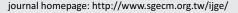


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Original Article

Association between Masticatory Function and Sarcopenia in Elderly People: A Systematic Review and Meta-Analysis

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SUMMARY

Background: The purpose of this systematic review was to explore the association between masticatory function (subjective and objective assessment) and sarcopenia in elderly people. Methods: Multiple electronic databases including PubMed, Embase, Web of Science, and Cochrane Central Register of Controlled Trials were searched for all years up to October 1, 2019. Articles that evaluated occlusal force or chewing ability or difficulties in eating scores to explore the association between sarcopenia in elderly patients and healthy elderly peoples were included. A modified version of the Newcastle Ottawa Scale was used to assess study quality. The pooled standardized effect size with its corresponding 95% confidence interval for each parameter was calculated. Results: Of the 45 articles identified, three retrospective observational comparison studies, which had a lower risk of bias, were included: objective (occlusal force or chewing gum) and subjective (difficulties in eating scores) assessment were reported. Meta-analysis revealed that maximum occlusal force (standardized mean difference (SMD) = 0.36, confidence interval (CI) = 0.19-0.53, p < 0.001) was significantly lower in subjects who were diagnosed with sarcopenia than in control groups. There were significant associations between sarcopenia and chewing ability using chewing gum (odds ratio (OR) = 2.34, CI = 1.09–5.02, p = 0.03) and difficulties in eating score (OR = 2.21, Cl = 1.65–2.97, p < 0.001). Conclusions: We found some limited evidence for an association between sarcopenia and masticatory

function. Our meta-analysis supports an association between sarcopenia and subjective and objective masticatory function. More evidence is needed to demonstrate the association between masticatory function and sarcopenia in elderly people.

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1. Introduction

The proportion of elderly in the general population is rapidly increasing due to improvements in living standards and medical technology worldwide.¹ In Korea, the proportion of the elderly population is expected to reach 20.8% in 2026, which means that one out of every five people will be part of a "super-aged society".² As the elderly population increases, elderly people are increasingly defined as having social problems. Particularly, interest in elder nutrition, health, and quality of life is becoming more important.³

Sarcopenia is the degenerative loss of skeletal muscle mass, quality, and strength associated with aging. Sarcopenia has recently been associated with various metabolic diseases, mortality, and quality of life, and the interest of society in this disorder is increasing.⁴ The major cause of sarcopenia has not been clearly identified, but lack of nutrition, exercise, and chronic inflammation have been identified as risk factors. Of these, malnutrition is known to be closely associated with sarcopenia.⁵

A recent study by Tanaka et al. reported that oral frailty could be a risk factor for physical frailty, mortality, and sarcopenia.¹⁰ It is important to recognize the importance of oral frailty, including masticatory function. Therefore, the purpose of this systematic review and meta-analysis was to evaluate the association between masticatory function (subjective and objective assessment) and sarcopenia in elderly people.

2. Materials and methods

2.1. Protocol and registration

This systematic review was conducted under the recommenda-

From a dental point of view, masticatory function and its interaction with nutritional status are especially important. The degree of masticatory function in the elderly plays an important role in maintaining balanced nutrition.⁶ Some studies have shown that elderly people who are uncomfortable chewing may not be able to adequately chew their food, which can lead to a decrease in the amount of food that can be consumed.^{7–9} Furthermore, improvement in maximum bite force and masticatory efficiency may be important prerequisites for adequate nutrition.⁶

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tions of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines¹¹ and the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions.¹² This systematic review was registered in the PROSPERO database, an international prospective register of systematic reviews in health and social care (National Institute for Health Research, UK; pre-protocol CRD 42017078945).

2.2. Eligibility criteria (PICOS)

The systematic review was designed to answer the following focused question: Is there evidence of an association between masticatory ability and sarcopenia in elderly people? The PICOS (Population/patient/participants/problem, Intervention, Comparison, Outcome, Study design) method was used to define the eligibility criteria as follows: the P (population) comprised people over 65 years of age with and without a diagnosis of sarcopenia; I (intervention) included participants who were diagnosed with sarcopenia; C (comparison) was elderly healthy people without sarcopenia; O (outcomes) were bite force, and/or masticatory ability, and/or difficulties in eating score; and S (study type) included all possible studies except case reports, letters, and review articles. Exclusion criteria were: 1) studies that did not evaluate masticatory ability (bite force or masticatory difficulty or low eating scores); 2) literature or systematic reviews, narrative reviews, and case reports; 3) protocols, comments, editorials, letters, and interviews; and 4) in vitro only studies.

2.3. Information sources and search strategy

2.3.1. Electronic search

A literature search was performed in the following databases from the earliest available date to October 1, 2019: MEDLINE, EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials. The search strategy was a combination of Mesh terms and free text words: ("mastication"[MeSH Terms] OR "mastication"[All Fields] OR "masticatory"[All Fields] OR "masticator"[All Fields] OR "masticatory ability"[All Fields] OR "bite force" [Mesh Terms] OR "bite force"[All Fields] OR "bite force" [Mesh Terms] OR "bite force"[All Fields] OR "bite] OR "biting"[All Fields] OR "occlusal"[All Fields]) AND ("sarcopenia" [Mesh Terms] OR "sarcopenia"[All Fields]). There was no language restriction. The detailed search strategy employed in this study is shown in Appendix 1.

2.3.2. Hand search

Reference lists of the included studies and previously published systematic reviews and meta-analyses related to the topic were screened for identification of any additional studies.

2.4. Study selection

Each identified article was independently screened by title and abstract by the two authors (D.W. and J.I.) to remove duplicate entries and studies that failed to meet the inclusion criteria. Any disagreement was resolved by discussion. Full-text articles of the remaining studies were assessed according to the previously defined inclusion and exclusion criteria, and then eligible articles were selected. The review authors were not blinded to authors, institutions, or publications. References of the included articles were further checked manually. If retrieved articles were unclear, we contacted the author by e-mail to clarify incomplete information.

2.5. Data collection process

Two of the authors (D.W. and J.I.) independently extracted the data from each included article into predesigned data collection forms in Microsoft Excel: 1) study identification: first author's name, year of publication, and country; (2) study design; (3) participants: sample size, mean age, and numbers of male and female participants; (4) interventions: details about diagnosis criteria for sarcopenia; (5) primary outcome measures; and (6) measuring tools. Discrepancies were resolved by discussion.

2.6. Data items

The primary outcome measures were objective masticatory function using chewing gum or maximum occlusal force and subjective masticatory function using questionnaire. When data were not provided, calculations were performed based on the raw data reported in the article if present or we contacted the author by e-mail to clarify incomplete information.

2.7. Risk of bias in individual studies

Two of the authors (D.W. and J.I.) independently evaluated the risk of bias of the enrolled studies in our meta-analysis using a modified version of the Newcastle-Ottawa (Appendix 2). The observational studies included were evaluated mainly through seven methodological items. Each study could be awarded only one score for each item; thus, the maximum possible score for each study was seven. The quality of the studies was assessed independently by two reviewers. If they disagreed, a consensus was reached by discussion.

2.8. Summary measures and results synthesis

To answer the research question, we aggregated previous study data that reported on the association between sarcopenia and bite force in the form of means (standard deviations) to produce a mean effect size (standardized mean difference, SMD). Difficulties in eating scores using questionnaire and chewing ability scores using chewing gum were summarized as odds ratios (95% confidence intervals), when provided or calculated. The standardized mean effect size was calculated using Comprehensive Meta-Analysis (version 2, Biostat Inc., USA) and the odds ratio was calculated using RevMan software v.5.1 (Cochrane Collaboration, Oxford, UK).¹³ We provided forest plots to describe the results of the meta-analysis. Heterogeneity analysis was conducted to examine whether all effect sizes in the sample were from the same population using the I^2 test, and the Q statistic. A p value for the Q statistic < 0.05 was defined as an indicator of heterogeneity and data were considered heterogeneous for an I^2 value higher than 40%.

2.9. Risk of bias across the studies

The funnel plot is a scatter plot showing the estimated effect sizes of the individual studies based on the sample size of the study. The interpretation of asymmetry can only be applied if at least 10 studies are included.

2.10. Additional analysis

In this study, we could not perform a sub-group analysis because of the small number of studies included. 240

3. Results

3.1. Study selection

Database searches identified 45 publications (Figure 1). After eliminating duplicates, 31 articles were selected; 20 of these were excluded after title and abstract screening as follows: Review (n = 5), articles not related to topic (n = 12), letter and commentary article (n = 2), and paper with only an abstract (incomplete data) (n = 1). A total of 11 articles were reviewed for eligibility by assessing the full text. The reasons for study exclusion during the final review were as follows: papers without masticatory force measurements (n = 1) and studies not related to sarcopenia (n = 7). We included the remaining three articles for quantitative and qualitative analyses.

3.2. Study design and population

The main characteristics of all included studies are described in Table 1. Included studies were published between 2013 and 2017. All trials were retrospective observational comparison studies.^{9,10,14} The three studies comprised a total of 3,879 patients, including diagnosed sarcopenia patients (n = 796).

3.3. Type of outcome measures

Characteristics of the included studies.

The included trials evaluated subjective masticatory function (difficulties in eating scores) and objective masticator function

Table 1

(chewing gum and occlusal force). To evaluate objective masticatory function, two studies^{9,10} used a color changeable chewing gum. For the analysis of occlusal force, two studies^{9,10} used an occlusal force meter. Subjective masticatory function (difficulties in eating score) were assessed in two studies^{10,14} by using a questionnaire.

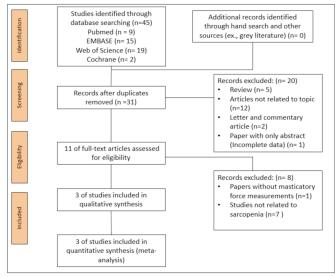


Figure 1. PRISMA flow of information through the different meta-analysis phases.

Study (year)	Country	Study design	Age range (mean), years	No. of subjects (sex)	Participants	Diagnosis criteria	Outcomes of interest	Measurement tool
Tanaka et al. (2017)	Japan	Retrospective comparative study	•	-	Japanese community- dwelling elderly subjects (Kashiwa city)	Asian Working Group for Sarcopenia (AWGS) guideline	Maximum occlusal force, chewing ability, and difficulties in eating	Occlusal force meter and a color-changeable chewing gum
Murakami et al. (2015)	Japan	Retrospective comparative study	73.0±5.1	761 (314 men and 447 women)	Japanese community- dwelling older adults with or without sarcopenia	Asian Working Group for Sarcopenia (AWGS) guideline	Occlusal force and chewing ability	An occlusal force measurement system film was used, Dental Prescale 50H Type R (Fuji Photo Film, Tokyo, Japan) and an Occuluser (Fuji Photo Film). A color-changeable chewing gum (Xylitol masticatory performance evaluating gum; Lotte, Saitama, Japan) was used to examine chewing ability.
Tanimoto et al. (2013)	Japan	Retrospective comparative study	•	1,074 (365 men and 709 women)	Japanese community- dwelling elderly subjects	AMM index (AMI, weight [kg]/height [m ²] as > 2 standard deviations below the mean AMI for normal young subjects. The lowest quartile for grip strength and usual walking speed was classified as low muscle strength and low physical performance, respectively. Sarcopenia was characterized by a low muscle mass, combined with a low muscle strength or low physical performance.	Difficulties in eating	Questionnaire

AMI, appendicular skeletal muscle index; SD, standard deviation.

3.4. Synthesis of results

3.4.1. Association of sarcopenia with subjective and objective masticatory function

The three included studies provided three effect sizes for the association of sarcopenia with three types of measurement outcomes (difficulties in eating scores for subjective methods and bite force scores and chewing gum scores for objective methods). Subjects diagnosed with sarcopenia showed decreased levels of masticatory ability scores using chewing gum (OR = 2.34, 95% CI = 1.09-5.02, p < 0.05) and difficulties in eating scores using questionnaire (OR = 2.21, CI = 1.65-2.97, p < 0.001) compared to a control group under the random model (Figure 2 and 3). Meta-analysis revealed that maximum occlusal force (SMD = 0.36, CI = 0.19-0.53, p < 0.001) was significantly lower in subjects who were diagnosed with sarcopenia than the control group. (Figure 4).

3.5. Risk of bias within individual studies

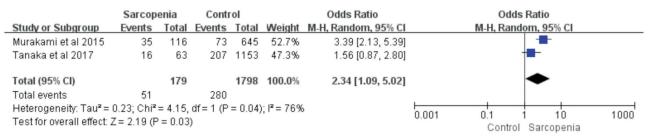
The quality assessment for retrospective observational comparison studies using the modified Newcastle-Ottawa Score Tool is summarized in Table 2. All of the included studies were described as observational studies. Sample size calculations were not performed in all studies. The representation of the selected samples was considered appropriate in all included studies. The ascertainment of the assessment tool for sarcopenia was considered as adequate in all observational studies because they were conducted through standardized diagnostic cut-off values. The response rate, consideration of important confounding factors, ascertainment of assessment tool, and statistical evaluation were reported in all studies. Overall, all of the included individual studies were considered to have a low risk of bias.

3.6. Risk of bias across the studies

Since the number of included studies was fewer than 10, funnel plot analysis was not performed. $^{\rm 15}$

4. Discussion

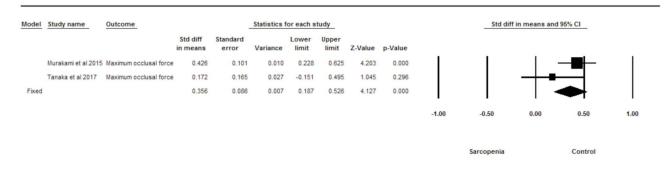
The term "masticatory function" includes both subjective and objective assessment. Patients' ratings of their ability to chew refers to the subjective assessment of the masticatory function by the patient and is evaluated using interviews or special questionnaires.¹⁶ Masticatory efficiency is evaluated using objective tests and is defined as "a measure of the comminution of food attainable under standardized testing conditions".¹⁷ The most common method is to use a chewing gum that changes color or a bite force measuring device. In this meta-analysis, three studies reported masticatory function outcomes (i.e., chewing gum, occlusal force meter, and





	Sarcop	enia	Contr	ol		Odds Ratio			Odds	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl			M-H, Rando	om, 95% Cl		
Tanaka et al 2017	18	63	173	1153	26.6%	2.27 [1.28, 4.01]				-	-	
Tanimoto et al 2013	138	617	53	457	73.4%	2.20 [1.56, 3.10]						
Total (95% Cl)		680		1610	100.0%	2.21 [1.65, 2.97]				٠		
Total events	156		226									
Heterogeneity: Tau ² = I		15.075-0708		= 0.93)); I ² = 0%		01	0.2	0.5 1	2	-	10
Test for overall effect: 2	Z = 5.30 (F	° < 0.00	001)				0.1	0.2	0.0	Sarcopenia	0	10

Figure 3. Forest plot of subjective masticatory function (difficulties in eating score).



self-reported chewing difficulty).

The principle finding of our meta-analysis was that masticatory function using chewing gum was significantly associated with sarcopenia. Evaluation of chewing ability using color changing gums may be useful for unhealthy patients, especially for patients with sarcopenia. Color changing gums are one of the most commonly used objective methods for the assessment of masticatory function.¹⁸ Sarcopenia can be measured by muscle mass, muscle strength, and general function.¹⁹ Unlike a single evaluation index, such as occlusal force or number of teeth, chewing ability is a global evaluation index related to muscles of mastication, tongue, teeth, and saliva.²⁰ This can be thought of as the background to the relationship with the sarcopenia.

In this review, occlusal force was significantly lower in subjects who were diagnosed with sarcopenia than in the control group. Evaluating maximum bite force is also an objective method, which evaluates masticatory-related muscle loss associated with jawclosing force. It is a test of strength in the static rather than dynamic state, so there is a limit to its ability to represent masticatory function, but it is useful to supplement this measure with chewing ability. In sarcopenia patients, masticatory-related muscle weakness can be identified. However, this may vary depending on the number of remaining teeth and the condition of any prosthesis. In Murakami et al.'s study, remaining teeth, age, and BMI were adjusted for and an association between occlusal force and sarcopenia was reported.⁹

Finally, statistical significance was also observed with respect to sarcopenia and subjective assessments such as difficulties in eating food as well as objective assessment of masticatory function. Some researchers have pointed out that subjective masticatory function measured by questionnaire and objective masticatory function measured by color changing chewing gum were associated with different factors, suggesting that both mental and physical factors should be taken into consideration when treating decreased masticatory function. Since mastication depends not only on tooth strength and the number of remaining teeth, but also on the amount of saliva, the movement of the tongue, and other factors, it is necessary to evaluate any subjective evaluation method, because it should include all of these variables.²¹ To date, sarcopenia, which is observed in people aged over 65 years, has been reported to be directly related to food shortages such as protein.²² In addition, recovery of mastication function is important in relation to effective protein intake.^{6,23} However, there are not many reports on the relationship between mastication function and sarcopenia, which is important for digestion and absorption of proteins.^{9,10,14} Although this study has shown that masticatory function is associated with sarcopenia, more trials are needed.

Sammnieng P et al.⁸ performed a cross-sectional study that included 612 older participants to evaluate the relationship between masticatory ability and nutritional status. They reported that retention of natural teeth with appropriate numbers of functional tooth units by replacing missing teeth with dentures and improving masticatory ability helps reduce the risk of malnutrition in older adults. Rémond D et al.²⁴ performed a study using a [1-(13)C]leucine balance with a single-meal protocol to assess the absorption rate of meat protein and to estimate the utilization of meat protein in elderly subjects with different masticatory efficiency. They found that postprandial whole-body protein synthesis was lower in denture wearers than in dentate subjects (30% compared with 48% of leucine intake, respectively; p < 0.05). This study showed that meat protein utilization for protein synthesis can be impaired by a decrease in the masticatory efficiency of elderly subjects.

Association of mastication function (occlusal force) on frailty

has also been reported in a community-dwelling healthy elderly study.^{6,25–28} Mediating effect of nutritional factors that influence the causal relationship between masticatory function and sarcopenia need to be evaluated. In a 2018 study by lkebe et al., the authors reported that maximum occlusal force was positively associated with direct cognitive function as well as indirectly through dietary intake, after controlling for all significant factors.²⁹ To demonstrate the causal relationship between masticatory function including occlusal force and sarcopenia, path analysis or multivariate analysis should be performed to demonstrate the mediating effects of food intake.

Nevertheless, this is the first meta-analysis of the association between masticatory function and sarcopenia in elderly people. However, this meta-analysis has several limitations. First, only three studies were included. So, the risk of bias could not be assessed because the included studies were less than 10. Second, there was heterogeneity in the assessment tool for masticatory function among the included studies. No information about occlusal force meters was mentioned in the 2017 Tanaka study. The occlusal force meters used in Tanaka's study in 2017 could not be identified. Therefore, we could not match the description for masticatory function (occlusal force). A standardized method is mandatory to evaluate the masticatory performance-related factor in the elderly. Hama et al.³⁰ reported that there was a relationship between masticatory performance and number of healthy natural teeth. However, there were no correlations with masticatory performance and maximal masticatory strength, height, weight, and age. To date, there are no standardized clinical guidelines for measuring masticatory function in patients with sarcopenia. Therefore, to search for an effective measurement tool to treat sarcopenia and to develop standardized strategies, more systematic research is needed.

In conclusion, through a systematic review, we found some limited evidence for the association between sarcopenia and masticatory function. Meta-analysis supporting the association of sarcopenia with occlusal force, chewing gum, and self-reported chewing difficulties. As the study involved were done by a specific research group in a particular area, more evidence is needed to demonstrate the association between masticatory function and sarcopenia in elderly people.

Disclosure statement

The authors declare no conflicts of interest.

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Association between Masticatory Ability and Sarcopenia in Elderly People

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Appendix

Appendix 1

Detailed search strategies for each database. Mesh terms, search terms, and combinations of the two were used for each database search.

Database	Detailed search strategies	Records found
MEDLINE/PUBMED	("mastication"[MeSH Terms] OR "mastication"[All Fields] OR "masticatory"[All Fields] OR "masticator"[All	9
	Fields] OR "chewing ability" [All Fields] OR "chewing" [All Fields] OR "bite force" [Mesh Terms] OR "bite	
	force"[All Fields] OR "bite"[All Fields] OR "biting"[All Fields] OR "occlusal"[All Fields]) AND	
	("sarcopenia"[Mesh Terms] OR "sarcopenia"[All Fields])	
EMBASE	('mastication'/exp OR 'mastication' OR 'masticatory' OR 'masticator' OR 'chewing ability' OR 'chewing' OR	15
	'bite force'/exp OR 'bite force' OR 'bite' OR 'biting' OR 'occlusal') AND ('sarcopenia'/exp OR 'sarcopenia')	
Cochrane Central Register of	("mastication" OR "masticatory" OR "masticator" OR "chewing ability" OR "chewing" OR "bite force" OR	2
Controlled Trials	"bite" OR "biting" OR "occlusal") AND ("sarcopenia")	
Web of Science	("mastication" [mesh] OR "mastication" OR "masticatory" OR "masticator" OR "chewing ability" OR	19
	"chewing" OR "bite force" [mesh] OR "bite force" OR "bite" OR "biting" OR "occlusal") AND	
	("sarcopenia"[mesh] OR "sarcopenia")	

Ultimately, 45 records were found, 9 from MEDLINE/PubMed, 15 from EMBASE, 2 from the Cochrane Library, and 19 from the Web of Science. Studies were further selected according to the inclusion criteria listed in the Material and Methods.

Appendix 2

Methodological Quality Appraisal Tool.

Selection

1. Did the authors present their reasons for selecting or recruiting the number of people included or analyzed?

- 0. No
- 1. Yes
- 2. Was study sample likely to be representative of the study population?
- 0. Non-probability sampling (including: purposive, quota, convenience and snowball sampling)
- 1. Probability sampling (including: simple random, systematic, stratified g, cluster, two-stage and multi-stage sampling)
- 3. Was the measurement tool used for ascertainment of sarcopenia valid and reliable?
 - 0. No
 - 1. Yes
- 4. Was a response rate mentioned within the study?
- 0. No

1. Yes

Confounding factors

5. Were there any considerations for important disturbance variables, such as age or socioeconomic status related to masticatory ability?

- 0. No
- 1. Yes

Outcome

6. Was the measurement tool used for assessment of outcome (masticatory ability) valid and reliable?

- 0. No
- 1. Yes

7. Was statistical adjustment adequately performed? (i.e., the effect of confounders when evaluating the influence of independent variables on masticatory ability)

0. No 1. Yes

Methodological Appraisal Score				
Bad	Satisfactory	Good		
0–33%	34–66%	67–100%		

0 - no or not reported; 1 - yes.

Note. Scoring: Total score divided by total number of items multiplied by 100.

Quality appraisal score: weak: 0-33.9%, moderate: 34%-66.9%, strong: 67%-100%.