The association between handgrip strength and depression in cancer survivors: a cross-section study

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Abstract

Background

The association between handgrip strength and depression in cancer survivors was unknown. We aim to examine the associations of handgrip strength and depression in cancer survivors by using public data (National Health and Nutrition Examination Survey).

Methods

We combined two waves of the data of the National Health and Nutrition Examination Survey during 2011-2014 to explore this important issue. The variable of handgrip strength was extracted by the maximum value of each hand. The depressive symptom was assessed by the Patient Health Questionnaire (PHQ-9) with the cut-off >=10 points indicating depressive symptoms. Other characteristics and health-related variables were evaluated. Multivariable logistic regression models were adopted to explore the associations between handgrip strength or low handgrip strength and depressive symptoms by adjusting for potential confounding factors.

Results

There were 992 cancer survivors in our final analysis, with 456 (45.97%) male and the mean (SD) age of this whole group being 64.75 (14.02) years. The prevalence of low handgrip strength and depression was 20.36% and 13.31%, respectively. The results showed that handgrip strength was negatively associated with depression (OR=0.97,95%CI:0.96-0.99; *P*=0.01). In addition, after adjusting age, race, education, marital status, sleep disorder, history of stroke, polypharmacy and BMI, cancer survivors with low handgrip strength had a 2.11-fold risk of depression, compared to those with normal handgrip strength (OR=2.11,95%CI:1.19-3.73; *P*=0.01).

Conclusions

Low handgrip strength, simple and modifiable parameter, is associated with a higher risk of depression in cancer survivors. Prospective cohort studies are warranted to confirm this association in the future.

Introduction

The number of cancer survivors is increasing thanks to the variety of multiple advances of technology and medicine and the aging society[1]. Meanwhile, cancer survivors were often suffering depression symptoms, with an estimated figure of 20%, as compared to 5% in the general population[2]. A meta-analysis reported that the prevalence of major depression and minor depression was 15% and 20%, respectively[3]. Cancer patients with depression could have an increased risk of adverse outcomes, such as poor adherence to medical treatment[4], lower survival time[5], even more likely to suicide[6], bringing

tremendous attention to clinicians and society. Therefore, early identification of risk and corresponding management for depression among cancer patients was essential.

Several factors, serious illness, female gender, social deprivation, and other health-related factors, are associated with depression[7]. Apart from these abovementioned factors, functional limitations such as low handgrip strength are becoming the hotpot topic for the researcher to explore with depression[8–10]. A previous study indicated that muscle mass could influence depression by secreting myokines[11] and muscle mass as the main component of organ to maintain the function of physical activity. Apparently, regular physical activity was associated with decreased risk of depression[12]. Handgrip strength, as an indicator of the function of muscle mass, can be easily obtained by dynamometer, widely applied in different settings. In addition, handgrip also used a parameter to assess the nutritional status of patients.

The association between handgrip and depression has been widely explored among community-dwelling older adults, with the results being that older adults with high handgrip strength had a lower risk of depression symptom[13, 14]. Furthermore, in a recent meta-analysis, handgrip strength was associated with depression (Pooling OR = 0.85,95%CI:0.80,0.89), indicating handgrip strength as a protective factor for depression[15]. However, most of the including studies for meta-analysis were conducted among community or nursing home settings where participants were relatively healthy. In contrast, the association between handgrip strength and depression among cancer patients was unknown.

Therefore, the aim of this present study was to explore the association between handgrip strength and depression among cancer patients and examine the association of low handgrip strength based on the definition of sarcopenia with depression by using the public internet database of the National Health and Nutrition Examination Survey.

Methods

Study design and participants.

This cross-sectional study of National Health and Nutrition Examination Survey (NHANES) was to explore the overall picture of nutrition, health, and risk factors among residents in various states across the USA (Centers for Disease Control and Prevention-http://www.cdc.gov/nchs/nhanes.htm). This survey is based on national-scale adopting multistage and clustered sample methods with the figure of being 5000 participants each year. Voluntary participants were asked to finish physical examination and this study was approved by Health Statistics Research Ethics Review Board from national center. All the participants have signed the written consent.

In this present study, data including handgrip strength, depression, sleep disorder, cancer type, baseline characteristics, and other health-related variables were extracted from NHANES ranging from 2011 to 2012 and 2013 to 2014, aggregating for final analysis.

Cancer diagnosis

Cancer patients was confirmed by asking about the question (Have you even been told by the doctor that you had been diagnosed with any type of cancer). We selected the patients whose answer is “YES.”

Handgrip strength

The detail of muscle strength measurement was depicted in NHANES Procedure Manual. Briefly, those participants who are able to finish the test obeyed the standard procedure. Investigators explained the detailed information and asked participants to squeeze the dynamometer as hard as possible for three times, recording the maximum value as the participant’s final handgrip strength. In our present study, the definition of low handgrip strength was <27kg for males and <16kg for females[16].

Depressive symptoms

According to the Questionnaire Instruments, Patient Health Questionnaire (PHQ-9) was used to assess the depressive symptoms of participants, consisting of 9-items with each item ranging from 0 to 3 points[17]. The total points of PHQ-9 ranged from 0 to 27. We categorized participants into depression and non-depression, with the cut-off being 10 points based on the previous study, which was reported good sensitivity (88%) and specificity (88%) for identifying major depression[18].

Covariates definition

We extracted demographic characteristics including age, gender, education, race, marital status, and smoking. Of which, the race was defined as Non-Hispanic Black, Non-Hispanic White, and others; marital status was classified as married, widowed or divorced, and others. Regarding of education, four categories including less than 12 grades, high school, some college, and college graduated above were confirmed. Other covariates such as BMI, cancer diagnosis, sleep disorder, history of stroke, and history of Congestive Heart Failure (CHF) were also extracted. In addition, Leisure-time physical activity was assessed by Global Physical Activity Questionnaire[19]. The detailed calculation method was reported the previous study. In brief, we combined the vigorous and moderate intensities of physical activity each week, and we defined it as inactive and physical activity, respectively, with the cut-off of zero min/week.

Statistical analysis

Continuous variables including age, BMI, Depression score were present as means and SD, and categorical variables including diagnosis, gender, race, education, marital status, sleep disorder, and other health-related variables were displayed as frequency (%). Comparisons for low handgrip strength versus normal handgrip strength and depression versus non-depression were conducted by Student’s-test and chi-squared test or Fisher’s Exact Test and Mann–Whitney tests, for appropriate. In addition, the generalized additive model (GAM) analysis was used to detect whether there is a non-linear relationship between handgrip strength and depression[20]. Before performing multivariable logistic regression analysis, we used Least Absolute Shrinkage and Selection Operator (LASSO) regression to select

variables for the final regression model. The results indicated that these variables (age, race, education, marital status, sleep disorder, history of stroke, polypharmacy, BMI, handgrip strength) were selected. Finally, Multivariable logistic regression analysis was adopted to identify the independent association between handgrip strength and depression after controlling for potential confounding factors including age, race, education, marital status, sleep disorder, history of stroke, polypharmacy, BMI. We also categorized handgrip strength into low handgrip and normal handgrip according to the sarcopenia of the revised European consensus on definition and diagnosis, with the cut-off value being <16kg for females and <27kg for males. The association between low handgrip strength and depression was also detected by multivariable logistic regression analysis with adjustment of the same variables. Unadjusted subgroup analysis between low handgrip strength and depression was performed in terms of different variables(inactive versus active, >=65 versus <65, sleep disorder, congestive heart failure, polypharmacy, history of stroke, marital status, race, and education.) All the statistics were conducted by software packages R and Empowerstats, with the significant P-value being <0.05.

Results

Baseline Clinical Characteristics

There were 992 cancer cases in this present study. Cancer patients include 222 Skin cancers (22.52%), 138 prostate cancers (14.00%), 64 melanoma cancers (6.49%),27 lung cancers (2.74%),117 gynecological cancers (11.87%),55 colon cancers (5.58%),157 breast cancers (15.92%) and 206 other cancers (20.89%). The mean (SD) age of this whole group was 64.75 (14.02) years, with 456 (45.97%) male. The prevalence of low handgrip strength and depression was 20.36% and 13.31%, respectively. Of these patients, 383(43.37%) participants experienced polypharmacy and 663 patients did not participate physical activity. Other detailed information was shown in Table 1.

Table 1
Baseline Clinical Characteristics

Variables	Total sample	Low handgrip strength		Standardize diff.	P-value
		No	Yes		
N		790(79.64%)	202(20.36%)		
Age (years)(mean, SD)	64.75 ± 14.02	63.21 ± 14.09	70.77 ± 12.00	0.58 (0.42, 0.73)	< 0.001
BMI (kg/m2) (mean, SD)	28.95 ± 6.72	29.11 ± 6.65	28.29 ± 7.00	0.12(-0.04,0.28)	0.171
Diagnosis (n,%)				0.29 (0.13, 0.44)	0.070
Skin	222(22.52%)	185 (23.54%)	37 (18.50%)		
Prostate	138(14.00%)	101 (12.85%)	37 (18.50%)		
Melanoma	64(6.49%)	55 (7.00%)	9 (4.50%)		
Lung	27(2.74%)	23 (2.93%)	4 (2.00%)		
Gynecological	117(11.87%)	98 (12.47%)	19 (9.50%)		
Colon	55(5.58%)	41 (5.22%)	14 (7.00%)		
Breast	157(15.92%)	116 (14.76%)	41 (20.50%)		
Others	206(20.89%)	167 (21.25%)	39 (19.50%)		
Depression score (mean, SD)	3.94 ± 5.56	3.70 ± 4.92	4.96 ± 7.65	0.20 (0.03, 0.36)	0.006
Gender (n, %)				0.04 (-0.12, 0.19)	0.619
Male	456 (45.97%)	360 (45.57%)	96 (47.52%)		
Female	536 (54.03%)	430 (54.43%)	106 (52.48%)		
Race (n, %)				0.16 (0.01, 0.32)	0.109
Other	185 (18.65%)	138 (17.47%)	47 (23.27%)		
Non-Hispanic White	642 (64.72%)	523 (66.20%)	119 (58.91%)		

CHF: Congestive Heart Failure

Variables	Total sample	Low handgrip strength		Standardize diff.	P-value
Non-Hispanic Black	165 (16.63%)	129 (16.33%)	36 (17.82%)		
Education (n, %)				0.36 (0.21, 0.52)	< 0.001
Less than 12 grades	200 (20.18%)	136 (17.22%)	64 (31.84%)		
High school graduate	198 (19.98%)	158 (20.00%)	40 (19.90%)		
Some college	302 (30.47%)	255 (32.28%)	47 (23.38%)		
College graduate above	291 (29.36%)	241 (30.51%)	50 (24.88%)		
Marital status (n, %)				0.27 (0.11, 0.43)	0.003
Married	555 (56.17%)	462 (58.56%)	93 (46.73%)		
Widowed or divorced	300 (30.36%)	220 (27.88%)	80 (40.20%)		
Other	133 (13.46%)	107 (13.56%)	26 (13.07%)		
Sleep disorder (n, %)				0.16 (0.03, 0.34)	0.046
Yes	371 (37.40%)	308 (38.99%)	63 (31.19%)		
No	620 (62.50%)	482 (61.01%)	138 (68.32%)		
History of stroke (n, %)				0.24 (0.09, 0.40)	< 0.001
Yes	84 (8.48%)	55 (6.97%)	29 (14.43%)		
No	906 (91.52%)	734 (93.03%)	172 (85.57%)		
CHF (n, %)				0.30 (0.14, 0.46)	< 0.001
Yes	69 (6.98%)	41 (5.20%)	28 (13.93%)		

CHF: Congestive Heart Failure

Variables	Total sample	Low handgrip strength		Standardize diff.	P-value
No	920 (93.02%)	747 (94.80%)	173 (86.07%)		
Leisure time physical activity (n, %)				0.56 (0.40, 0.71)	< 0.001
Inactive	663 (66.83%)	490 (62.03%)	173 (85.64%)		
Active	329(33.17%)	300(37.97%)	29 (14.36%)		
Depression (n, %)				0.22 (0.06, 0.38)	0.004
No	827 (86.69%)	681 (88.21%)	146 (80.22%)		
Yes	127 (13.31%)	91 (11.79%)	36 (19.78%)		
Polypharmacy (n, %)				0.37 (0.21, 0.53)	< 0.001
< 5	500 (56.63%)	421 (60.49%)	79 (42.25%)		
>=5	383 (43.37%)	275 (39.51%)	108 (57.75%)		
CHF: Congestive Heart Failure					

Baseline characteristics between low handgrip strength and normal handgrip strength.

Overall, cancer patients with low handgrip strength were more likely older, had poor sleep, and were less likely to participate in physical activity. In addition, the proportions of depression and polypharmacy were higher in cancer patients with low handgrip strength as compared to those with normal handgrip strength. Those patients who suffered a history of stroke or congestive heart failure tended to have low handgrip strength.(Table 1)

Univariate Analysis For The Factors Related To Depression

The results of univariate analysis showed that female, low handgrip strength, sleep disorder, stroke, and polypharmacy were associated with depression. In addition, cancer patients who were not married were more likely to have a risk of depression. Other related variables with depression were displayed in Table 2.

Table 2
Comparison between depression and non-depression.

Variables	Statistics	Depression	P-value
Gender (n,%)			
Male	456 (45.97%)	1.0	
Female	536 (54.03%)	1.64 (1.11, 2.42)	0.0123
AGE	64.75 ± 14.02	0.97 (0.96, 0.98)	< 0.0001
Race (n,%)			
Other	185 (18.65%)	1.0	
Non-Hispanic White	642 (64.72%)	0.60 (0.37, 0.95) 0.0309	0.0309
Non-Hispanic Black	165 (16.63%)	1.17 (0.67, 2.05) 0.5726	0.5726
Diagnosis (n,%)			
Others	206(20.89%)	1.0	
Skin	222(22.52%)	0.84 (0.46, 1.55)	0.5834
Prostate	138(14.00%)	0.84 (0.41, 1.68)	0.6146
Melanoma	64(6.49%)	1.04 (0.44, 2.46)	0.9229
Lung	27(2.74%)	0.28 (0.04, 2.17)	0.2242
Gynecological	117(11.87%)	1.82 (0.98, 3.38)	0.0589
Colon	55(5.58%)	1.25 (0.53, 2.97)	0.6108
Breast	157(15.92%)	1.28 (0.69, 2.36)	0.4395
Low handgrip strength (n,%)			
No	790 (79.64%)	1.0	
Yes	202 (20.36%)	1.85 (1.21, 2.82)	0.0048
Education (n,%)			
Less than 12 grades	200 (20.18%)	1.0	
High school graduate	198 (19.98%)	0.69 (0.40, 1.18)	0.1766
Some college	302 (30.47%)	0.68 (0.42, 1.09)	0.1109
College graduate above	291 (29.36%)	0.27 (0.15, 0.49)	< 0.0001
Marital status (n,%)			
CHF: Congestive Heart Failure			

Variables	Statistics	Depression	P-value
Married	555 (56.17%)	1.0	
Widowed or divorced	300 (30.36%)	2.30 (1.51, 3.52)	0.0001
Other	133 (13.46%)	3.02 (1.80, 5.05)	< 0.0001
Sleep disorder (n,%)			
Yes	371 (37.40%)	1.0	
No	620 (62.50%)	0.27 (0.18, 0.40)	< 0.0001
History of stroke (n,%)			
Yes	84 (8.48%)	1.0	
No	906 (91.52%)	0.40 (0.23, 0.68)	0.0008
CHF (n,%)			
Yes	69 (6.98%)	1.0	
No	920 (93.02%)	0.59 (0.31, 1.12)	0.1051
Leisure time physical activity (n,%)			
Inactive	744 (75.00%)	1.0	
Active	248 (25.00%)	0.85 (0.55, 1.33)	0.4815
Polypharmacy (n,%)			
<5	500 (56.63%)	1.0	
>=5	383 (43.37%)	2.43 (1.62, 3.64)	< 0.0001
CHF: Congestive Heart Failure			

The association between handgrip strength or low handgrip strength and the risk of depression.

Multivariable logistic regression analysis was used to identify the association between handgrip strength or low handgrip strength and depression among cancer patients. the results showed that handgrip strength was a protective factor for depression in an unadjusted model, the OR being 0.979(95%CI:0.966–0.992; $P = 0.005$). After adjusting potential confounding factors, this association was still exited (OR = 0.977,95%CI:0.960–0.994; $P = 0.01$). When handgrip strength was classified into low handgrip strength and normal handgrip strength, the multivariable logistic regression analysis also indicated that cancer patients with low handgrip strength had increased risk of depression after adjusting age, gender, marital status, sleep disorder, physical activity, history of stroke and polypharmacy (OR = 2.11,95%CI:1.19–3.73; $P = 0.001$).(Table 3)

Table 3
multivariable logistic regression analysis for the association between handgrip strength or low handgrip strength and the risk of depression.

Exposure	Non-adjusted	Adjust
Depression		
Lower handgrip strength		
NO	1.0	1.0
Yes	1.845 (1.206, 2.823) 0.0047	2.11 (1.19, 3.73) 0.01
Depression		
Handgrip strength(kg)	0.979(0.966, 0.992) 0.005	0.977(0.960,0.994) 0.01
Restults: β (95%CI) Pvalue / OR (95%CI) P-value		
Non-adjusted model adjust for: None		
Adjust model adjust for: age, BMI, marital status, race, education, sleep disorder, history of stroke; pharmacology		

Non-linear Relationship Analyses

The generalized additive model (GAM) analysis was adopted to detect whether there is a non-linear relationship between handgrip strength and depression and the results suggested the association between handgrip strength and the risk of depression was negative, meaning that with the increase of handgrip strength, the possibility of depression was decreased. (Shown in Fig. 1)

Subgroup analysis between low handgrip strength and depression in terms of different variables.

The subgroup analysis showed that the association between low handgrip strength and depression among cancer patients was almost unchanged in various stratum, indicating that this was reliable and stable (Fig. 2)

Discussion

This present study showed that cancer patients with low handgrip strength had an increased risk of depression as compared to those with normal handgrip strength, implying cancer patients need to take measures such as resistance training and nutritional program to improve handgrip strength, eventually reducing the risk of depression among cancer patients.

To the best of our knowledge, this is the first study to explore the association between handgrip strength and depression among cancer survivors. Many studies had examined the association between handgrip and depression among the community-dwelling population. In a cross-sectional study consisting of 24,109 Chinese adults (41. 5 ± 11.9 years), the authors found that participants with higher handgrip strength were associated with lower risk of depression and this association was particular in female[21]. Furthermore, another prospective cohort study conducted in rural Chinese populations, reporting the reversely association between handgrip and depression[22]. Our study was in line with these abovementioned previous studies. However, most of these studies were performed among relatively healthy people. Only a few studies focused on hospitalized patients. A study in 2020 was reported this association among participants suffering from different chronic diseases with inconsistent results[23]. The results found that those participants with high strength tertile had decreased depression both among people with no disease or metabolic diseases; however, this association was not observed in patients with arthritis diseases, which need more study for further exploration. Our study focused on a special population, cancer survivors, which are prevalent of suffering from depression[24]. Additionally, co-morbid depression had an adverse impact for treatment and recovery for cancer patients. Therefore, early prevention and treatment for depression were essential for cancer survivors.

Prior studies mainly focused on other aspects of risk factors for depression, which consisting of social factors (family, social support, stressful life event), characteristic of cancer (type of cancer, recurrence, prognosis), cancer treatment (radiotherapy, chemotherapy, treatment burden), individual characteristics (age, gender, marital status) and psychological response to diagnosis. To the best of our knowledge, no study explores the handgrip strength, a modifiable parameter, with the association of depression. Obviously, handgrip strength had many merits, simple, convenient, and not time-consuming, compared to these abovementioned factors, which were widely used in clinical settings and other primary community healthcare[25]. The most significant merit is that handgrip strength can be modified by interventions. Given our study indicated that lower handgrip strength increased the risk of depression (OR = 2.31,95%CI:1.37–3.89; P = 0.001), it is reasonable that improvement of handgrip strength by multiple measures such as resistance training program and national intervention can had benefit for reducing the risk of depression, which had a positive impact for cancer treatment and recovery. In a randomized controlled trial, the author reported that aerobic exercise intervention increased the amount of muscle mass among patients with major depression, which was beneficial for improving depression[26].

The mechanism between low handgrip strength and depression was complicated. First, low handgrip strength as the core component for defining sarcopenia, which was reported by multiple studies[27, 28], was associated with a high risk of depression. Second, cancer patients with low handgrip strength are unlikely to participate in physical activity. In this present study, cancer survivors with low handgrip strength experienced a higher proportion of inactive than those with normal handgrip strength (85.64% versus 62.03%). Given recent meta-analysis covering 97 randomized controlled trials reporting that exercise program was associated with a lower level of depression with the pooled OR = 2.24(95%CI:1.77–2.84)[29]. Therefore, cancer patients with low handgrip strength, hardly participating in physical activity would not

gain the beneficial effect for reducing depression producing by exercise. Third, some studies reported that a muscle–brain crosstalk can be medicated by myokines and metabolites, which were secreted by muscle, playing a role in regulating hippocampal function that was closely related to depression[11, 30]. Although there were some possible reasons for the association between low handgrip strength and depression, future studies were warranted to explore this underlying mechanism.

This study possessed strengths and drawbacks. First, based on our knowledge, this is the first study to examine the association of handgrip strength and depression among cancer survivors, which was a fundamental issue for the prevention and management of depression among oncology Patients. Second, our study suggests that by using a simple and convenient dynamometer to measure handgrip strength, clinicians can identify the high-risk group of depression. Given the characteristic of modification of handgrip strength, appropriate and personalized exercise and nutritional programs are beneficial for reducing the risk of depression. Third, our study used comprehensive statistical analysis such as Lasso regression, by using shrinkage, to better select variables for minimizing multicollinearity. However, some drawbacks need to be mentioned. First, the feature of cross-section study limited the ability to identify a completely causal association, which needs more prospective cohort study for further exploration. Secondly, the NHANES study database did not provide some other important information about cancer treatment (radiotherapy and chemotherapy), length of time of first cancer diagnosis, and advanced disease stages, which might overestimate or underestimate the association between low handgrip strength and depression. Our study indicated that cancer survivors with low handgrip strength had an about 2.1-fold risk of depression, implying that clinicians need to perform corresponding interventions (physical activity and nutrition) to improving handgrip strength with the benefit for reducing depression.

Abbreviations

LASSO: Least Absolute Shrinkage and Selection Operator; PHQ-9: Patient Health Questionnaire; HANES: National Health and Nutrition Examination Survey; CHF: Congestive Heart Failure

LASSO
Least Absolute Shrinkage and Selection Operator
PHQ-9
Patient Health Questionnaire
HANES
National Health and Nutrition Examination Survey
CHF
Congestive Heart Failure

Declarations

Ethics approval and consent to participate

This study included data from NHANES 2011-14, all the participants agreed with this study and signed written informed consent, approving by the National Center for Health Statistics research ethics review board.

Consent for publication

Not Applicable

Consent to participate

Not applicable

Availability of data and materials

Data that support the findings of this study are available NHANES, https://www.cdc.gov/nchs/nhanes/index.htm

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

XMZ and ZBZ were responsible for drafting the manuscript

XJW and WC were responsible for the concept and design

XMZ and ZBZ participated in data analysis.

All the authors have read and approved the manuscript.

References

1. Miller KD, Nogueira L, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2019. *CA: a cancer journal for clinicians* 2019; **69**: 363–85. doi: 10.3322/caac.21565
2. Steel Z, Marnane C, Iranpour C, et al. The global prevalence of common mental disorders: a systematic review and meta-analysis 1980–2013. *International journal of epidemiology* 2014; **43**:

476–93. doi: 10.1093/ije/dyu038

3. Mitchell AJ, Chan M, Bhatti H, et al. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *The Lancet Oncology* 2011; **12**: 160–74. doi: 10.1016/s1470-2045(11)70002-x
4. Manning M, Bettencourt BA. Depression and medication adherence among breast cancer survivors: bridging the gap with the theory of planned behaviour. *Psychology & health* 2011; **26**: 1173–87. doi: 10.1080/08870446.2010.542815
5. Zhou L, Sun H. The longitudinal changes of anxiety and depression, their related risk factors and prognostic value in colorectal cancer survivors: a 36-month follow-up study. *Clinics and research in hepatology and gastroenterology* 2021; **45**: 101511. doi: 10.1016/j.clinre.2020.07.016
6. Pitman A, Suleman S, Hyde N, Hodgkiss A. Depression and anxiety in patients with cancer. *BMJ (Clinical research ed)* 2018; **361**: k1415. doi: 10.1136/bmj.k1415
7. Niedzwiedz CL, Knifton L, Robb KA, Katikireddi SV, Smith DJ. Depression and anxiety among people living with and beyond cancer: a growing clinical and research priority. *BMC cancer* 2019; **19**: 943. doi: 10.1186/s12885-019-6181-4
8. Ashdown-Franks G, Stubbs B, Koyanagi A, et al. Handgrip strength and depression among 34,129 adults aged 50 years and older in six low- and middle-income countries. *Journal of affective disorders* 2019; **243**: 448–54. doi: 10.1016/j.jad.2018.09.036
9. Marques A, Gaspar de Matos M, Henriques-Neto D, et al. Grip Strength and Depression Symptoms Among Middle-Age and Older Adults. *Mayo Clinic proceedings* 2020; **95**: 2134-43. doi: 10.1016/j.mayocp.2020.02.035
10. Zhang XM, Jiao J, Cao J, et al. Handgrip Strength and Depression Among Older Chinese Inpatients: A Cross-Sectional Study. *Neuropsychiatric disease and treatment* 2021; **17**: 1267–77. doi: 10.2147/ndt.S301064
11. Pedersen BK. Physical activity and muscle-brain crosstalk. *Nature reviews Endocrinology* 2019; **15**: 383–92. doi: 10.1038/s41574-019-0174-x
12. Ernstsen L, Rangul V, Nauman J, et al. Protective Effect of Regular Physical Activity on Depression After Myocardial Infarction: The HUNT Study. *The American journal of medicine* 2016; **129**: 82–88.e1. doi: 10.1016/j.amjmed.2015.08.012
13. Han KM, Chang J, Yoon HK, et al. Relationships between hand-grip strength, socioeconomic status, and depressive symptoms in community-dwelling older adults. *Journal of affective disorders* 2019; **252**: 263–70. doi: 10.1016/j.jad.2019.04.023
14. Wang H, Hai S, Liu Y, et al. Association between depressive symptoms and sarcopenia in older Chinese community-dwelling individuals. *Clinical interventions in aging* 2018; **13**: 1605–11. doi: 10.2147/cia.S173146
15. Marques A, Gomez-Baya D, Peralta M, et al. The Effect of Muscular Strength on Depression Symptoms in Adults: A Systematic Review and Meta-Analysis. *International journal of environmental research and public health* 2020; **17**doi: 10.3390/ijerph17165674

16. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age and ageing* 2019; **48**: 16–31. doi: 10.1093/ageing/afy169
17. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine* 2001; **16**: 606–13. doi: 10.1046/j.1525-1497.2001.016009606.x
18. Manea L, Gilbody S, McMillan D. Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. *CMAJ: Canadian Medical Association journal = journal de l'Association medicale canadienne* 2012; **184**: E191-6. doi: 10.1503/cmaj.110829
19. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet (London, England)* 2012; **380**: 247–57. doi: 10.1016/s0140-6736(12)60646-1
20. Yang L, Qin G, Zhao N, Wang C, Song G. Using a generalized additive model with autoregressive terms to study the effects of daily temperature on mortality. *BMC medical research methodology* 2012; **12**: 165. doi: 10.1186/1471-2288-12-165
21. Gu Y, Li X, Zhang Q, et al. Grip strength and depressive symptoms in a large-scale adult population: The TCLSIH cohort study. *Journal of affective disorders* 2021; **279**: 222–28. doi: 10.1016/j.jad.2020.08.023
22. Zhao Z, Ji C, Liu Y, Gao S, Xia Y. Higher handgrip strength predicts a lower risk of depressive symptoms in rural Chinese populations. *Journal of affective disorders* 2020; **269**: 12–17. doi: 10.1016/j.jad.2020.03.028
23. Marconcin P, Peralta M, Ferrari G, et al. The Association of Grip Strength with Depressive Symptoms among Middle-Aged and Older Adults with Different Chronic Diseases. *International journal of environmental research and public health* 2020; **17**doi: 10.3390/ijerph17196942
24. Wang YH, Li JQ, Shi JF, et al. Depression and anxiety in relation to cancer incidence and mortality: a systematic review and meta-analysis of cohort studies. *Molecular psychiatry* 2020; **25**: 1487–99. doi: 10.1038/s41380-019-0595-x
25. Lee WJ, Peng LN, Chiou ST, Chen LK. Relative Handgrip Strength Is a Simple Indicator of Cardiometabolic Risk among Middle-Aged and Older People: A Nationwide Population-Based Study in Taiwan. *PloS one* 2016; **11**: e0160876. doi: 10.1371/journal.pone.0160876
26. Kerling A, Hartung D, Stubbs B, et al. Impact of aerobic exercise on muscle mass in patients with major depressive disorder: a randomized controlled trial. *Neuropsychiatric disease and treatment* 2018; **14**: 1969–74. doi: 10.2147/ndt.S167786
27. Kirk B, Zanker J, Bani Hassan E, Bird S, Brennan-Olsen S, Duque G. Sarcopenia Definitions and Outcomes Consortium (SDOC) Criteria are Strongly Associated With Malnutrition, Depression, Falls, and Fractures in High-Risk Older Persons. *Journal of the American Medical Directors Association* 2021; **22**: 741–45. doi: 10.1016/j.jamda.2020.06.050
28. Nishikawa H, Enomoto H, Yoh K, et al. Association between Sarcopenia and Depression in Patients with Chronic Liver Diseases. *Journal of clinical medicine* 2019; **8**doi: 10.3390/jcm8050634

29. Bigarella LG, Ballotin VR, Mazurkiewicz LF, et al. Exercise for depression and depressive symptoms in older adults: an umbrella review of systematic reviews and Meta-analyses. *Aging & mental health* 2021: 1–11. doi: 10.1080/13607863.2021.1951660
30. Campbell S, Macqueen G. The role of the hippocampus in the pathophysiology of major depression. *Journal of psychiatry & neuroscience: JPN* 2004; **29**: 417–26.

Figures

Subgroup	No. of patients	OR(95%CI)	P- value
Leisure time physical activity			
Inactive	663	1.73 (1.08, 2.80)	0.024
Active	329	2.07 (0.73, 5.89)	0.172
Gender			
Male	456	2.30 (1.18, 4.50)	0.015
Female	536	1.63 (0.93, 2.83)	0.085
Age			
<65	425	2.80 (1.45, 5.39)	0.002
>=65	567	2.07 (1.13, 3.82)	0.019
Sleep disorder			
Yes	371	1.70 (0.91, 3.17)	0.093
No	620	2.85 (1.51, 5.40)	0.001
Congestive Heart Failure			
Yes	69	0.63 (0.17, 2.29)	0.479
No	920	2.10 (1.33, 3.30)	0.001
Polypharmacy			
<5	500	1.91 (0.89, 4.07)	0.094
>=5	383	1.55 (0.89, 2.70)	0.125
Stroke			
Yes	84	0.76 (0.26, 2.25)	0.623
No	906	2.07 (1.30, 3.29)	0.002
Marital			
Married	555	1.48 (0.70, 3.09)	0.302
Widowed or divorced	300	1.46 (0.75, 2.83)	
Other	133	3.59 (1.36, 9.46)	0.009
Education			
Less than 12 grades	200	1.29 (0.61, 2.76)	0.505
High school graduate	198	1.51 (0.59, 3.88)	0.396
Some college	302	1.93 (0.87, 4.28)	0.103
College graduate above	291	2.90 (1.03, 8.17)	0.044
Race			
Other	185	1.44 (0.60, 3.43)	0.413
Non-Hispanic White	642	1.89 (1.05, 3.39)	0.033
Non-Hispanic Black	165	2.03 (0.82, 5.01)	0.126

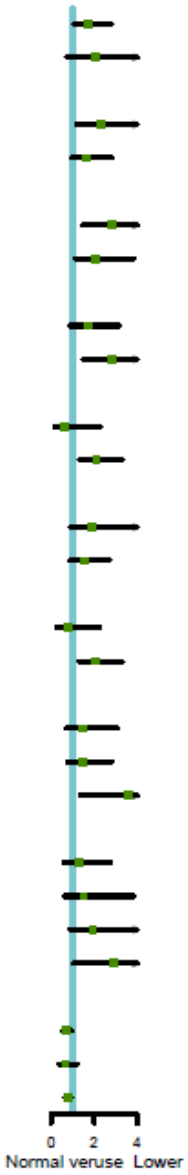

Figure 1

A linear relationship between handgrip strength and probability of depression by a generalized additive model

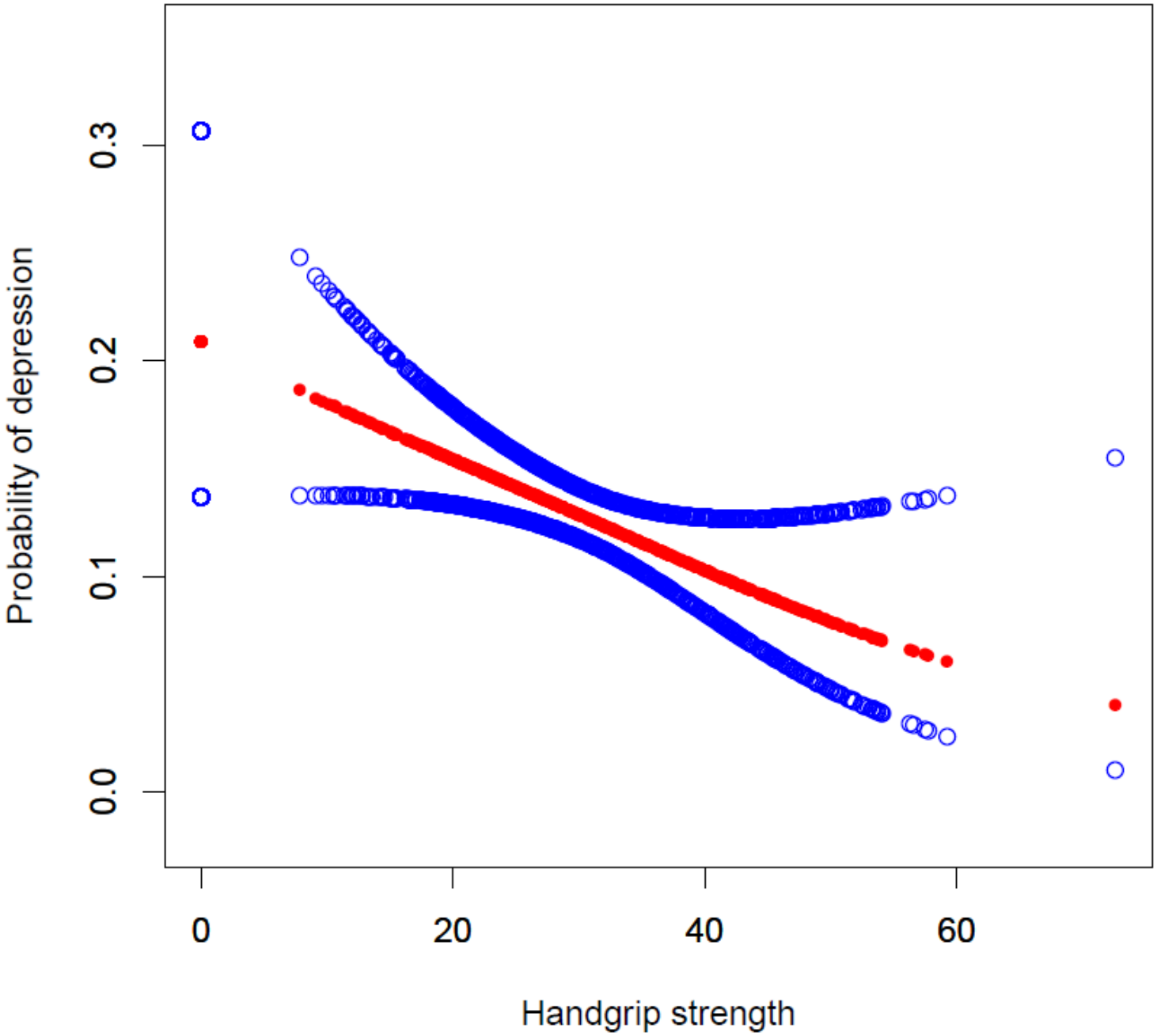

Figure 2

Subgroup analysis between low handgrip strength and depression in terms of different variables.