The association between blood concentration of 25-hydroxyvitamin D and sarcopenia: a meta-analysis

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Jing Luo MS[1], Zhenyu Quan PhD[2], Song Lin PhD[1], Lianhua Cui PhD[1]

[1]Department of Public Health, Medical College of Qingdao University, Qingdao, Shandong Province, China
[2]Medical School of Yanbian University, Yanji City, Yanbian Korean Autonomous Prefecture, Jilin, China

Authors' contributions:
Yoko Saino: conception and design of the study, generation, collection, assembly, analysis and interpretation of data, drafting and revising the manuscript, and approval of the final version of the manuscript. Hidetaka Wakabayashi, Keisuke Maeda, Shinta Nishioka, Takako Hao and Kenji Mimatsu: conception and design of the study, analyzing and interpreting data, revising the manuscript, and approval of the final version of the manuscript.

Authors' e-mail address:
Jing Luo, luojing0610@163.com;
Zhenyu Quan, zyquan@ybu.edu.cn;
Song Lin, 15146001303@163.com;
Lianhua Cui, clhqd_lh@163.com

Corresponding author: Dr Lianhua Cui, Department of Public Health, Medical College of Qingdao University, Dengzhou Road 38, Qingdao, Shandong Province, China. Tel: +86 15966845887. Email: clhqd_lh@163.com

ABSTRACT

Objectives: Associations between blood25-hydroxyvitamin D (25(OH)D) concentration and sarcopenia remain controversial; thus, this meta-analysis was conducted to explore the relationship between blood25(OH)D concentration and sarcopenia. **Design:** We searched the PubMed and EMBASE databases for relevant published observational studies that investigated blood 25(OH)D concentration and sarcopenia up to June 2017.We then investigated data from these studies that compared blood 25(OH)D concentrations between the sarcopenia and healthy control groups. A random-effect model was used to calculate the pooled weighted mean difference (WMD) of blood 25(OH)D concentration with a 95% confidence interval (95% CI). **Results:** Twelve studies (eight cross-sectional, two matched case-control, and two prospective cohort studies) with a total of 22,590 individuals were included. Sarcopenic individuals had lower blood 25(OH)D concentrations than healthy controls (WMD=−2.14, 95% CI: −2.81–−1.48; I^2=74.6%). Subgroup analysis showed that the methods of assessing both blood 25(OH)D concentrations and sarcopenia might be sources of heterogeneity, and further showed that studies excluding obese individuals and different sarcopenia assessment criteria enhanced the relationship. Sensitivity analysis by one-study-removed confirmed the robustness of these results. **Conclusions:** Our study shows that sarcopenic adults have lower blood 25(OH)D concentrations. Further high-quality large-scale prospective cohort studies are needed to confirm these findings.

Key Words: sarcopenia, vitamin D, 25-hydroxyvitamin D, muscle mass, meta-analysis

INTRODUCTION

Sarcopenia, which is characterized by a reduction in muscle mass and strength, as well as a decline in physical performance with age, has become an important worldwide public health problem. Sarcopenia has long been regarded as a characteristic of natural aging rather than a disease; however, recent studies have shown that sarcopenia is associated with various diseases such as cancer, heart failure, chronic obstructive pulmonary disease, rheumatoid arthritis, and neurodegenerative disorders.[1] Additionally, sarcopenia is also accompanied by worse health outcomes, including increased mortality rates, longer hospitalization times, and greater need for rehabilitation care after hospital discharge.[2] As a major clinical problem associated with age, there is a progressive reduction in the size and number of muscle fibers, which can result in a decrease in muscle mass of approximately 40% between the ages of 25

and 80.[3,4] Many studies have shown that vitamin D deficiency contributes to sarcopenia development and that vitamin D supplements can increase muscle quality (e.g., gait speed, handgrip strength).[5,6]

Vitamin D is a fat-soluble vitamin that regulates calcium and phosphorous homeostasis, as well as bone mineralization.[7] Its active form is 1,25 dihydroxy vitamin D_3 ($1,25(OH)_2D$)[8] and the major circulating metabolite is 25-hydroxyvitamin D(25(OH)D).[9] Although the latter is not the most active metabolite, blood concentrations of total 25(OH)D are routinely used to assess blood vitamin D status in clinical practice.[10] There has been an increasing appreciation of the role of vitamin D in maintaining muscle health and physical activity,[11,12] as its insufficiency can cause muscle weakness and a decline in bone mineral density, as well as an increase in the risk of recurrent falls in elderly adults.[13] The association between low blood 25(OH)D concentration and increased risk of falls has been reported in many studies.[14,15] Falls are the primary clinical sign of reduced muscle function, which is the long-term outcome of losing muscle mass.

Several recent studies have focused on sarcopenia and its related risk factors. Yoshimura et al[16] performed a systematic review and meta-analysis based on randomized controlled trials to explore the effectiveness of exercise, nutrition, drugs, and combinational interventions for treating sarcopenia in older people. Another systematic review and meta-analysis[17] based on randomized controlled trials assessed the effects of vitamin D supplementation on muscle strength and muscle mass. However, no comprehensive meta-analysis has addressed the role of blood 25(OH)D concentration on sarcopenia. Some studies have shown a relationship between blood 25(OH)D concentration and sarcopenic adults;[5,18-21] however,these results are not unequivocal. Thus, we conducted this meta-analysis to investigate the underlying association between blood 25(OH)D concentration and sarcopenia.

PARTICIPANTS AND METHODS

This meta-analysis was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[22]

Search strategy

Two authors (J.L. andS.L.) independently searched the PubMed and EMBASE databases for relevant observational published studies that investigated serum, plasma and blood 25(OH)D

concentration and sarcopenia up to June 2017 (Supplemental figure 1). A manual search using references from the retrieved studies was also performed.

Eligibility criteria and quality assessment

Our inclusion criteria were as follows: (i) observational original articles evaluating the blood concentration of 25(OH)D in both sarcopenia patients and the general population; (ii) sarcopenia was diagnosed based on the adjusted appendicular muscle skeletal muscle mass measured by dual-energy x-ray absorptiometry (DEXA)[23] or bioelectrical impedance (BIA);[24] and (iii) sarcopenia was considered the case and non-sarcopenia was considered the control.

Our exclusion criteria were as follows: (i) participants were clinical patients from hospital or care settings; and (ii) studies not published as full reports, letters, or case-only studies.

The quality of all studies was also independently assessed by the two authors listed above using the Newcastle-Ottawa scale for cohort, case-control studies in three aspects, including the selection of study participants, the comparability of the groups, and assessment of outcome measures. Cross-sectional studies were evaluated by the modified Newcastle-Ottawa Scale.[25] Any differences were resolved by consensus. Studies with a Newcastle-Ottawa scale score ≥5 were regarded as high quality.

Data extraction

The following study characteristics were extracted from each study using a standardized record form: surname of the first author, year of publication, study location, characteristics of the study population (e.g., cohort size and demographics) assessment criteria of sarcopenia, and blood 25(OH)D concentration. Data extraction was independently extracted by the two authors (J.L. and S.L.). Any disagreement was resolved by referring back to the original studies.

Statistical analysis

All analyses were conducted using Stata11.0 software (StataCorp, College Station, TX, USA). Unless otherwise specified, a p-value <0.05 was considered significant. The pooled weighted mean difference (WMD) and its 95% confidence interval (CI) were used for this meta-analysis of blood 25(OH)D concentration and sarcopenia. We pooled the estimates across studies using the random-effect model (DerSimonian–Larid). Study heterogeneity was measured using the Cochran's Q and I^2 statistics, assuming that $p \leq 0.10$ for the former and

$p \geq 50\%$ for the latter indicated significant and substantial heterogeneity.[26] We conducted subgroup analyses to investigate the potential differences and heterogeneity according to methods used to detect blood 25(OH)D concentrations, methods of measuring skeletal muscle mass, whether studies excluded obese individuals, and the assessment criteria of sarcopenia (muscle mass alone or combined with muscle quality) were conducted. Sensitivity analysis was conducted to evaluate the robustness of results. When the blood 25(OH)D concentration were reported in nmol/L, we divided both the mean and SD by 2.5 to convert to ng/ml.[27] Small-study effects were evaluated using a funnel plot and Egger's test.[28]

RESULTS

Literature search

We initially identified 761 potential articles, including 594 from EMBASE and 167 from PubMed. After excluding duplicate articles and reviewing titles and abstracts, 559 were removed. Then, 50 articles underwent full-text review according to the inclusion criteria, which excluded 38. In total, 12 articles were included in our final meta-analysis for estimating the association between blood 25(OH)D concentration and sarcopenia. The selection process is shown in Figure 1.

Study characteristics

All investigated subjects, which included 6,357 sarcopenic individuals and 16,233 healthy controls, were from the community. The mean age of sarcopenic individuals ranged from 50[29]–88[30] years, and that of healthy controls ranged from 50[29]–86[30] years; 54.65% of all individuals were women. As for study design, eight studies were cross-sectional studies,[5,18,29-34] two were matched case-control studies[19, 20] and two were prospective cohort studies.[21,35] With regard to study location, eight studies were conducted in Korea,[5,18,21,29,31,32,34,35] and one study was conducted in each of following countries: Australia,[30] United Kingdom,[19] Netherlands,[33] and Brazil.[20] All studies provided blood 25(OH)D concentrations; six studies[5, 18, 21, 31, 32, 35] used a radioimmunoassay kit (RIA)[36] to detect 25(OH)D, three[19,31,33] used the chemiluminescence micro-particulate immunoassay (CIA)[37] method, one[21] used HPLC[38] and two[29,34] did not report their methods. Sarcopenia was diagnosed by dual energy x-ray absorptiometry (DEXA)[39] in 10 articles[5,18,20,21,29-32,34,35] and by bioelectric impedance analysis (BIA)[40] in two articles.[19, 33] The data from eight articles[5,19,20,30-34] were reported as mean±SD, three studies[18,21,35] gave mean±inter quartile

range, and one (Park S et al) provided mean±95% CI. All data were converted to weighted mean difference (WMD)±SD. The characteristics of the included articles are summarized in Table 1. The Newcastle–Ottawa scores of each study were not less than 5, indicating that the methodological quality was generally good. The quality assessments of the included studies are shown in Supplemental table 1.

Association between blood 25(OH)D concentration and sarcopenia

Figure 2 shows the results of the meta-analysis of the 12 studies regarding blood 25(OH)D concentration and sarcopenia. These results revealed that sarcopenic patients had lower blood 25(OH)D concentrations compared with the healthy controls (WMD=−2.14, 95% CI: −2.81–−1.48). The statistical heterogeneity was high with an I^2 of 74.6%.

Considering that high heterogeneity was found, sub-analyses were conducted to explore the possible sources of heterogeneity. Subgroup analyses of the methods used to detect blood 25(OH)D concentrations, methods of measuring skeletal muscle mass, whether studies excluded obese individuals, and the assessment criteria of sarcopenia were conducted. We first conducted a sub-analysis between different measurement methods for blood 25(OH)D (Supplemental figure 2). Sub-analyses showed a negative association between blood 25(OH)D concentrations and sarcopenia in RIA studies (WMD=−1.59, 95% CI, −2.30–−0.89; k=6), CIA studies (WMD=−3.83, 95% CI, −6.38–−1.29; k=3), and N/A studies (WMD=−2.57, 95%CI, −3.03–−2.12; k=2); however this effect was not seen in the HPLC study,[25] which might be explained by the small number of included studies and their sample sizes. Both RIA and CIA studies continued to demonstrate moderate heterogeneity, with I^2 of 65.6% and 53.9%, respectively. While the N/A subgroup showed low heterogeneity, with an I^2 of 0.Then we conducted a sub-analysis between the different measurement methods for skeletal muscle mass (Supplemental figure 3). DEXA studies (WMD=−2.08, 95% CI, −2.76–−1.41; I^2= 77.2%, k=10) showed a negative association between blood 25(OH)D concentration and sarcopenia. This effect was not seen in BIA studies (WMD=−3.21, 95% CI, −7.55–1.14; I^2=67.5%, k=2). The next sub-analysis aimed to distinguish between studies that excluded obese individuals or not (Supplemental figure 4). Both studies that excluded (WMD=−1.89, 95% CI, −3.19–−0.59; k=4) and those that did not exclude obese individuals (WMD=−2.27, 95% CI, −2.98–−1.57; k=8) showed a significant association between blood 25(OH)D concentrations and sarcopenia. They all also continued to demonstrate moderate heterogeneity with I^2 of 74.0% and 63.0%, respectively. The last sub-analysis was conducted

to distinguish the sarcopenia assessment criteria, which included muscle quality (e.g., gait speed, handgrip strength) or not (Supplemental figure 5). Both assessment criteria demonstrated moderate heterogeneity, with I^2 of 53.9% and 75.2%, respectively. Studies in which sarcopenia was evaluated by combined muscle mass and muscle quality showed lower blood 25(OH)D concentrations (WMD=−3.83, 95% CI, −6.38–−1.29, k=3) than studies that only focused on muscle mass (WMD=−1.90, 95% CI, −2.54–−1.25, k=9); however, they all showed a negative association between blood 25(OH)D concentrations and sarcopenia.

Sensitivity analysis

Finally, a sensitivity analysis was performed to evaluate the robustness of these results. We conducted a one-study-removed sensitivity analysis (Supplemental figure 6) and we excluded studies that were only conducted on men or women. These statistical results still showed a significant difference (WMD=−2.37, 95% CI, −3.21–−1.62; k=10). Thus, these sensitivity analyses suggested that the results were stable and reliable.

Small-study effect evaluation

To investigate potential small study effects, funnel plots and quantitative assessments via Egger's test were performed (Figure 3). The results of the funnel plot and an Egger's test (p=0.301) did not suggest any obvious small study effects.

DISCUSSION

The purpose of this study was to evaluate if blood 25(OH)D concentration was associated with sarcopenia. Pooled results from 12 studies showed that individuals with sarcopenia had lower blood 25(OH)D concentrations compared with the non-sarcopenia population. Interestingly, we found that this effect was not seen in sub-analyses of studies that used HPLC to measure blood 25(OH)D and those that used BIA methods to assess skeletal muscle mass. Compared with the RIA and CIA methods for measuring blood 25(OH)D, the pooled effects of HPLC studies might be explained by the small number of included studies and sample sizes (35 with sarcopenia and 70 non-sarcopenia). A previous study[41] showed that DEXA estimates of percentage body fat were higher and that lean mass was lower than the values obtained using BIA, meanwhile sarcopenia is characterized by a higher fat accumulation in the muscle, which might be a reason for inconsistencies of sub-analyses that used body composition. It is worth mentioning that the assessment criteria of sarcopenia were

extremely varied among the included studies, which might confound the association between blood 25(OH)D concentration and sarcopenia. A lower pooled blood 25(OH)D concentration was found in our included studies that evaluated sarcopenia based on muscle mass and strength compared with those that used muscle mass alone. Evaluating sarcopenia by combining muscle mass and strength, which considers both structure and function, was better for predicting disability than muscle mass alone. Additionally, another meta-analysis[17]that included 30 randomized controlled trials shows that vitamin D supplementation had a small but significant positive effect on muscle strength, but had no significant effect on muscle mass. Another study[42] demonstrated that the loss of muscle mass was a major determinant of muscle strength loss during aging; therefore, blood 25(OH)D concentrations may play an important role that bridges loss of muscle mass and decline of muscle strength. Reduced muscle mass may lead to a decline in blood 25(OH)D concentration, which contributes to the development of reduced muscle strength, and this decline in strength is much more rapid than the concomitant loss of muscle mass, demonstrating reduced muscle quality.[42] This result implies that there is a certain link between sarcopenia and vitamin D. The potential physiological mechanisms of the association between blood 25(OH)D and sarcopenia still require more exploration.

Potential biological mechanisms

Several potential biological links might exist between blood 25(OH)D and sarcopenia. First, muscle fibers are associated with blood 25(OH)D concentration. Histological sections of 25(OH)D-deficient individuals show muscle fiber atrophy, enlarged inter fibrillar spaces, fat infiltration, fibrosis and glycogen granules,[43]all of which can lead to a decline in muscle function. Moreover, individuals with low vitamin D demonstrate a preferential atrophy of type 2 muscle fibers, combined with reduced muscle strength and proximal muscle weakness.[43] These changes include denervation of motor units and a net conversion of fast type 2 muscle fibers into slow type 1 fibers with the resulting loss in muscle quality necessary for daily activities.[44] Second, both the decline in blood 25(OH)D and muscle mass loss are age-related changes.[45,46] The latter is closely related to the decline in the expression of vitamin D receptors (VDRs),[47] which may limit the biologically active form of vitamin D. This suggests that vitamin D exerts its principal actions by binding to VDRson muscle tissues.[43,48] Furthermore, decreased vitamin D levels in older persons may lead to a decline in VDR expression because of decreased stimulation, and thus down regulation of receptor

expression.[49-51] Over time, this may impair protein synthesis in muscle cells,[53,54] which also results in a decrease in type 2 fibers and reduces muscle strength,[49,55] eventually leading to sarcopenia. The presence of VDR in skeletal muscle myocytes could demonstrate the relationship between blood 25(OH)D concentration and muscle synthesis and/or altered contractility.[56] In addition to the aging process, a number of studies have shown that physical activity is associated with both sarcopenia and low blood25(OH)D concentrations.[57] Some studies have shown that physical inactivity contributes to sarcopenia development.[58] In middle-aged and older adults, low skeletal muscle mass may contribute to the development of low blood 25(OH)D levels due to reduced physical activity, which promotes a sedentary lifestyle that is linked with reduced sunlight exposure,[59] which is the most important source of vitamin D. Considering most adjusted variables included factors such as age, gender, smoking and alcohol consumption, the association between sarcopenia and blood 25(OH)D concentration could not be explained simply by aging and physical inactivity, suggesting that other specific mechanisms may exist. As mentioned previously, chronic inflammation has been recognized as another key component of sarcopenia,[60,61] while vitamin D also has an active role in reducing inflammation.[62] In summary, exercise and nutritional interventions may be a good choice for treating sarcopenic adults with vitamin D deficiency; however, the details will need to be researched in future high-quality randomized controlled trials.

Directions for further research

Blood 25(OH)D concentrations vary by sex; yet how gender influences the prevalence and effects of blood 25(OH)D concentration on sarcopenia remains an open question. Additionally, the impact of blood 25(OH)D concentration on sarcopenia in middle-aged and older obese adults is unknown. Despite the study population including obese individuals, aging muscles can be infiltrated by fat, and most methods for measuring skeletal muscle mass use DEXA, which does not distinguish between fat and lean muscle, so it is unclear what is being measured to ensure it is "lean muscle mass." As critical confounders, the degree to which skeletal muscle adipose tissue infiltration (myosteatosis) and vitamin D deficiency impact sarcopenia still require further study.

Strengths and limitations

Our study had multiple strengths. First, our analysis focus on the association between blood 25(OH)D concentration and sarcopenia primarily in middle-aged and older adults. It was also

a representative sample in which a decrease in total lean body mass began to appear. Additionally, the pooled effect estimates did not change significantly whether adjusted for potential confounders or not, indicating that our results were reliable. Nevertheless, this meta-analysis also had several limitations. First, we were limited to performing this meta-analysis on observational studies. This meta-analysis mainly came from cross-sectional studies, thus, a directional causality between blood 25(OH)D concentrations and sarcopenia in middle-aged and older adults cannot be ascertained and will require future cohort studies for confirmation. Second, several factors, such as sex, obesity, methods for measuring blood 25(OH)D and sarcopenia, could lead to heterogeneity. Third, the subjects of this meta-analysis were mostly Asian (and most of them Korean), which may lead to potential publication bias; better-designed studies with populations from other countries are needed.

In summary, our meta-analysis demonstrated a significant negative association between blood 25(OH)D concentration and sarcopenia. However, related studies are still deficient. Further well-designed cohort and randomized controlled trials studies are required to confirm the relationship between blood 25(OH)D and sarcopenia.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Table 1. Basic characteristics of studies.

Vitamin D assessment	Sarcopenia assessment	Gender (Female %)	Sample size, n		Baseline age, years		Study design	Country	Authors (Year)
CIA	BIA	M/F (59.1%)	sarcopenia 66	control 66	sarcopenia 71.1±4.4	control 71.0±4.4	matched case-control	United Kingdom	Verlaan et al (2017)
RIA	DEXA	M/F (56.67%)	sarcopenia 746	control 217	sarcopenia 71.54±0.31	control 69.61±0.22	cross-sectional	Korea	Oh et al (2017)
RIA	DEXA	M	sarcopenia 91	control 720	sarcopenia 74.5±5.6	control 71.5±5.0	cross-sectional	Korean	Kim et al (2017)
RIA	DEXA	M/F (50.31%)	sarcopenia 835	control 3096	sarcopenia 57.9±14.6	control 51.3±14.6	cross-sectional	Korean	Hwang et al (2017)
CIA	BIA	M/F 51.54%	sarcopenia 53	control 174	≥65		cross-sectional	Netherlands	Ter et al (2016)
CIA	BIA	M/F (59.1%)	sarcopenia 66	control 66	sarcopenia 71.1±4.4	control 71.0±4.4	matched case-control	United Kingdom	Verlaan et al (2017)
RIA	DEXA	M/F (56.67%)	sarcopenia 746	control 217	sarcopenia 71.54±0.31	control 69.61±0.22	cross-sectional	Korea	Oh et al (2017)
RIA	DEXA	M	sarcopenia 91	control 720	sarcopenia 74.5±5.6	control 71.5±5.0	cross-sectional	Korean	Kim et al (2017)
RIA	DEXA	M/F (50.31%)	sarcopenia 835	control 3096	sarcopenia 57.9±14.6	control 51.3±14.6	cross-sectional	Korean	Hwang et al (2017)
CIA	BIA	M/F 51.54%	sarcopenia 53	control 174	≥65		cross-sectional	Netherlands	Ter et al (2016)
CIA	DEXA	65%	sarcopenia:284	control 1	sarcopenia: 81±7	control: 79±7	cross-sectional	Australia	Huo et al (2016)
HPLC	DEXA	100%	sarcopenia 35	control 70	sarcopenia 70.6 ±5.7	control: 70.6±4.9	matched case-control	Brazil	de Souza Genaro et al (2015)
RIA	DEXA	63.05%	sarcopenia 128	control 324	sarcopenia 60±11.11	control: 51±17.04	baseline data of cohort study	Korea	Hong et al (2014)
N/A	DEXA	58.25%	sarcopenia 4611	control 2597	≥50		cross sectional analysis	Korea	Park S et al (2014)
N/A	DEXA	57.53%	Sarcopenia 1248	control1695	male: sarcopenia 69.7±6.6; control 68.5±6.0 female: sarcopenia 69.4±6.2; non-sarcopenia 69.3±6.6		cross-sectional	Korea	Chung JY et al (2013)
RIA	DEXA	63.49%	Sarcopenia 28	non-sarcopenia 186	Male/Female: sarcopenia: 53.0/50·9±10·7 non-sarcopenia: 49·9±16·9/43·1±14·3		baseline data of cohort study	Korea	Kim TN et al (2013)
RIA	DEXA	56.45%	sarcopenia 246	non-sarcopenia 2923	sarcopenia 68.0±8.9 non-sarcopenia 63.6±9.2		cross-sectional study	Korea	Kim MK et al (2011)

DEXA: Dual energy x-ray absorptiometry; BIA: bioelectric impedance analysis; RIA: radioimmunoassay kit; CIA: chemiluminescense micro-particulate immunoassay; HPLC: high performance liquid chromatography; N/A: not available.

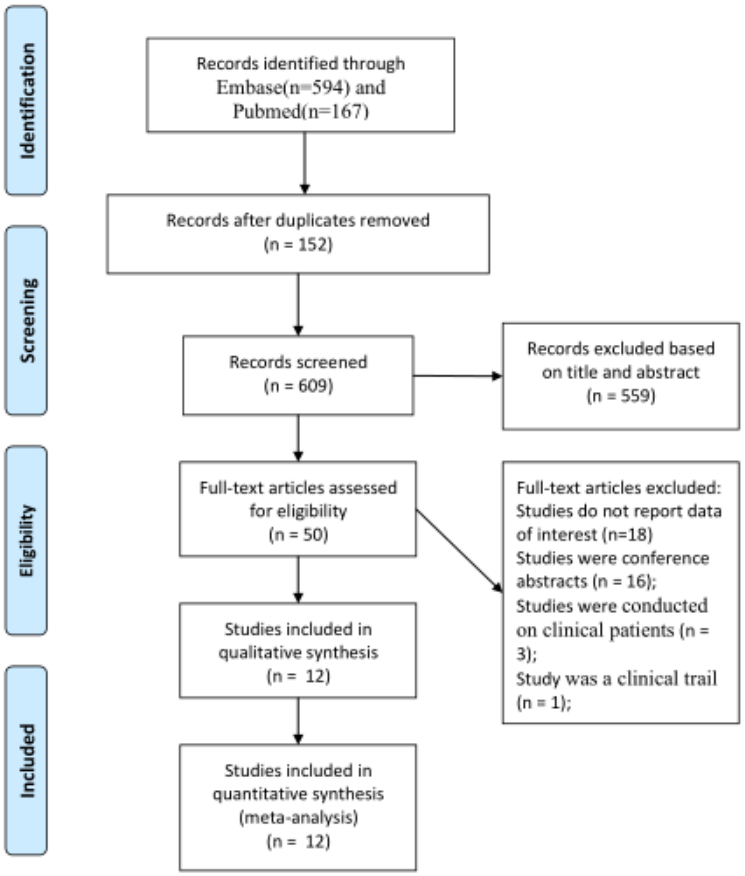

Figure 1. Flow diagram of literature search.

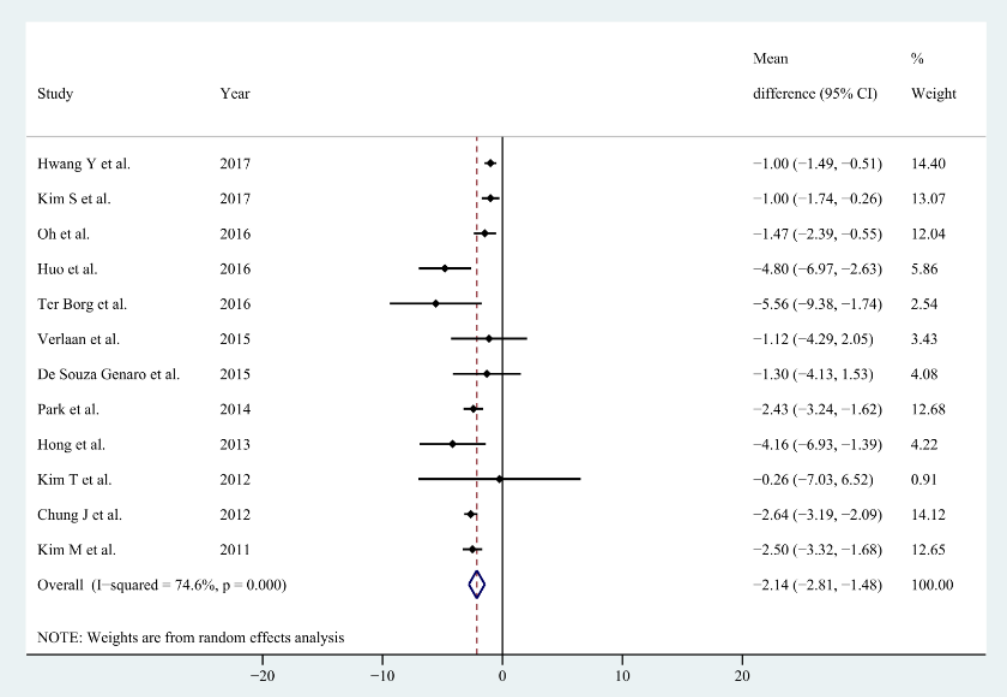

Figure 2. Forest plot of all included studies.

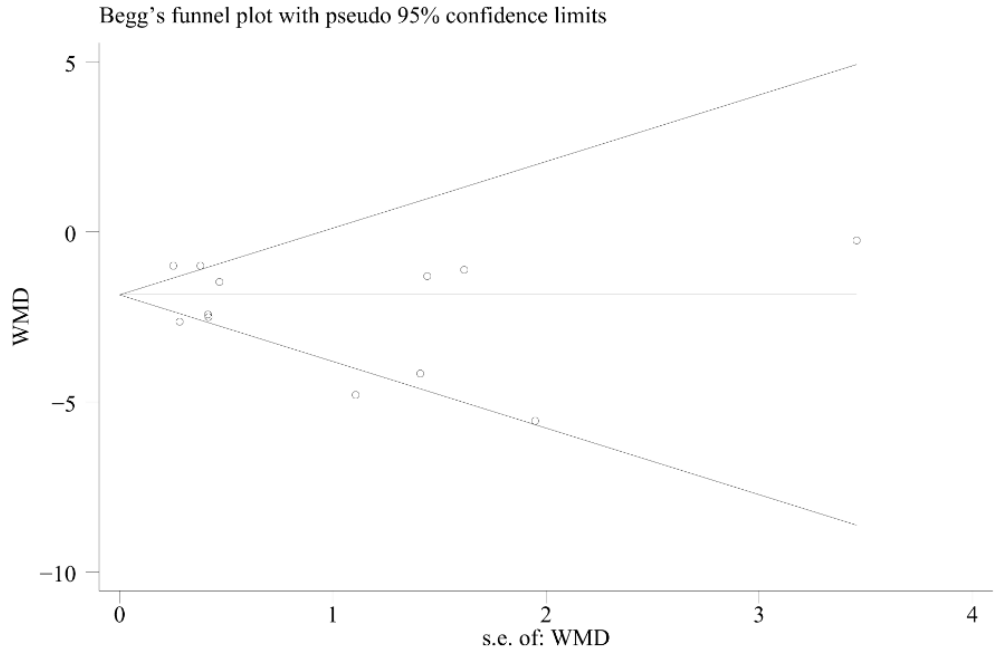

Figure 3. Small-study effect evaluation.

Supplement table 1. Quality assessment by using the Newcastle-Ottawa Scale for the included studies.

Author(Year)	Selection				Comparability	Outcome		Total points
	Representative of patients with sarcopenia	Sample size	Non-respondents	Ascertainment of exposure		Assessment of outcome	Statistical test	
Verlaan et al[23](2017)	+			++	+	+	+	6
Oh et al[35](2017)	+	+	+	+		++	+	7
Kim et al[36](2017)	+		+	+	+	++	+	7
Hwang et al[22](2017)	+	+	+	+		++	+	7
Ter et al[37](2016)			+	++	+	++	+	7
Huo et al[34](2016)		+	+	++	+	++	+	8
De et al[24](2015)				+	+	++	+	5
Hong et al[39](2014)	+	+		+		++	+	6
Park et al[33](2014)	+	+	+	+	+	+	+	7
Kim et al[25](2013)	+			+	+	++	+	6
Chung et al[38](2013)	+	+	+	+	+	+	+	7
Kim et al[5](2011)	+	+	+	+	+	++	+	8

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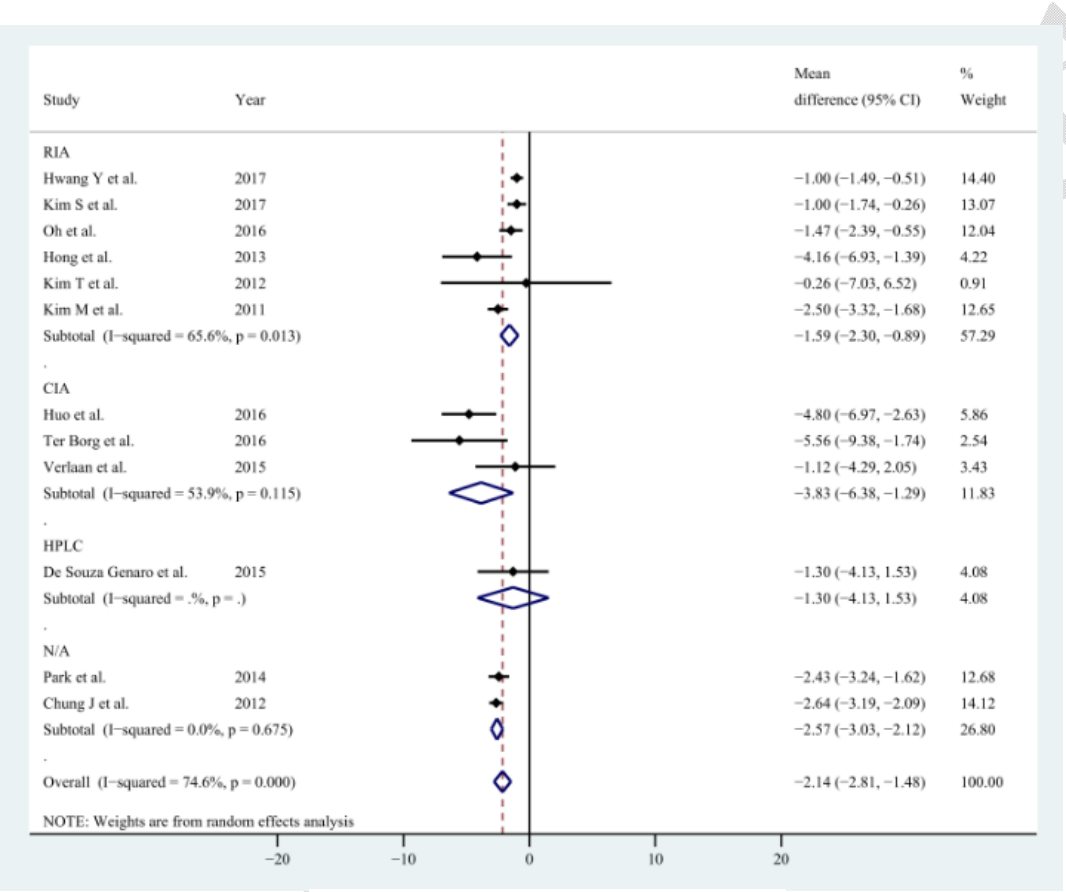
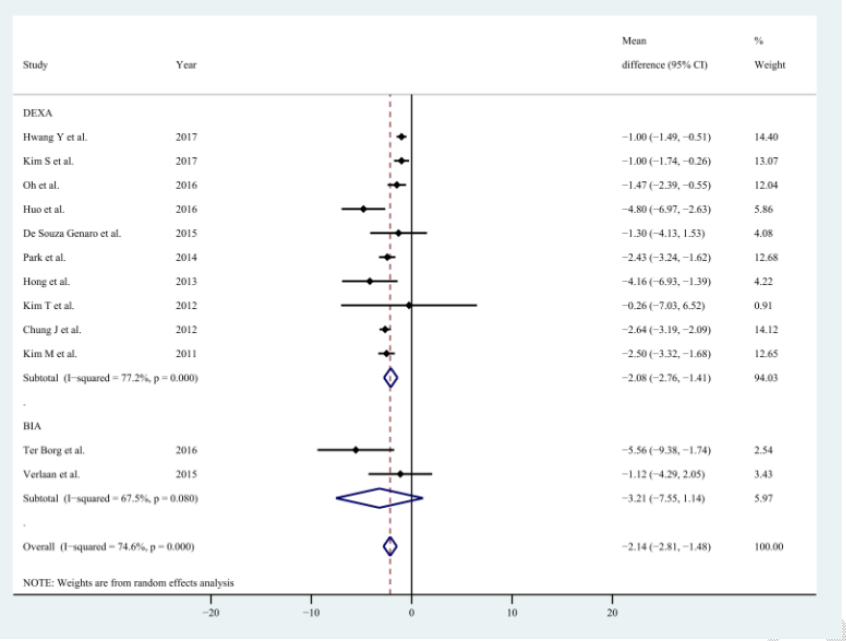
((((((((((avitaminosis) OR Ergocalciferol) OR "vitamin D deficiency") OR "hypovitaminosis D") OR calcitriol) OR cholecalciferol) OR "25-Hydroxyvitamin D 2") OR "25-Hydroxyvitamin D") OR ("Vitamin D"[Mesh] OR "Ergocalciferols"[Mesh]))) AND sarcope*

Supplement figure 1. Search strategy for "vitamin D" and "sarcopenia".



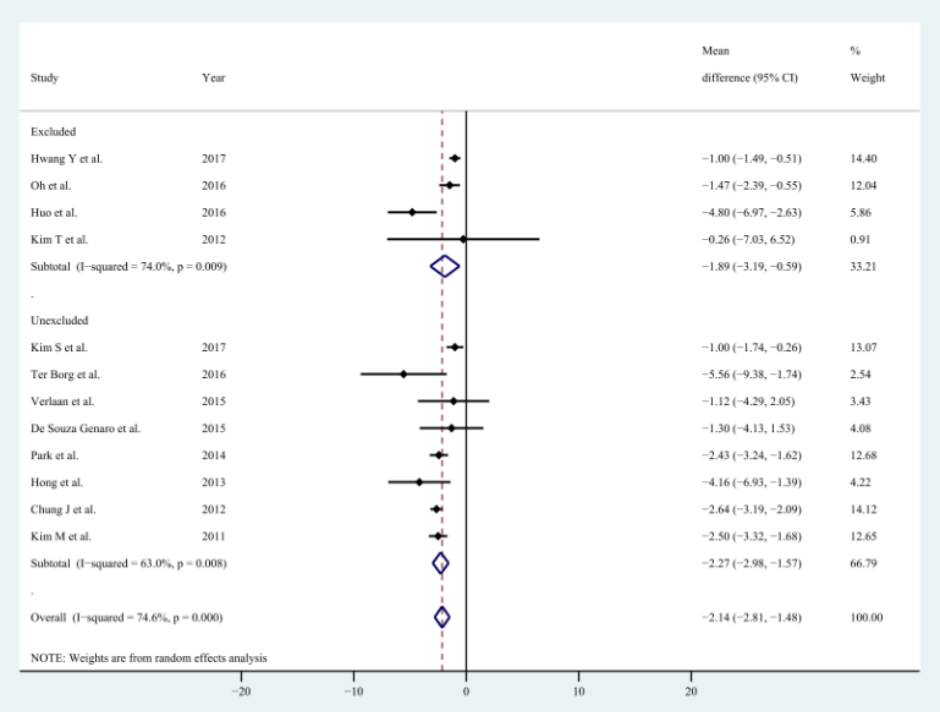
RIA: radioimmunoassay kit; CIA: chemiluminescence micro-particulate immunoassay; 95% CI: 95% confidence interval.

Supplement figure 2. Subgroup analysis of the methods used to detect serum 25(OH)D concentrations.

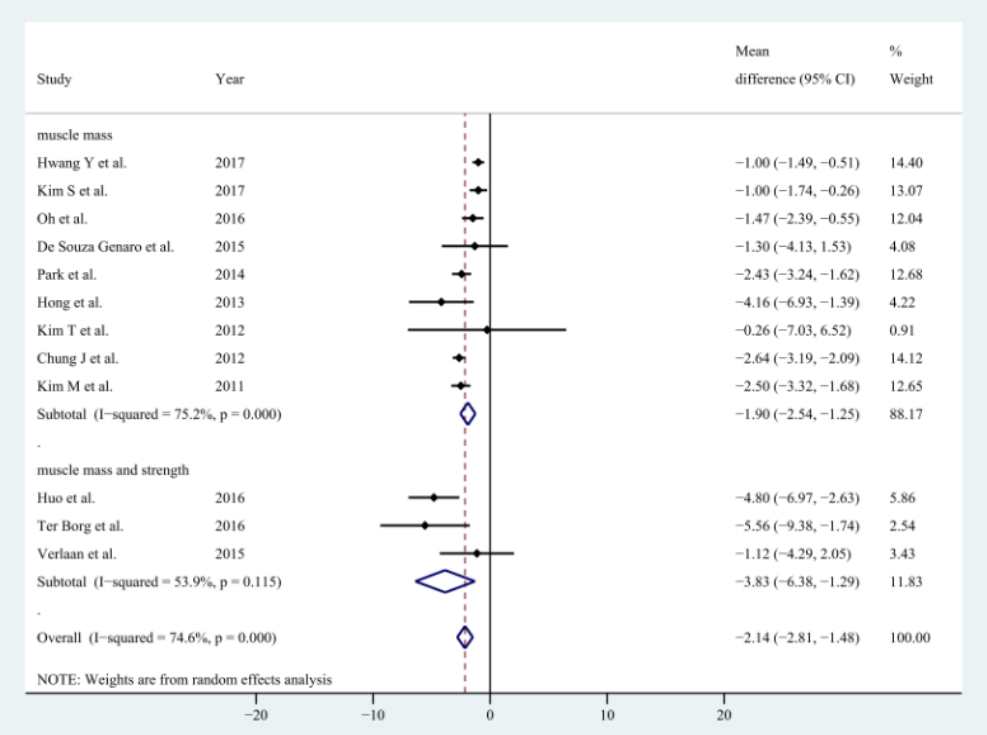


DEXA: dualenergy x-ray absorptiometry; BIA: bioelectric impedance analysis.

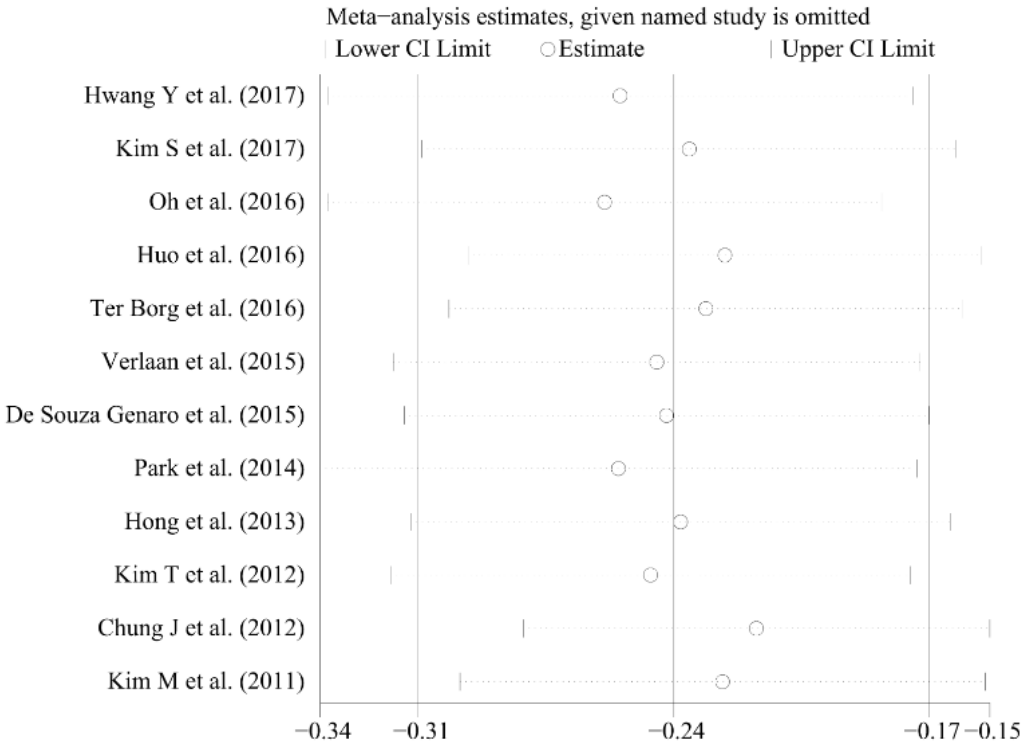
Supplement figure 3. Sub-analysis of the methods used to measure skeletal muscle mass.



Supplement figure 4. Sub-analysis whether studies excluded obese individuals.



Supplement figure 5. Sub-analysis of the assessment criteria of sarcopenia.



Supplement figure 6. One-study-removed sensitivity analysis.