Association between muscular strength and depressive symptoms

A narrative review

Konstantinos Volaklis · Temur Mamadjanov · Christa Meisinger · Jacob Linseisen

Summary There is increasing evidence for an association between low muscular strength and depressive symptoms. In this review the existing literature on the association between muscular strength and depression particularly in older people as reported in epidemiological studies is summarized. From the literature search, conducted in PubMed (January 1980–May 2018), 17 papers (8 cross-sectional and 9 longitudinal studies) were selected. All cross-sectional studies reported significantly lower odds of having depressive symptoms with increased levels of muscular strength and this association persisted even after adjusting for several confounders including the level of physical activity. The majority of the longitudinal studies also reported that low muscular strength was independently associated with a higher risk of developing depression but more studies are needed to confirm this evidence. Furthermore, future investigations are needed to explore the exact mechanisms of muscular strength in relation to depression. Low muscular strength is a modifiable factor for depression, which is of great public health interest.

Keywords Muscular strength · Depression · Public health · Epidemiological studies · Risk

Assoziation zwischen Muskelkraft und depressiven Symptomen
Ein narrativer Review

Zusammenfassung Es gibt zunehmend wissenschaftliche Hinweise auf einen Zusammenhang zwischen niedriger Muskelkraft und depressiven Symptomen. Ziel dieser Übersichtsarbeit ist eine Zusammenfassung der Daten zum Zusammenhang von Muskelkraft und Depressionsrisiko vor allem bei älteren Menschen. Die Literaturrecherche, die in PubMed durchgeführt wurde (Januar 1980 bis Mai 2018), erbrachte 17 Veröffentlichungen (8 Quer- und 9 Längsschnittstudien). In allen Querschnittstudien wurde eine signifikant geringere Wahrscheinlichkeit für depressive Symptome mit erhöhter Muskelkraft beobachtet, und diese Assoziation blieb auch nach Adjustierung für verschiedene Störfaktoren, einschließlich der körperlichen Aktivität, bestehen. In der Mehrzahl der Längsschnittstudien wurde berichtet, dass eine niedrige Muskelkraft mit einem höheren Risiko für die Entstehung einer Depression einhergeht, jedoch sind weitere Studien erforderlich, um diese Evidenz weiter zu belegen. Zusammenfassend lässt sich ableiten, dass Muskelkraft als ein modifizierbarer Risikofaktor im Zusammenhang mit der Entstehung von Depressionen zu verstehen ist, was von großem Interesse für die öffentliche Gesundheit ist. Zukünftige Studien sind erforderlich, um die genauen Mechanismen der Muskelkraft in Bezug auf Depressionen zu untersuchen.

Schlüsselwörter Muskelkraft · Depression · Öffentliche Gesundheit · Epidemiologische Studien · Risiko

K. Volaklis, Ph.D. · T. Mamadjanov · C. Meisinger · J. Linseisen
Lehrstuhl für Epidemiologie, LMU München am UNIKA-T, Neusaesser Str. 47, 86156 Augsburg, Germany
k.volaklis@unika-t.de

Introduction

Depression is an important public health problem affecting approximately 350 million people of all ages worldwide and is associated with reduced quality of life, decreased cognitive functioning, higher risk of cardiovascular disease and increased mortality [1–3]. The global prevalence of depression has been increasing in the last decades and varies significantly between published studies according to among others country, age, gender, health status and living setting [3]. The World Health Organization predicted that by the year 2020 depression will rank second in global disease burdens worldwide while in Europe each year approximately 7% of the population suffer from a major depression [4].

Older age, physical comorbidities, low income, cognitive decline, stressful life events and genetic predisposition have been identified as important risk factors for the occurrence of depression [5, 6]. On the other hand, it has been recognized that increased levels of cardiorespiratory fitness and regularly performed aerobic exercises have a preventive effect regarding the development of depressive symptoms later in life [7–10]. Another important component of physical fitness is muscular strength, which plays an independent role in the prevention of many chronic diseases, such as cardiovascular diseases and type 2 diabetes [11–14]. In addition, studies among older people have further suggested that there is a strong association between low muscle strength and both cognitive impairment and the risk of neurodegenerative diseases, such as dementia, Alzheimer's disease and Parkinson's disease [15–18]. More recently, there is a growing body of evidence to also suggest that muscular weakness is strongly and independently related to the development of depressive symptoms. This association seems to be irrespective of age and other potential confounders including the level of physical activity. According to the recent literature the assessment of handgrip strength in the clinical practice could be a useful instrument to identify those individuals at risk for depression. All the above are very important given that the early identification of objective predictors of future depression is essential not only for the individual patient but also for the healthcare system.

In this review, the association between muscular strength and depression particularly in older people, as reported in epidemiological studies (both cross-sectional and longitudinal investigations) will be presented, in order to provide recent scientific evidence. The clinical implications of the existing studies are discussed and some possible explanations on the association between muscular strength and depression are provided.

Methods

An electronic literature search was carried out using PubMed from January 1980 to May 2018. Key words used for the electronic search were "handgrip strength", "depression or depressive symptoms" and "elderly". The following inclusion criteria were used: (a) muscle strength was assessed by handgrip strength measurement (handgrip dynamometry), (b) adult participants of any gender in a community or clinical setting, (c) depressive symptoms as one of the primary outcomes, (d) studies involving healthy participants or participants with current depressive disorders and (e) English as the publication language. Although the primary focus was to examine the older population age was not used as an inclusion or exclusion criterion. Case reports, letters to the editor, conference paper, dissertations, commentaries and papers not written in English were excluded.

For the quality assessment and risk of bias of the included studies the Newcastle Ottawa Scale (NOS) was used, which is one of the most frequently used tools worldwide. The NOS evaluates three quality parameters (selection, comparability and outcome) divided across eight specific items. The maximum score for cross-sectional studies is 10 and for longitudinal studies 9 and studies having less than 5 points are identified as representing at high risk of bias [19].

Results

The electronic search identified 222 articles and the titles and abstracts were reviewed to find out whether they met the stated inclusion criteria. The remaining 17 eligible full text articles were analyzed and included in this review. Of the articles four reported data on participants younger than 50 years (these studies were also included due to the limited scientific data on this field). Quality assessment revealed that all studies included in the review had scores higher than 5, so they were considered as moderate or good quality (Tables 1 and 2). More specifically, 6 of the cross-sectional studies reached a score of 8/10 and 2 reached score 7/10. From the longitudinal studies 5 reached a score of 8/9, 2 reached a score of 7/9, 1 reached a score of 6/9 and 1 reached a score of 9/9. Of the studies eight examined the cross-sectional relationship between handgrip strength and depressive symptoms, nine articles assessed prospective association and four focused on both cross-sectional and longitudinal relationships. The majority of the studies focused on individuals aged >50 years, some of them also included younger individuals.

A number of different dynamometers were used to measure handgrip strength. The majority of studies used a Jamar Hand Dynamometer [20, 23, 26, 28, 30], others used dynamometers from Takei Scientific Instruments [22, 27], Newtest [21], TTM-YD [32], Stoelting [29] and Practical Metrology and Fabrication Enterprises [24, 25]. The hand that was used to measure handgrip strength varied as well. Generally, the dominant hand was used and in some studies both hands were used for measurement. In one study the hand used for the measurement was not specified. Either the best value out of multiple measurements or the mean results of the measurements were reported. In the studies two body positions were used for the measurement: (i) sitting in a straight-backed chair with elbows flexed at 90° [20, 27, 30] and (ii) standing with the forearm held parallel to the body [21, 22, 24, 26]

Table 1 Results of the Newcastle-Ottawa scale adapted for cross-sectional studies

Reference	Selection				Score	Comparability	Score	Outcome		Score	Total Score
	Representativeness of the sample	Sample size	Non-respondents	Ascertainment of exposure		Based on design and analysis		Assessment of outcome	Statistical test		
Taekema et al. 2010 [26]	–	+	–	++	3/5	+	1/2	++	+	3/3	7/10
van Miligen et al. 2012 [20]	+	+	–	++	4/5	+	1/2	++	+	3/3	8/10
Suija et al. 2013 [21]	+	+	–	++	4/5	+	1/2	++	+	3/3	8/10
Fukumori et al. 2015 [22]	+	+	–	++	4/5	+	1/2	++	+	3/3	8/10
Gariballa and Alessa 2018 [25]	–	+	–	++	3/5	+	1/2	++	+	3/3	7/10
Stessman et al. 2017 [27]	+	+	–	++	4/5	+	1/2	++	+	3/3	8/10
McDowell et al. 2018 [24]	+	+	–	++	4/5	+	1/2	++	+	3/3	8/10

++ quality criterion completely satisfied; + quality criterion satisfied; – quality criterion not satisfied or insufficient information to adjudicate as satisfied

and four studies failed to report the position used for handgrip measurement [23, 25, 28, 29].

As outcome measurement, different types of depression assessment methods were used. The Geriatric Depression Scale (GDS) was used as a screening instrument for depressive symptoms in most of the identified studies whereas the Hospital Anxiety and Depression Scale (HADS), the Hopkins' Symptom Checklist-25 (HSCL-25), the 5-item version of the Mental Health Inventory (MHI-5), the Self-reported 8-item Centre of Epidemiological Studies Depression Scale, the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatry Association (DSM-IV), the Brief Symptom Inventory and the EURO-D scale were also used (Tables 3 and 4).

Evidence from cross-sectional studies

Van Milligen et al. [20] were among the first who examined the association between physical functioning and the presence of depressive symptoms in adults using handgrip strength measurements in a large cohort study. They analyzed data from the Netherlands Study of Depression and Anxiety (NESDA), which included 1629 subjects (1086 women and 543 men, aged 41.1 ± 13.1 years) with depressive and/or anxiety disorders and 629 healthy controls. Women with depressive disorders had significantly poorer muscular strength compared to healthy controls, especially those with a late age of depression onset (≥40 years) after adjustment for several covariates (age, education, BMI, lung medication, chronic diseases, smoking and physical activity) but no such association was found in men.

On the other hand, Suija et al. [21] reported a positive association between handgrip strength and depressive symptoms in men only. The study included 5497 males and females, participating in the northern Finland birth cohort, who completed fitness tests at the age of 31 years and filled in a questionnaire about depressive symptoms (Hopkins' Symptom Checklist-25) and physical activity. After adjustment for several covariates, the odds ratio (OR) of having depressive symptoms in the lowest quintile of handgrip strength was 1.64 (95% confidence interval, CI 1.11–2.42) in males and 0.86 (95% CI 0.63–1.18) in females.

In a large population-based Japanese study, Fukumori et al. [22] analyzed data from 4314 women and men (aged 40–79 years). Using national representative data classified by age and gender, the authors showed that subjects with lower handgrip strength (per 1SD decrease) had higher odds (by 15%) of having depressive symptoms even after adjustment for several cofactors in the regression analysis.

Gale et al. [23] used data from five different studies ($n = 5570$) to examine the relationship between muscular strength and presence of depression. The overall odds to be depressive was markedly lower in people with better physical performance, as assessed by grip strength (OR: 0.50 per 1 SD increase in grip strength). This association changed little after adjustment for potential confounding or mediating variables.

Recently, McDowell et al. [24] examined the association between handgrip strength and depression in the Irish Longitudinal Study on Ageing (4505 community dwelling adults, 56.5% females, aged ≥50 years). In the total population, the highest tertile of grip strength was significantly associated with a 51% and 31% lower odds of having depressive symptoms for men and women, respectively, after adjustment for age, waist circumference, social class, smoking and health status. Interestingly, Gariballa and Alessa [25] investigated the association between poor muscle strength and depression in older adults ($n = 432$) during acute illness. Compared to those with normal

Table 2 Results of the Newcastle-Ottawa scale for longitudinal studies

Reference	Selection					Comparability			Outcome				
	Representative of cohort	Selection of non-exposed cohort	Ascertainment of HGS	Outcome of interest was not present at baseline	Score	Controls for sex	Controls for age and BMI	Score	Assessment of outcome	Follow-up for outcome to occur	Lost-to-follow-up	Score	Total Score
Taekema et al. 2010 [26]	+	+	+	–	3/4	+	+	2/2	+	+	–	2/3	7/9
Van Milligen et al. 2012 [20]	+	+	+	+	4/4	+	+	2/2	+	–	+	2/3	8/9
Fukumori et al. 2015 [22]	+	+	+	+	4/4	+	+	2/2	+	–	+	2/3	8/9
Hamer et al. 2015 [29]	+	+	+	+	4/4	+	+	2/2	–	+	+	2/3	8/9
Van Milligen et al. 2017 [30]	+	+	+	–	3/4	+	+	2/2	+	–	+	2/3	7/9
Gariballa and Alessa 2018 [25]	–	+	+	–	2/4	+	+	2/2	+	–	+	2/3	6/9
Stessman et al. 2017 [27]	+	+	+	+	4/4	+	+	2/2	+	+	–	2/3	8/9
Veronese et al. 2017 [28]	+	+	+	+	4/4	+	+	2/2	+	+	+	3/3	9/9
McDowell et al. 2018 [24]	+	+	+	+	4/4	+	+	2/2	+	–	+	2/3	8/9

++ quality criterion completely satisfied; + quality criterion satisfied; – quality criterion not satisfied or insufficient information to adjudicate as satisfied

muscle strength, hospitalized patients with low muscle strength showed higher depressive symptoms using the 15-item geriatric depression questionnaire at admission.

It is important to note that poor handgrip strength has also been associated with depressive symptoms in the oldest old populations. Taekama et al. [26] in the Leiden 85-plus study reported that lower handgrip strength was significantly correlated with higher depression score among 555 individuals aged 85 years and over, whereas Stessmann et al. [27] also found an elevated risk of having depressive symptoms at age 78 years and 90 years (OR: 2.38 and 2.04, respectively) for those in the lowest tertile of handgrip test.

Of the existing studies discussed above, all reported significantly lower odds of having depressive symptoms with increasing levels of muscular strength (Table 3). This association persisted even after adjusting for several confounders such as age, gender, BMI, education, smoking, alcohol intake, chronic diseases or even the level of physical activity; however, the conclusion drawn from the above studies should be treated with caution due to some limitations. The fact that several different instruments were used for the assessment of depressive symptoms makes a comparison between studies difficult. Furthermore, the self-reported nature of these questionnaires may be subject to bias and limited specificity (misdiagnosis of depression). Since significant interactions occurred between race/ethnicity in relation to prevalence of dysthymic disorders it is important to examine how these factors may affect the association between muscle strength and depression. Only one study reported data from hospitalized patients and given that older adults in institutions suffer from higher rates of depression (and probably have also lower levels of muscle strength), further studies in these populations are needed to fully confirm the strong association reported in community-dwelling older adults. Finally, due to the cross-sectional design of the reported studies, no causal relationships could be established; thus, this study also searched for the association between muscular strength and depression risk, as reported in prospective studies.

Evidence from longitudinal studies

Fukumori et al. [22] prospectively investigated the association between muscular strength and the risk of depressive symptoms among individuals aged 40–79 years after 1 year of follow-up. They reported higher odds of developing depressive symptoms by 13% for the participants within the lowest quartile of handgrip strength after multivariable adjustment. In another study Veronese et al. [28] tested the hypothesis if objective physical performance can predict the incidence of depression among older adults ($n = 970$) in the Progetto Veneto Anziani study. During the 4 years of follow-up the participants within the low-

Table 3 Cross-sectional association between muscular strength and depression

Reference	Sample characteristics	Depression assessment method	Adjustments for cofactors	Statistical analysis	Main findings
Taekema et al. 2010 [26]	555 subjects: 361 (65%) women, 194 (35%) men. Age: 85 years	GDS-15	Gender, height, weight, income	Linear regression analysis	β: −0.008 (SE: 0.02) per 1 kg change in handgrip strength, $p<0.001$
van Milligen et al. 2012 [20]	1629 subjects with depressive and/or anxiety disorder: 1086 (67%) women, 543 (33%) men. 629 healthy controls. Age: 41.1 ± 13.1 years	CIDI	Age, sex, years of education, BMI, somatic diseases, lung medication, physical activity, and smoking	Linear regression analysis	Only in women, those with a depressive and/or anxiety disorders had lower handgrip strength
Suija et al. 2013 [21]	5497 subjects: 51% women, 49% men. Age: 31 years	HSCL-25	Alcohol intake, smoking, obesity, somatic diseases	Logistic regression analysis	OR: 1.64 (95% CI: 1.11–2.42) among males in the lowest quintile of handgrip strength. OR: 0.86 (95% CI: 0.63–1.18) among females in the lowest quintile of handgrip strength
Fukumori et al. 2015 [22]	4314 subjects: 58.5% women, 41.5% men. Age: 66.3 ± 9.0 years	MHI-5	Age, sex, BMI, smoking status, daily activities, comorbid conditions (coronary artery disease, respiratory disease, stroke)	Logistic regression analysis	AOR: 1.15 (1.06–1.24) per 1 SD decrease in handgrip strength
Gariballa and Alessa 2018 [25]	432 hospitalized older patients: 205 women, 227 men. Age: >65 years	GDS-15	Age, gender, disability, comorbidity, BMI, and severity of acute illness (inflammation)	Linear regression analysis	β: −0.09, (95% CI: −0.14–0.034) per 1 kg change in handgrip, $p=0.001$
Stessman et al. 2017 [27]	327 subjects aged 70 years: 157 women, 170 men; 384 subjects aged 78 years: 197 women, 187 men; 1187 subjects aged 85 years: 650 women, 537 men; 406 subjects aged 90 years: 210 women, 196 men	BSI	Education, self-rated health, physical activity level, depression, difficulty in performing ADL, cognitive impairments, diabetes mellitus	Logistic regression analysis	In subjects aged 78 years: OR: 2.31(1.14–5.66); AOR: 2.38(1.04–5.44); In subjects aged 85 years: OR: 2.44(1.83–3.24); AOR: 1.22(0.86–1.72) In subjects aged 90 years: OR: 3.89(2.33–6.50); AOR: 2.04(1.11–3.77)
McDowell et al. 2018 [24]	4505 community-dwelling adults: 56.5% women, 43.5% men. Age: >50 years	CES-D	Age, waist circumference, social class, smoking, health status	Logistic regression analysis	Males: OR: 0.81 (95% CI: 0.67–0.99) per 1 SD increase in strength OR: 0.49 (95% CI: 0.29–0.82) in the highest strength tertile; Females OR: 0.85 (95% CI: 0.74–0.97) per 1 SD increase in strength OR: 0.69 (95% CI: 0.50–0.95) in the highest strength tertile; Total population: OR: 0.84 (95% CI: 0.75–0.93) per 1 SD increase in strength OR: 0.62 (95% CI: 0.47–0.82) in the highest strength tertile

GDS-15 the 15-item Geriatric Depression Scale, *CIDI* Composite International Diagnostic Instrument, according to DSM-IV, *HSCL-25* Hopkins' Symptom Checklist-25, *MHI-5* 5-item version of the Mental Health Inventory, *BSI* Brief Symptom Inventory, *CES-D* Center for Epidemiological Studies Depression Scale, *BMI* body mass index, *ADL* activities of daily living, *OR* odds ratio, *SD* standard deviation, *CI* confident intervals, *AOR* adjusted odds ratio, *SE* standard error

est handgrip tertile had the highest risk (OR: 1.75, $p=0.01$) of developing depression compared to individuals scored in the highest strength tertile.

Hammer et al. [29] examined the role of sarcopenic obesity (defined as a BMI ≥30 kg/m^2 in the lowest tertile of sex-specific grip strength) as a risk factor for the new onset of depressive symptoms among 3862 community-dwelling participants in the English Longitudinal Study of Ageing. After multivariable adjustment they found that a reduction in grip strength over 6 years was associated with a significantly higher risk of depressive symptoms in obese participants only (OR: 1.79 vs. 1.47 for obese and normal weight individuals, respectively). This was the first study providing evidence for the importance of sarcopenic obesity regarding the risk of depression.

Interestingly, muscular strength also seems to protect against the development of depressive symptoms during the recovery period from an acute illness. A study including 432 hospitalized patients and mental health outcome measures including depression symptoms were assessed at admission and 6 weeks

Table 4 Longitudinal association between muscular strength and depression

Reference	Sample characteristics	Follow up	Depression assessment method	Adjustments for cofactors	Statistical analysis	Main findings
Taekema et al. 2010 [26]	555 subjects: 361 (65%) women, 194 (35%) men. Age: 85 years	4 years	GDS-15	Gender, height, weight, income	Linear regression analysis	$\beta = 0.002$ (SE: 0.003) per 1 kg change in handgrip strength, $p = 0.626$
Van Milligen et al. 2012 [20]	1206 subjects with depressive and anxiety disorders at baseline: 796 women, 410 men. Age: 42.0 ± 12.3 years	2 years	CIDI	Age, sex, years of education, BMI, somatic diseases, lung medication, physical activity, and smoking	Logistic regression analysis	OR: 0.81 (95%CI: 0.67–0.98) per 1 SD increase in handgrip strength among subjects with depression, $p = 0.03$ OR: 0.82(95% CI: 0.69–0.99) per 1 SD increase in handgrip strength among subjects with depression/anxiety, $p = 0.04$
Fukumori et al. 2015 [22]	1936 subjects: 60.2% women, 39.8% men. Age: 67.2	1 year	MHI-5	Age, sex, BMI, smoking status, daily activities, co-morbid conditions (coronary artery disease, respiratory disease, stroke)	Logistic regression analysis	AOR: 1.13 (95% CI: 1.01–1.27) per 1 SD decrease in handgrip strength
Hamer et al. 2015 [29]	3862 community-dwelling participants: 2083 women, 1779 men. Age: 64.6 ± 8.3 years	6 years	CES-D	Age, sex, physical activity, smoking, alcohol, wealth, time varying accumulative cardiovascular disease (angina, heart disease, heart failure, heart murmur, arrhythmia, and stroke), diabetes, cancer and arthritis	Logistic regression analysis	OR: 1.47 (95% CI: 0.98–2.20) among non-obese participants with low handgrip strength OR: 1.79 (95% CI: 1.10, 2.89) among obese participants with low handgrip strength
Van Milligen et al. 2017 [30]	2480 participants: 65.7% women, 34.3% men. Age: 41.9 ± 13.1 years	6 years	CIDI IDS-SR30	Time, group, sociodemographics, and time × group/severity score interaction term	Linear regression analysis	β: –1.34 (SE: 0.36), $p < 0.001$ in women with the current depressive disorder β: –0.04 (SE: 0.01) per 1 unit change in IDS-SR30, $p < 0.001$
Gariballa and Alessa 2018 [25]	432 hospitalized older patients: 205 women, 227 men. Age: >65 years	6 weeks, 6 months	GDS-15	Age, gender, disability, comorbidity, BMI, and severity of acute illness, inflammation	Analysis of variance	GDS score at the 6th week: 5.2 ± 4 in patients with low muscle strength 3.0 ± 3.7 in patients with normal muscle strength $p < 0.05$
Stessman et al. 2017 [27]	327 subjects aged 70 years: 157 women, 170 men; 384 subjects aged 78 years: 197 women, 187 men; 1187 subjects aged 85 years: 650 women, 537 men; 406 subjects aged 90 years: 210 women, 196 men	From age 70 to 78 From age 78 to 85 From age 85 to 90 From age 90 to 95	BSI	Education, self-rated health, physical activity level, depression, difficulty in performing ADLs, cognitive impairments, diabetes melitus	Logistic regression analysis	From age 70 to 78 years OR: 1.87 (95% CI: 0.58–6.02) from age 78 to 85 years OR: 0.88 (95% CI: 0.23–3.42) from age 85 to 90 years OR: 2.68 (95% CI: 1.19–6.00) AOR: 2.36 (95% CI: 0.96–5.82)
Veronese et al. 2017 [28]	970 subjects: 54.6% women, 45.4% men Mean age: 72.5 ± 6.0 years	4 years	GDS-30	Age, BMI, ADL, MMSE and GDS, cardiovascular disease, hypertension, fractures, chronic obstructive pulmonary disease, cancer, physical activity, smoking habits, and monthly income	Logistic regression analysis	OR: 1.75 (95% CI: 1.14–2.68), $p = 0.01$ in the highest tertile

as well as 6 months after hospital discharge [25]. The longitudinal analysis revealed that patients with low muscle strength at admission had poorer cognitive function and higher depressive symptoms compared to those with normal muscle strength throughout the study period.

In another study Van Milligen et al. [30] examined whether objective physical function is a predictor for the persistence of depressive disorders in a large group of depressive and anxious patients. In that study 1206 (66.1% women) subjects with depression and/or anxiety, aged 42.0 ± 12.3 years, were followed-up for a period of 2 years. After full adjustment for potential confounders (age, sex, education, BMI, somatic diseases, use of lung medication, physical activity and smoking), a one standard deviation increase in hand-

Table 4 (Continued)

Reference	Sample characteristics	Follow up	Depression assessment method	Adjustments for cofactors	Statistical analysis	Main findings
McDowell et al. 2018 [24]	4104 community-dwelling adults Age: >50 years	2 years	CES-D	Sex, age, waist circumference, social class, smoking status, & health status	Logistic regression analysis	Males: OR: 0.83 (95% CI: 0.64–1.08) per 1 SD increase OR: 0.90 (95% CI: 0.49–1.68) in the highest strength tertile OR: 0.79 (95% CI: 0.65–0.96) per 1 SD increase OR: 0.58 (95% CI: 0.37–0.91) in the highest strength tertile OR: 0.80 (95% CI: 0.69–0.93) per 1 SD increase. OR: 0.67 (95% CI: 0.47–0.96) in the highest strength tertile

GDS-15 The 15-item Geriatric Depression Scale, *CIDI* Composite International Diagnostic Instrument, according to DSM-IV, *IDS* 30-item Inventory of Depressive Symptomatology, *MHI-5* 5-item version of the Mental Health Inventory, *BSI* Brief Symptom Inventory, *CES-D* Center for Epidemiological Studies Depression Scale, *BMI* body mass index, *ADL* activities of daily living, *MMSE* Mini Mental State Examination

grip strength resulted in 18% lower odds (OR = 0.82, p = 0.04) of having persistent depression, showing that muscular strength predicts the worse course of the disease. This is very important finding because half of people who suffer from persistent depression will experience at least one episode of major depression.

Recently, McDowell et al. [24] examined the gender-related differences in the prospective association between muscular strength and depression development in the Irish longitudinal study of aging (n = 4505 community dwelling adults, aged ≥50 years, 56.5% females). After 2 years of follow-up a significant protective effect of increased muscle strength against the development of depression in women was shown. One standard deviation increase in grip strength resulted in a 42.0% lower odds of depression in women but this association was not significant in men (reduced odds by 10%). This was the first study showing the gender-specific impact of muscular strength on depression.

Of the existing studies discussed above, the majority reported significantly lower risk of developing depressive symptoms over time with increasing levels of muscular strength and this association persisted even after adjusting for several confounders (Table 4). Since other researchers, however, failed to show such an association [26, 27] there is a need for further studies on this topic. Discrepancies in the findings from the various studies may be due to differences in the characteristics of the participants. Interestingly, in the studies whithout an association between muscle strength and depressive symptoms participated older adults who were fitter compared to those in the other studies. Furthermore, although the authors adjusted for several confounders it may be that other unmeasured factors might have affected the observed associations (e.g. oxidative stress or inflammatory status which both influence muscle strength and depressive symptoms). More studies are needed in diseased and/or hospitalized patients to prove if muscular strength is longitudinally associated with the development of depressive symptoms.

Discussion

This review summarizes the existing literature on the association of muscular strength with depression risk in older people as reported in epidemiological studies. All cross-sectional studies reported significantly lower risks of having depressive symptoms with increased levels of muscular strength and this association persisted in community-based settings [20–24] among the oldest old population [25, 26] as well as in hospitalized patients [25]. Furthermore, most of the longitudinal studies [22, 24, 25, 28–30] but not all [26, 27] also reported that low muscular strength was independently associated with higher odds of developing depression.

This is the first review presented on this topic including studies of good methodological quality (see Methods) and highlights the importance of low muscular strength as a potential risk factor for the occurrence as well as the progression of depression.

Mechanisms of resistance exercise

Several possible mechanisms have been proposed to explain the strong association between muscular strength and risk of depression. It is well known that low physical performance (and thus low muscular strength) is associated with increased oxidative stress and inflammation [31, 32] and these factors may also influence the onset of depression [33]. Furthermore, low muscular strength may be an early marker of nervous system deterioration causing impaired balance and thus increased risk of falls as well as reduced functional mobility [34]. Thus, a vicious circle of physical inactivity due to the fear of falling and social isolation develops, and it is possible that people with low muscular strength are therefore at higher risk of depression. In addition, a low level of muscle strength has been associated with inadequate dietary intake [35] and it is further known that malnutrition is common among older depressed people [36]; thus, it is hypothesized that this is another explanation in the relationship between dynapenia and depression.

It has also been reported that atrophy in the hippocampus and other brain regions is associated with depression [37] and given that resistance exercise has beneficial effects on hippocampus volume and neurogenesis [38] it can be assumed that this can be one possible explanation for the findings. Taken the above mechanisms into consideration the strong, independent association between muscular strength and depression risk observed in this review is not surprising.

Clinical implications

The strong association between low muscle strength and the risk of depressive symptoms would be of great interest from a public health perspective. Depression is a common condition among older adults and is associated with reduced quality of life, higher cardiovascular disease risk and increased mortality [1–3]. Numerous risk factors for depression have been identified including physical comorbidities, stressful life events, cognitive decline, lower socioeconomic status and genetic predisposition [4, 5]. According to recent scientific evidence, low muscular strength is a strong and independent determinant of depressive symptoms among older and middle aged individuals and it is also known that muscular weakness is a modifiable risk factor for chronic disease [39].

Based on these findings it is suggested that measuring handgrip strength could be a useful instrument (being noninvasive, inexpensive and quickly administered) to identify those adults at risk for depression. Thus, individuals, particularly those with very low muscle strength or specific predisposition may be encouraged to participate in resistance-type activities in order to improve their health status and reduce the manifestation of depression later in life. Interestingly, handgrip strength among people with bipolar depression has been found to have the highest reproducibility of all physical functional assessments [40]. Furthermore, as suggested by the majority of the longitudinal studies, muscular strength also seems to be a good prognostic indicator in depressive persons. All the studies cited have significant clinical consequences, given that the early identification of objective predictors of future depression is essential not only for the individual patient but also to the healthcare system. Since depression is a mood disorder that can lead to suicidal thoughts, it is very important to predict the worse course of the disease. Indeed, in a cohort study of 1 million participants, Ortega et al. [41] reported that stronger adolescents had a 20–30% lower risk of death from suicide and were 15–65% less likely to have any psychiatric diagnosis (such as schizophrenia and mood disorders).

As the population ages, a central focus is to help older people to avoid sarcopenia and frailty syndrome. In this context the role of resistance exercises is crucial to achieving this. This is of critical importance since age-related low-grade inflammation and increased oxidative stress have been postulated as mechanisms linking low muscle mass and sarcopenia with cognitive impairment and higher depressive symptoms [42, 43]. Indeed, some prospective studies have also shown that resistance training helps to reduce depressive symptoms in older adults [44, 45] but more studies are needed on this topic; however, this review examined how low muscle strength leads to depression and not vice versa (how can depression causes muscle weakness). The relationship between these two factors is complex given that depression is characterized by fatigue and asthenia [46], which further lead these patients to decrease physical activity and thus muscular strength. It seems possible that a strong bidirectional association exists and further studies are needed to identify the direction of this association.

Conclusion and future directions

According to recent scientific evidence, low muscle strength is strongly and independently related to the existence and the development of depressive symptoms among middle aged and older adults even after adjusting for several confounders including the levels of physical activity. For this reason and because muscle strength is known to decline with age, muscle-strengthening exercises are necessary not only to improve physical fitness and other health-related parameters but also specifically to reduce the risk of depression; however, several issues must be further considered. Given that depressive symptoms were higher among females than males and that there are differences in the age-related loss of muscle mass and strength [47], it is important to examine how gender may affect the association between muscle strength and depression. Since the prevalence of depression or depressive symptoms is higher in patients than in the general population the results cannot be generalized to diseased or hospitalized/institutionalized patients. Furthermore, only one study provided information regarding medication use as a confounder and because drugs may affect both muscle strength and depressive symptoms more studies are needed to examine the impact of medications on this relationship. In addition, more studies are needed to prove if oxidative stress and inflammation could play important roles in mediating the association between low muscle strength and depression. The use of handgrip test (and not whole body strength tests) as the only muscle strength assessment in order to detect associations with depressive symptoms may also represent some selection bias; thus, more studies are required on this topic.

As there are only few studies among younger individuals, the protective role of muscular strength regarding depression risk at a young age must be interpreted with caution. In addition, little is known about the level of muscular strength required to protect against the risk of depression and this issue must be further clarified. Finally, more studies are needed on specific groups of patients where depression prevalence is high (e.g. stroke patients) or under clinical conditions where muscle atrophy is a common feature (e.g. advanced cancer or heart failure patients).

Conflict of interest K. Volaklis, T. Mamadjanov, C. Meisinger, and J. Linseisen declare that they have no competing interests.

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