there was a negative correlation between sarcopenia and improvement in ADLs in the rehabilitation setting. Our finding concurred with those of the studies as well.

Implications for practice

Our study found that sarcopenia was correlated with physical functional status of patients with stroke. The ability to perform ADLs was essential for the improvement of the quality of life for stroke patients and their families. Previous studies showed that increased nutritional or exercise interventions could improve the muscle mass, strength, and physical function of patients with sarcopenia and stroke^{37,38}. Increased muscle mass was found to improve ADLs, which was important for stroke rehabilitation. It highlighted the significance of managing skeletal muscle mass of this population.

Sarcopenia is not a consideration in current recommendations for stroke treatment and rehabilitation guidelines. Measurement tools for sarcopenia are infrequently used in the clinical setting^{39,40}. Considering this situation, we strongly suggest that screening, diagnosis, treatment, and prevention of sarcopenia should be part of the routine clinical practice in patients with stroke.

Limitations

This study has some limitations. Firstly, several different definitions and measures were used to determine sarcopenia or physical functional outcomes. In addition, there was no defined threshold for muscle mass loss for patients with stroke⁴. Secondly, because some studies utilized a retrospective approach, there might be unexplored confounders, such as rehabilitation and psychiatric symptoms, which might affect physical functional prognosis. Thirdly, majority of the studies had follow-up periods ending at discharge, which was a short length of time. Future studies should require longer follow-up periods.

Conclusion

This review provided an overview of the available literature identifying the relationship between sarcopenia and physical functional outcomes of patients with stroke. Early identification of sarcopenia in stroke patients is imperative for outcome improvement. We are hoping to see further investigations into the disease mechanism as well as more research on sarcopenia as a clinical outcome predictor among this patient population.

Conflict of Interest

The authors declare no conflict of interest.

Funding

This study received no special grant from any funding agency.

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