Sarcopenic is associated with hypertension in older adults: a systematic review and meta-analysis

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Research article

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Abstract

Background

Both sarcopenia and handgrip strength have been observed association with hypertension. However, the results in different studies were inconsistent. In the current study, we conducted a systematic review and meta-analysis to reveal the association between sarcopenia, handgrip strength, and hypertension in older adults.

Methods

PubMed, MEDLINE, Cochrane Library, and EMBASE databases were searched from inception to 15 November, 2019for original research studies. The studies that addressed the association between sarcopenia, handgrip strength, and hypertension were included and summarized.

Results

19 studies met the inclusion criteria and a total of 21301 were included in the meta-analysis. Eight eligible studiesreported the odd ratios (ORs) of hypertension and the ORs ranged from 0.41 to 4.38. When pooled the ORs together, the summarized ORs was 1.29 [95% confidence interval (CI) =1.00-1.67]. The summarized ORs for the Asian group 1.50 (95% CI=1.35-1.67) was significantly higher than that of Caucasian group 1.08 (95% CI=0.39-2.97). Eleven studies provided the data on association between handgrip strength and hypertension. The overall ORs and 95% CI was 0.99 (95% CI=0.80-1.23), showing no association.

Conclusion

Sarcopenia was associated with hypertension but no correlation was found between handgrip strength and hypertension in older adults.

Background

In 2050, the number of elderly people of the world population is expected to reach about 30% [1]. The aging process is accompanied with alterations in some physiological systems collaborating to the development of geriatric syndromes and chronic diseases. Hypertension is affecting more than 70% of the older people [2] and show an increased risk of stroke (i.e., hemorrhagic and ischemic) and myocardial infarction [2, 3]. In the past few years, number of studies have indicated that hypertension is associated with elevated cardiovascular risk [4–6].

Recently, data from population studies have demonstratedthat sarcopenia, a neuromuscular disease characterized by a progressive muscular atrophy accompanied by low muscle strength and/or lower muscle limb function, could be a risk factor of hypertension[7–9]. Meanwhile, sarcopenia has been demonstrated have associations with the aging process and can lead to significant morbidity and disability, including loss of independence, poor quality of life, and mortality[10–13]. Sarcopenia had several contributing factors, such as primarily advanced age, immobility, inadequatenutrition, neurodegenerative disease, malignancy, chronicmultiple endocrine disorders, and cardiometabolic disease. The rate of sarcopenia in the elderly is expected to increase in the future [14]and is becoming a major public health problem[15].

The handgrip strength examination is often applied as a sarcopenia filtering technique in clinical setting such measurement is considered inexpensive, simple, easy, and can be done with portable measuring tool. Up to now, the associations between sarcopeniahandgrip strength, and hypertension in older adults were controversial [7–9, 16, 17]and has not been systemic summarized. Given the hypothesis that sarcopenia could be a risk factor of hypertension, a systemic investigation of on the topic would allow early identification one of the hypertension key risk factors in elderly patients undergoing sarcopenia and conduct prevention or treatment strategies associated with specific vulnerability factors.

Methods

Literature Search

The individual and joint keywords of “Handgrip Strength”, “grip strength”, “sarcopenia”, and “hypertension” were conducted for the literature search following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[18]. To

include more potential literatures, we kept the search termsas broadly aspossible to identify the relevant publications. A systematic electronic search of PubMed, MEDLINE, Cochrane Library, and EMBASE databases were performed up to 15 November, 2019. Moreover, the bibliographies of all relevant studies and reviews, and Google Scholar for studies citing relevant studies were also checked and identified.

Eligibility Criteria

The inclusion criteria were as follows: (1) observational studies that addressing the association between sarcopenia and hypertension, or handgrip strength and hypertension; (2) provided clear diagnostic criteria of sarcopenia and hypertension; (3) necessary data extracted from original studies; (4) studies published in English; and (5) only the study provided more detailed information was included if the population was reported in duplicate.

Reviews, case reports, abstracts or posters for conferences, studies focused on animal experiments or experiments *in vitro*, and studies in languages other than English were also excluded.

Data extraction

Two investigators (TTB and FF) extracted the necessary information of included studies using a customized and standardized form independently, and the consensus were reached on all items by the two authors. For each included study, the following information were extracted: the author and year of publication, country, study design, sample size, patient characteristics (e.g., age, sex, and nation), diagnostic criteria of sarcopenia and hypertension, sample size and characteristics for each group, follow-up period, and outcomes of each group.

Quality scoring of studies

Two reviewers (FKL and JMC) assessed the methodological strength of included studies independently in order to aid interpretation the validity of any findings by the Newcastle-Ottawa Scale (NOS), a procedure to independently assess the methodological quality of for meta-analysis of observational studies[19]. Newcastle-Ottawa Scale included three categories three factors: (1) patient selection (three items); (2) comparability of the two study arms (two items); and (3) assessment of the outcomes (two items). The detailed criteria for the three assessments are: if the cases were defined adequately, the representativeness of the cases, the process of selection and definition for controls, comparability of cases and controls based on the design or analysis, ascertainment of exposure, the same method of ascertainment for cases and controls, and nonresponse rate.

Studies were awarded a maximum of one star for each numbered item within the selection and exposure categories and a maximum of two stars can be given for comparability. Studies were graded on an ordinal scoring scale. The score was ranged from 2 stars to 9 stars. Therefore, a scale of 0 to 4 stars was considered to be of poor quality, 5 to 6 stars as moderate quality, and 7-9 stars as high quality.

Statistical analysis

The inverse variance method with random effects was conducted to summarize the dichotomous outcomes, odd ratios (ORs), and 95% confidence intervals (CIs). Stratified analyses were also performed with respect to the characteristics of the study population and outcome. Heterogeneity between included studies was assessed using the I^2 and Q tests. Heterogeneity was defined as low, moderate, and high to I^2 values of 25%, 50%, and 75%, respectively [20]. The Begg rank correlation [21] and Egger weighted regression methods [22] were used to assess the publication bias (P< 0.05 was considered indicative of a statistically significant publication bias). Review Manager(version 5.3, The Cochrane Collaboration, Oxford, UK) was used for generation of forest plot and statistical analyses. The Begg and Egger tests were assessed by STATA 15.0 (Stata Corporation, College Station, TX, USA). A P value of <.05 was considered significant for all analysis.

Results

Study selection

In total, 1221 studies through the initial searches in different datasets as potentially relevant literature reports and 1013 were left after duplicates removed. Majority of potentially relevant literatures were excluded by browsing title or abstract. After retrieving 30 full-length

manuscripts,finally, 12 articles [7-9, 16, 17, 23-29] of 19 studieswere eligible for data extraction and meta-analysis. The flow chart of the studies recruited in the current study can be found in **Figure 1**.

Study characteristics

19 studies met the inclusion criteria and a total of 21301 were included in the study.Eight studies [7-9, 17, 26-28] addressed the association between sarcopenia and hypertension, and 11 studies [16, 23-25, 29] focused on the association between handgrip strength and hypertension.The included studies were published between 2013 and 2019 and the sample size ranged from 72 to 4771. The study participants' characteristics of the included studies can be found in **Supplementary Table 1** and **Supplementary Table 2.**

Six studies were conducted in China[16, 17, 26, 29], two in Republic of Korea [8]and Japan [24], andUnited States [9, 23, 30, 31], one in Turkey[28], Switzerland [25], Italy [7], and Spain [27]. Most of the studies were cross-sectional studies except two cohort studies [7, 9]. The characteristics of the included studies and patients were summarized in **Table 1** and **Table 2**.

Quality assessment of studies

Newcastle-Ottawa Scales for the eligible studies were presented in **Supplementary Table 3** and all included studies were found to exhibit a higher quality. Four studies were evaluated as 6 stars, 6 studies were 7 stars, and 2 studies were 8 stars.

The association between sarcopenia and hypertension

All of theeight eligible studiesreported the ORs of hypertension, and the ORs ranged from 0.41 to 4.38. When pooled the ORs together, the summarized ORs was 1.29 (95% CI=1.00-1.67, P=0.04) with a moderate heterogeneity (I^2 = 74%). The detailed information could be found in **Figure 2 and Supplementary Figure 1**.

To explore the sources of heterogeneity, subgroup analysis was performed by categorizing the studies according to the ethnicity of the participants and the Newcastle-Ottawa Scales than were equal to or more than 7 stars.The Asian group included 4 studies from China and Korea, the Caucasian group included four studies conducted in United States, Italy, Spain, and Turkey.The summarized ORs for the Asian group 1.50 (95% CI=1.35-1.67, P=0.00) was significantly higher than that of Caucasian group1.08 (95% CI=0.39-2.97, P=0.88).The heterogeneities for the two subgroups were significantly decreased to I^2 = 34% and I^2 =40%.When removed the studies that with lower quality (Newcastle-Ottawa Scales<6), the overall OR were 1.53 (95%CI=1.37-1.71, P=0.00) with lower heterogeneity (I^2 =2.62%). More data was presented in **Figure 3** and **Figure 4**.

The association between handgrip strength and hypertension

Eleven studies provided the data on association between handgrip strength and hypertension. Ten studies reported the odds ratios and 95% CI. The overall odds ratios and 95% CIwas 0.99 (95% CI=0.80-1.23, P=0.93) with a higher heterogeneity (I^2 = 76%) and significant public bias (P<0.01). The detailed data can be found in **Figure 5**.

As shown in **Figure 6** and **Figure 7**, to explore the sources of heterogeneity and public bias, the included studies were categorized into two groups by the gender of the participants. For the males, the pooled OR was 1.14 (95%CI=0.91-1.43, P=0.27) with an acceptable heterogeneity (I^2 = 31%) and public bias (P>0.05). The fameless group had a slightly lower OR (0.81, 95%CI=0.52-1.26,P=0.34, I^2 = 45%) without public bias (P>0.05).

Seven studies reported the β value and stand error of the linear regression on hypertension and the pooled β value was -1.57 with an SE equal to 1.03, and the heterogeneity was 99%. As two studies provided the data on different body mass indexes, two more subgroup analysis were done, underweight or normal body mass index group (OR=1.04, 95%CI=0.81-1.33, P=0.77), overweight or obese body mass index group (OR=1.18, 95%CI=0.94-1.41, P=0.16). The data was presented in **Supplementary Figure 3** and **Supplementary Figure 4.**

Publication bias

Most of the analysis except one was found potential publication bias among the included trials according to Begg rank correlation analysis and Egger weighted regression analysis (P value of the analysis was more than 0.05). For the analysis with public bias, when grouped the studies by the gender of the participants, the public bias was disappeared (P>0.05, **Figure 6** and **Figure 7**). The detailed potential publication bias of each analysis can be found in **Supplementary Table 4**

Discussion

To the best of our knowledge, the current meta-analysis is the first study systematic review and meta-analysis summarized the association between sarcopenia, handgrip strength, and hypertension. 19 studies with 21301 participants were included in the study. Eight studies addressed the association between sarcopenia and hypertension and indicated that sarcopenia was a risk factor for the hypertension. 11 studies focused on the association between handgrip strength and hypertension and no association was found by the pooled results.

Being limited by lacking a standard definition for the sarcopenic, the current study proved sarcopenic was a risk factor for hypertension. Several prospective and cross-sectional studies have found the link between sarcopenic and hypertension[8, 17].The prevalence of sarcopenic can vary dramatically depend depending on the definition of sarcopenic obesity. In the current study, Asian Working Group for Sarcopenia (AWGS) criteria and the European Working Group on Sarcopenia in Older People (EWGSOP) criteria were used and the odds ratios were slightly different. This might partly explain Asian groups had a stronger association with hypertension than that ofCaucasian group. Precious study [32] observed that obesity or sarcopenia, or both might be the initiation of sarcopenic. The obesity is caused by the surplus of energy intake relative to energy expenditure. Therefore, sarcopenia may result from a discrepancy in anabolism and catabolism of skeletal muscle protein [33].

In the current study, handgrip strength was negatively associated with hypertension in both men and women. The result was controversial in various studies [24, 25]. The specific biological mechanism linking grip strength and sarcopenia with hypertension is keeping unknown. However, of note, regular exercise, which has been shown consistently in plenty of studies to improve the blood pressure, may improve mitochondrial function and reducing inflammation and result in improving metabolic function and decrease sarcopenia [34].

It is necessary to consider the limitations of the present meta-analysis while interpreting the results. First, the definition of sarcopenia inconsistent in different studies and the variations in assessment of sarcopenia across studies could have caused methodological limitations and compromised the results. Second, the number of the included studies was limited and majority of them were from Asian countries. As the sarcopenia might be affected by the economic level, medical level, and genetic factors, the associations betweensarcopenia, handgrip strength, and hypertension in different countries could be slightly different. Therefore, the result in the current can only partly annotate the associations. Three, almost all of studies addressing the sarcopenia did not provided the specific sarcopenia by gender and age. Due to the limited sample size of each studies, we cannot perform more subgroups or sensitivity analyses.Therefore, due to the limited information, we cannot perform more subgroups or sensitivity analyses, especially on the sensitivity analyses on age and sex. Four, potential language bias might exist because our literature searches only considered articles published in English.

Conclusions

In conclusion, our meta-analysis provided pooled results based 19 studies from eight different regions or countries, and summarized a large data set of 21301 participants. The current study highlighted that sarcopenia was associated with hypertension. In the future, by stratifying patients, efforts must be made to prevent and treat sarcopenia in the older population, which would also decrease the risk of hypertension and the comorbidities of hypertension. At the same time, limited by smaller number of included studies, in the future, more studies with lager sample size from different counties are needed to support the conclusion.

Abbreviations

ORs: odd ratios;

CI: confidence interval;

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses;

NOS: Newcastle-Ottawa Scale;

AWGS: Asian Working Group for Sarcopenia;

EWGSOP: European Working Group on Sarcopenia in Older People.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Study concept: JMC and TTB. Study design: JMC, TTB and FF. Data acquisition: TTB, FF and FKL. Quality control of data and algorithms: JMC and FKL. Data analysis and interpretation: TTB, YR and JAH. Manuscript preparation: TTB and FF. Manuscript editing: TTB and FKL. Manuscript review: JMC and JAH. All authors (TTB, FF, FKL, YR, JAH, JMC) have read and approved the final version of the manuscript.

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Tables

Table 1. Characteristics of the included studies that focused on sarcopenia

Study included	NO. of sarcopenia patients		NO. of HTN patients		Means±SD (mmHg)		Taking antihypertensive drugs (%)	Odd ratios (95% CI)
	sarcopenia (-)	sarcopenia (+)	sarcopenia (-)	sarcopenia (+)	SBP	DBP		
Landi, et.al., 2013	154	43	126	28	NA	NA	NA	NA
Han, et.al., 2014 [a]	2326	894	1156	544	126.40±0.50/ 129.30±0.90	74.30±0.30/ 75.10±0.50	33.00±1.30/ 45.30±1.90	1.50 (1.23-1.84)
Han, et.al., 2014 [b]	594	1032	393	771	129.90±0.80/ 131.20±0.70	76.90±0.50/ 77.60±.40	52.00±2.40/ 62.30±1.90	NA
Koo, et.al., 2016	239	70	98	41	98.10 ± 14.8/ 127.9 ± 17.4	77.8 ± 11.0/77.2 ± 11.5	NA	NA
Can, et.al., 2016	36	36	4	12	NA	NA	NA	NA
Han, et.al., 2017	634	77	267	36	NA	NA	NA	NA
Montes, et.al., 2017	148	52	116	33	NA	NA	NA	NA
Xu, et.al., 2019	4459	312	NA	NA	NA	NA	NA	1.44 (1.16–1.78) 0.001

)breviations: HTN, Hypertension; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; , confidence interval; NA, not available.

participants whose BMI was less than 25.00 kg/m^2.

participants whose BMI was equal or more than 25.00 kg/m^2.

Table 2. Characteristics of the included studies that focused on handgrip strength

Study included	Sample size	Handgrip strength (kg)	Handgrip strength/body weight ratio	odd ratios (95% CI) for High blood pressure	β of linear regression (stand error)
Mainous, et.al., 2015	1469	60.8±1.61 [a]/71.5±0.84 [b]	NA	NA	-4.93 (0.03)
Kawamoto, et.al., 2016 [a]	742	33.40±7.50	0.55±0.11	0.78 (0.66, 0.94)	NA
Kawamoto, et.al., 2016[b]	937	21.30±4.10	0.43±0.09	0.72 (0.62, 0.83)	NA
Ji, et.al., 2018 [a]	2184	41.50 ± 8.80	NA	1.23 (1.04, 1.46)	0.21 (0.09)
Ji, et.al., 2018 [b]	2413	26.70 ± 5.70	NA	1.01 (0.80, 1.27)	0.01 (0.12)
Ji, et.al., 2018 [c]	563	NA	NA	1.14 (0.83, 1.55)	0.13 (0.16)
Ji, et.al., 2018 [d]	1292	NA	NA	1.29 (1.04, 1.59)	0.030 (0.17)
Ji, et.al., 2018 d [e]	636	NA	NA	0.88 (0.58, 1.33)	-0.13 (0.21)
Ji, et.al., 2018 d [f]	1323	NA	NA	1.02 (0.76, 1.38)	0.02 (0.15)
Zhang, et.al., 2019 [a]	515	35.94±19.72	NA	0.55 (0.28, 1.08)	NA
Zhang, et.al., 2019 [b]	637	14.45±10.41	NA	0.19 (0.07, 0.55)	NA

Abbreviations: CI, confidence interval; NA, not available.

[a], males.

[b], females.

[c], Underweight or normal body mass index of males.

[d], Underweight or normal body mass index of females.

[e], Underweight or normal body mass index of males.

[f], Overweight or obese body mass index of females.

Figures

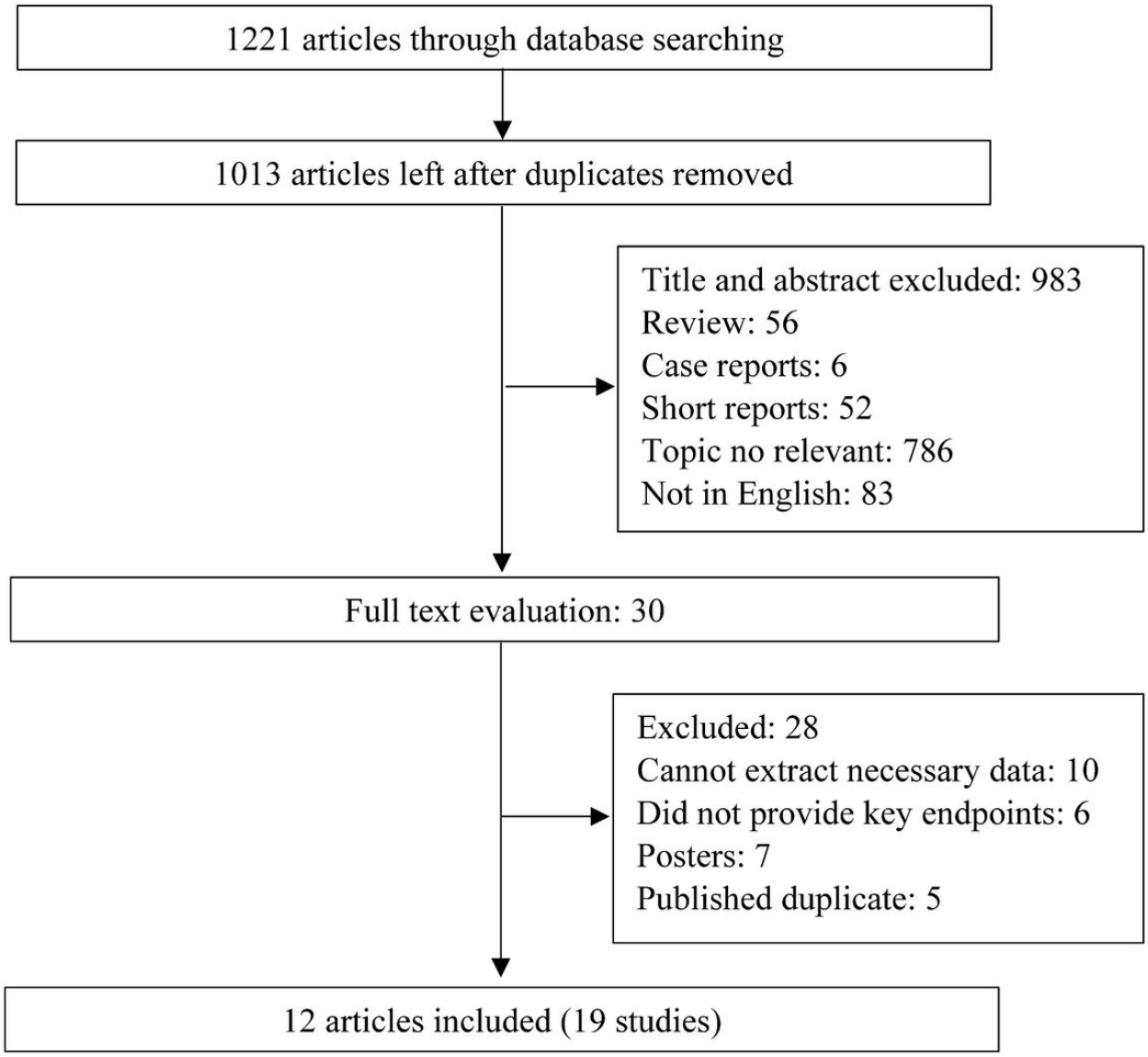


Figure 1

Flow chart of the study selection.

Study name	OR	95% CI		Z-value	P-value
Landi, et.al., 2013	0.410	0.195	0.860	-2.359	0.018
Han, et.al., 2014 a	1.570	1.340	1.840	5.576	0.000
Han, et.al., 2014 b	1.510	1.211	1.882	3.666	0.000
Koo, et.al., 2016	2.030	1.180	3.491	2.559	0.010
Can, et.al., 2016	4.380	1.261	15.213	2.325	0.020
Han, et.al., 2017	1.210	0.752	1.946	0.786	0.432
Montes, et.al., 2017	0.480	0.241	0.955	-2.091	0.037
Xu, et.al., 2019	1.440	1.162	1.784	3.338	0.001
Overall odds ratio	1.294	1.004	1.669	1.991	0.046

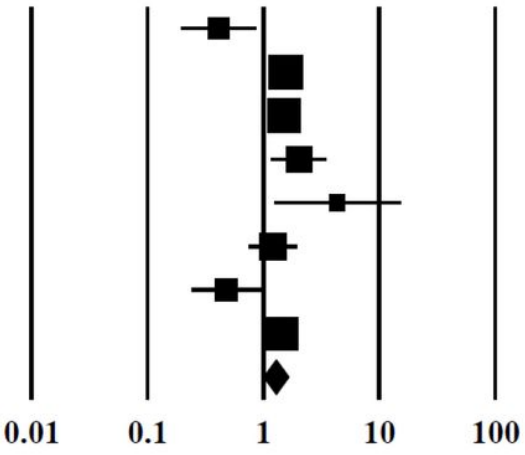
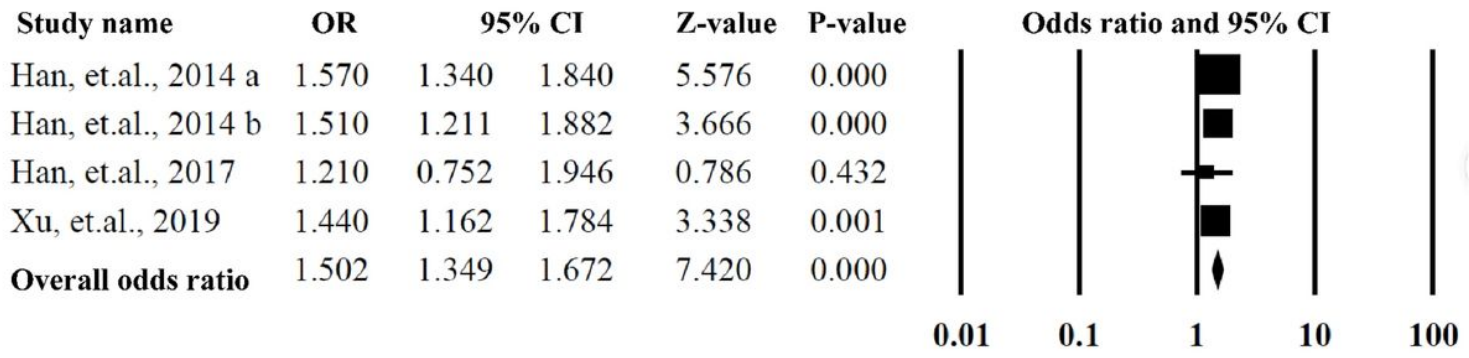
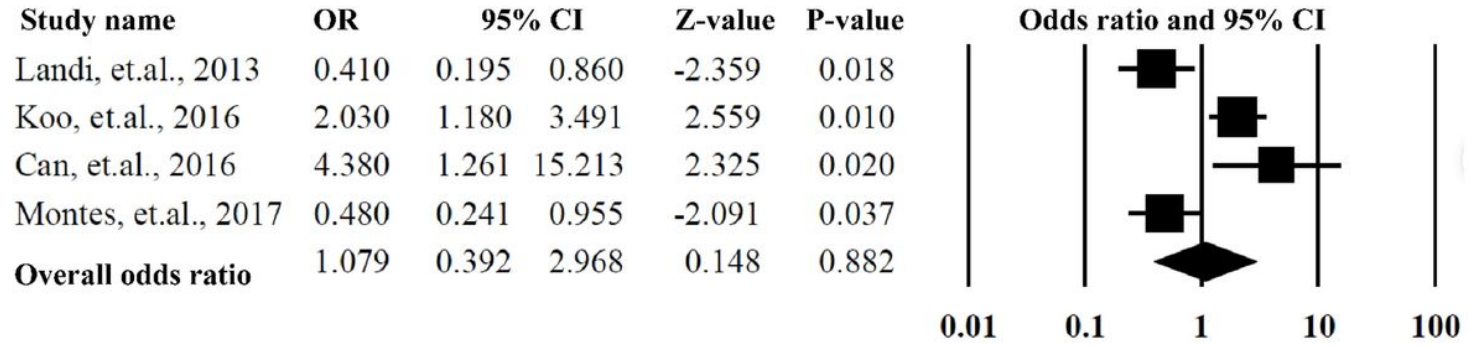


Figure 2

Summarized overall odds ratio of hypertension



a. Summarized overall odds ratio of hypertension of the studies from Asia



b. Summarized overall odds ratio of hypertension of the studies from Europe

Figure 3

Summarized overall odds ratio of hypertension of the studies grouped by ethnicity of the participants

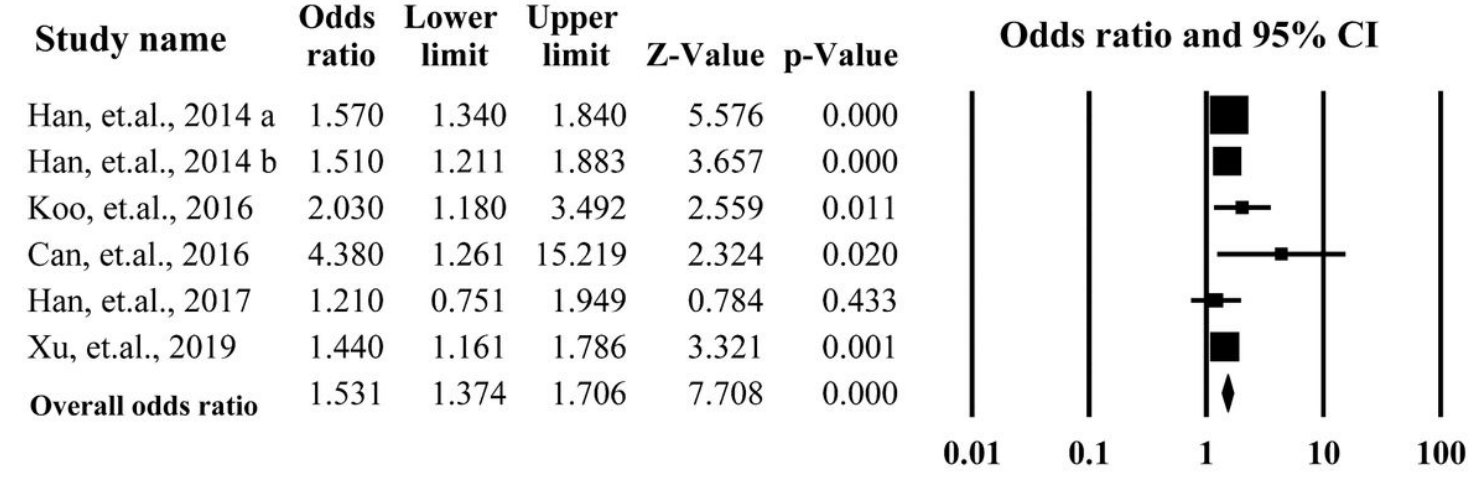


Figure 4

Summarized overall odds ratio of hypertension of the studies that with equal to or more than 7 stars of the Newcastle-Ottawa Scales

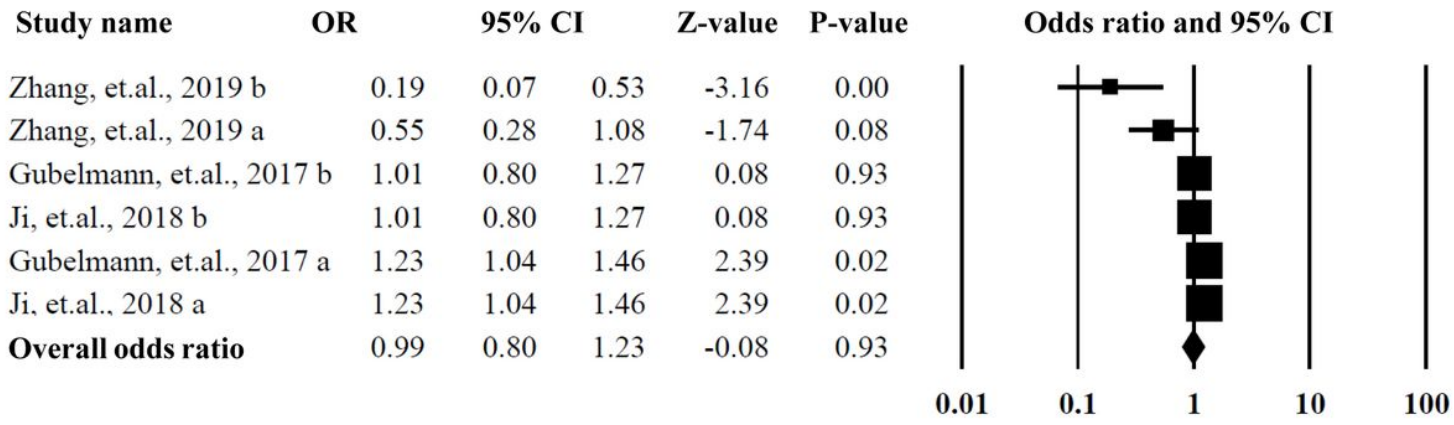


Figure 5

Summarized overall odds ratio of handgrip strength

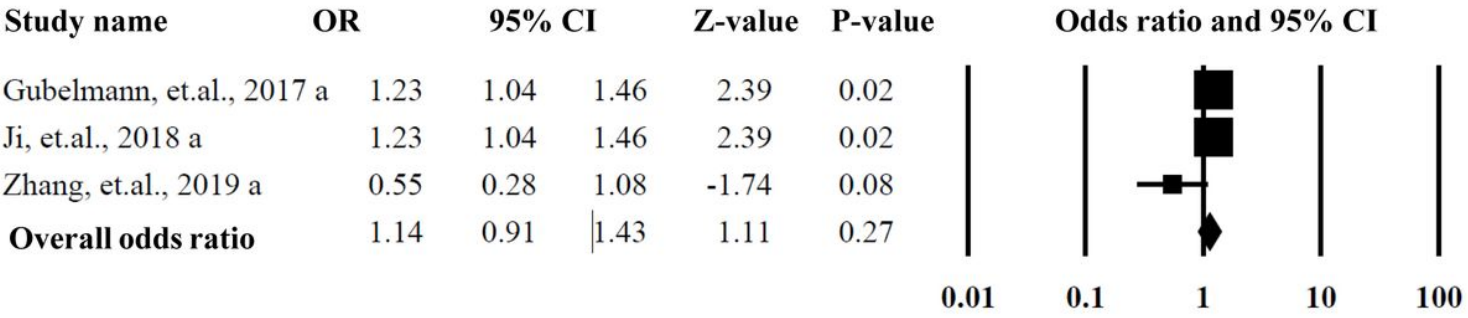


Figure 6

Summarized overall odds ratio of handgrip strength based on male participants

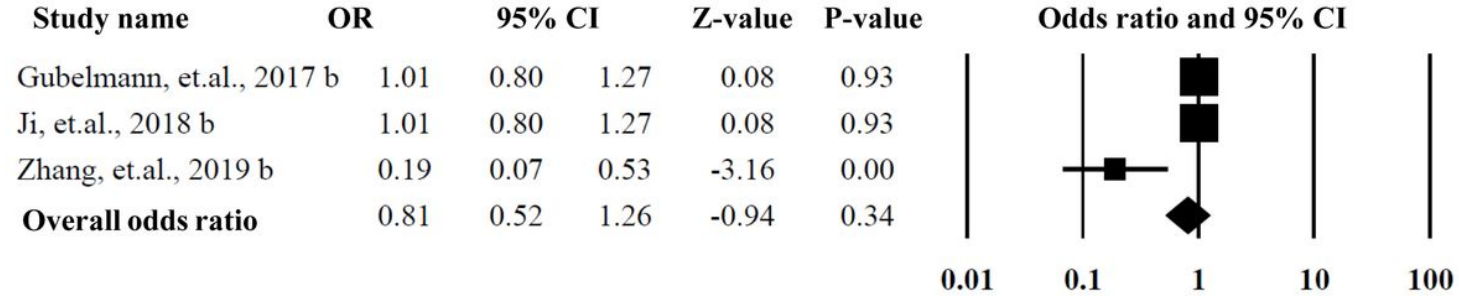


Figure 7

Summarized overall odds ratio of handgrip strength based on female participants

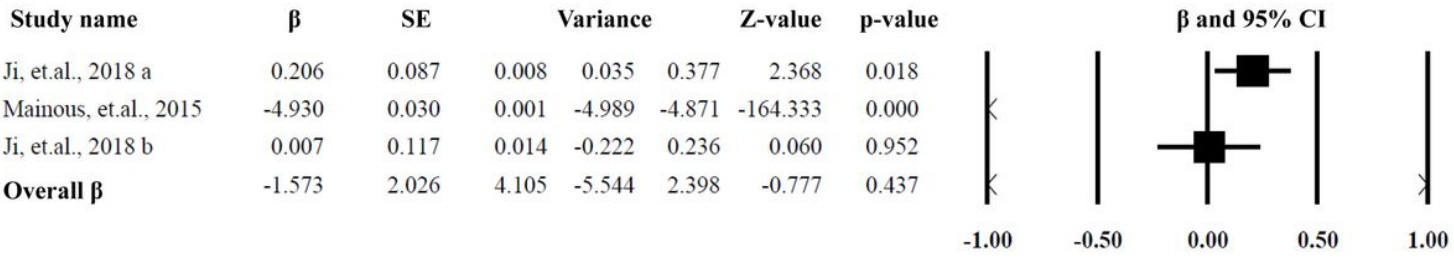


Figure 8

Summarized overall β for the linear regression and stand error

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile2.docx
- Additionalfile1.docx