

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email editorial.bmjopen@bmj.com

BMJ Open

Body Mass Index, Waist-to-Hip Ratio and Cognitive Function among Chinese Elderly

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-022055
Article Type:	Research
Date Submitted by the Author:	01-Feb-2018
Complete List of Authors:	Zhang, Tao; Zhejiang Provincial Center for Disease Control and Prevention Yan, Rui; Zhejiang Provincial Center for Disease Control and Prevention Chen, Qifeng; Shaoxing Center for Disease Control and Prevention Ying, Xuhua; Yuhuan Center for Disease Control and Prevention Zhai, Yujia; Zhejiang Provincial Center for Disease Control and Prevention Li, Fudong; Zhejiang Provincial Center for Disease Control and Prevention Wang, Xinyi; Zhejiang Provincial Center for Disease Control and Prevention He, Fan; Zhejiang Provincial Center for Disease Control and Prevention Ye, Chiyu; Zhejiang Provincial Center for Disease Control and Prevention Lin, Junfen; Zhejiang Provincial Center for Disease Control and Prevention
Keywords:	cognitive impairment, body mass index, abdominal obesity, elderly, Chinese

SCHOLARONE™
Manuscripts

1
2
3 **Body Mass Index, Waist-to-Hip Ratio and Cognitive Function among Chinese Elderly**
4

5 Tao Zhang ^{a,1}, Rui Yan ^{a,1}, Qifeng Chen ^{b,1}, Xuhua Ying ^c, Yujia Zhai ^a, Fudong Li ^a, Xinyi
6 Wang ^a, Fan He ^a, Chiyu Ye ^a, Junfen Lin ^{a,*}
7

8
9 ^a *Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, Zhejiang, China*
10

11 ^b *Shaoxing Center for Disease Control and Prevention, Shaoxing, Zhejiang, China*
12

13 ^c *Yuhuan Center for Disease Control and Prevention, Taizhou, Zhejiang, China*
14

15 ¹ These authors contributed equally to this work
16

17
18
19 **Correspondence to:** Junfen Lin, No.3399, Binsheng Rd., Binjiang District, Hangzhou,
20

21 P.R.China; +86-571-87115131; zjlinjunfen@163.com
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Objectives: To investigate the associations between body mass index (BMI), waist-to-hip ratio (WHR) and cognitive function among Chinese elderly.

Design: Cross-sectional study.

Setting: Community.

Participants: Data was obtained from the baseline survey of a community based cohort in Zhejiang Province, and enrolled 9 326 persons aged 60 years and older.

Primary outcome measures: We investigated the effect of BMI on cognition, and then explored the effect of WHR on cognition across different quartiles of BMI.

Results: A sample of 9 087 persons was used in this study, including 4 375 men and 4 712 women. Higher WHR increased cognitive impairment risk in those with BMI > 25.3 kg/m² (OR (per 0.1 increase), 1.39, 95% CI, 1.13-1.70). No statistically significant association was found in other BMI categories.

Conclusions: WHR could increase risk for cognitive impairment among elderly with BMI > 25.3 kg/m². Our results suggest that it could be of benefit for the elderly with high BMI to control WHR.

Strengths and limitations of this study:

The strength of this study was the in-depth analysis of the effect of waist-to-hip ratio on cognitive impairment across different body mass index categories.

High fat diet, which is an important influence factor for cognitive function as mentioned above, was not included in this study.

Since this was a cross-sectional study, caution would be needed when generalizing the

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

present findings.

Keywords: cognitive function, body mass index, abdominal obesity, elderly, Chinese

For peer review only

Introduction

Cognitive impairment is an important health issue in the elderly. An estimated 46.8 million people currently have dementia in the world, the most well-known form of cognitive impairment, and this number will rise to 131.5 million in 2050. It was estimated over 9.5 million people with dementia in China, which was 20% of the total number of people in the world with dementia. By 2030, the number of people living with dementia in China is expected to rise to over 16 million [1]. The incidence of dementia in people aged 60 years and older [2], is 9.87 cases per 1000 person-years in China, and the situation of cognitive impairment would be more serious [3].

Obesity was widely recognized as an influence factor of dementia [4 5]. Body mass index (BMI) and waist-to-hip ratio (WHR) are common index assessing obesity around the world. Both too high and low BMI are harmful to health, such as increasing risk for development of numerous chronic disease, and even associated with increased mortality [6 7]. Studies of BMI and cognitive impairment in the elderly have shown conflicting results: both positive and negative association have been reported [8-12]. One possible explanation for the heterogeneous findings is that BMI is affected by both fat and fat-free mass, which may have opposite effects on health [13]. This is a limitation of BMI when comparing individuals with same weight and height but different body fat content. The use of BMI as a surrogate for body fat may be particularly problematic in the elderly due to the effect of aging on fat distribution [14]. Therefore, WHR, as a proxy for body fat distribution, would be a complementary indicator in health related studies for the elderly. It has been reported that high WHR was associated with adverse health outcomes independent of BMI [15 16].

1
2
3 However, to our knowledge, few studies have evaluated the effect of BMI and WHR on
4 cognitive impairment in a large Chinese elderly population. To help shed light on this area,
5
6 we investigated the associations between BMI, WHR and cognitive impairment among
7
8 Chinese aged 60 years and older.
9
10

11 **Materials and Methods**

12 **Study Population**

13
14
15 The present study used data collected from the baseline survey of a community-based
16 cohort study focusing on aging and health problems among the elderly in Zhejiang Province,
17
18 China since 2014. In brief, 6 out of 90 counties were randomly selected from Zhejiang
19
20 Province, with at least 1 500 permanent residents aged 60 years and above were randomly
21
22 recruited in each county for participation in 2014. Finally 9 326 subjects were enrolled.
23
24 During the baseline survey, we performed questionnaire based interview, physical
25
26 examinations and laboratory tests for each participant. Informed consent was obtained from
27
28 all participants, and the study was approved by the Ethics Committee of Zhejiang Provincial
29
30 Center for Disease Control and Prevention. A sample of 9 087 of 9 326 participants was
31
32 included in this study. The remained 239 were excluded because of missing values in age,
33
34 Chinese language version of the Mini-Mental State Examination (MMSE) score, or BMI.
35
36
37
38
39
40
41
42
43
44

45 **Cognitive Function**

46
47 Cognitive function was determined by MMSE, which included 30 items. The maximum
48
49 score of MMSE is 30, and higher scores indicate better cognitive function. According to
50
51 Wang et al., The questionnaire of MMSE has good reliability and validity as an instrument to
52
53 detect cognitive impairment among Chinese [17]. The widely accepted cut-off score of
54
55
56
57
58
59
60

1
2
3
4 cognitive impairment in China is education-specific: 17/18 for illiteracy, 20/21 for people
5
6 with primary education level, 24/25 for people with higher than primary education level [18].
7

8 **Body Mass Index (BMI)**

9
10 BMI (kg/m^2) was calculated as the body weight (by kilograms) divided by the square of
11
12 the body height (by meters). All the participants were asked to remove shoes, heavy clothing,
13
14 and hats prior to height and weight measurements, and have the participants stand straight
15
16 with heels together, legs straight, and looking straight ahead.
17
18

19 **Waist-to-hip Ratio (WHR)**

20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
Waist circumference was measured midway between the lower rib margin and iliac crest.
Hip circumference was measured at the level of the widest circumference over the greater
trochanters. In the baseline survey, waist circumference and hip circumference were
measured twice, and the difference of two measured values were restricted in ± 2 centimeters.
Waist-hip ratio was calculated as waist circumference divided by hip circumference. In this
study, waist circumference and hip circumference were calculated as mean of two measured
values.

60 **Covariates**

Covariates were collected by face-to-face interview with questionnaire, including: age,
race, education level, marital status, economic status, smoking, alcohol drinking, physical
exercise, hypertension (diagnosed by doctors), diabetes (diagnosed by doctors), coronary
heart disease (diagnosed by doctors), and depressive symptom. Depressive symptom was
determined using the Patient Health Questionnaire- 9 scale (PHQ-9). Those scored 5 or above
were defined as depression [19].

Statistical Analysis

Descriptive statistics were applied to illustrate the socio-demographic and health characteristics of the enrolled participants. Differences of the characteristics across different cognitive status groups were assessed by *t*-test for continuous variables, and by Chi-square test for categorical variables. Logistic regressions were used to examine the effects of BMI and WHR on cognitive impairment. BMI was evaluated as categorical variable, divided by quartiles. WHR was evaluated under different BMI levels. Both BMI and WHR were assessed by 3 logistic models. In the basic model (model 1), no covariate was included when assessing the effect of BMI on cognitive impairment, and BMI was adjusted when assessing the effect of WHR. Model 2 was based on model 1, with adjusting for additional socio-demographics variables (age, sex, nation, education, marital status, and family economics). Model 3 was based on model 2, with additional adjustments of lifestyles (smoking, drinking, and physic exercise) and health variables (hypertension, stroke, and depression).

All statistical analyses were performed by SAS 9.4 (SAS Institute Inc., Cary, NC), and two tailed *P*-value <0.05 was considered statistically significant.

Results

Socio-demographics and health Characteristics

Of the 9 087 subjects, 1 339 (14.7%) were defined as cognitive impairment by MMSE. The mean age of all the subjects was 69.8 (\pm 8.3). More than a half (51.9) was female. Among the subjects with cognitive impairment, the mean MMSE score was 13.6 (\pm 5.1), while the

mean score was 25.8 (± 3.1) in normal cognition group. The mean values of BMI and WHR were 22.7 \pm 3.6, 0.9 \pm 0.1, respectively in the cognitive impairment group, and the mean values were 23.3 \pm 3.3, 0.9 \pm 0.1, respectively in normal cognition group. Differences of BMI and WHR between the two groups were both significant statistically. The subjects with cognitive impairment tended to be older, female, minority ethnic group, without physical exercise, with hypertension, with stroke, with depression. Also, cognitive impairment was associated with education, marital status, family economics, smoking, and drinking. More details were shown in Table 1.

Table 1. Socio-demographics and health characteristics of 9087 participants by cognitive status

Characteristics	Normal cognition (n=7748)	Cognitive impairment (n=1339)	Overall	<i>P</i>
Age, years(mean, SD)	68.8 \pm 7.8	75.4 \pm 8.5	69.8 \pm 8.3	<0.001
Sex				<0.001
Male	3877(50.0)	498(37.2)	4375(48.1)	
Female	3871(50.0)	841(62.8)	4712(51.9)	
Nation				<0.001
Han	7489(96.7)	1213(90.6)	8702(95.8)	
Minority	259(3.3)	126(9.4)	385(4.2)	
Education				<0.001
Illiteracy	3703(47.8)	893(66.7)	4596(50.6)	
Primary school	3461(44.7)	379(28.3)	3840(42.3)	
Middle school or higher	584(7.5)	67(5.0)	651(7.2)	
Marital status				<0.001
Single	104(1.4)	38(2.8)	142(1.6)	
Married	6060(78.4)	776(58.0)	6836(75.4)	
Windowed/Divorced	1566(20.3)	525(39.2)	2091(23.1)	
Family economics				<0.001
Rich	796(10.3)	77(5.8)	873(9.6)	
Median	6135(79.2)	984(73.5)	7119(78.4)	
Poor	817(10.5)	277(20.7)	1094(12.0)	
Smoking				<0.001
Current smokers	1749(22.6)	173(12.9)	1922(21.2)	
Ex-smokers	768(9.9)	121(9.0)	889(9.8)	
Never smokers	5231(67.5)	1045(78.0)	6276(69.1)	

Drinking					<0.001
Current drinkers	2079(26.8)	204(15.2)	2283(25.1)		
Ex-drinkers	662(8.5)	158(11.8)	820(9.0)		
Never drinkers	5007(64.6)	977(73.0)	5984(65.9)		
Physic exercise	1499(19.4)	190(14.2)	1689(18.6)		<0.001
Hypertension	3462(44.7)	648(48.4)	4110(45.2)		0.011
Diabetes	667(8.6)	113(8.4)	780(8.6)		0.838
Coronary heart disease	230(3.0)	48(3.6)	278(3.1)		0.227
Stroke	204(2.6)	91(6.8)	295(3.2)		<0.001
Depression	664(8.6)	275(20.5)	939(10.3)		<0.001
Body mass index	23.3±3.3	22.7±3.6	23.2±3.4		<0.001
Waist-to-Hip ratio	0.9±0.1	0.9±0.1	0.9±0.1		0.026
MMSE score	25.8±3.1	13.6±5.1	24.0±5.6		<0.001

Association between BMI and cognitive impairment

The mean MMSE scores were calculated by quartiles of BMI. The highest quartile of BMI had the highest mean MMSE score (24.36±5.28), and the lowest quartile had the lowest mean value (23.33±5.94). Compared with the 2nd quartile of BMI, the odds ratio (OR) of the lowest quartile was 1.42 (95% confidence interval (CI), 1.21-1.67), the OR of the highest quartile was 0.86 (95% CI, 0.72-1.02), and the 3rd quartile had an OR value of 0.92 (95% CI, 0.77-1.08). In model 3, the OR of Q1 BMI was close to being statistically significant, and these results were essentially unchanged after adjustment for more covariates (Table 2).

Table 2. Association between body mass index and cognitive impairment

Quartiles of body mass index	Odds ratio (95% confidence interval)		
	Model 1 ^a (n=9087)	Model 2 ^b (n=9068)	Model 3 ^c (n=9068)
Q1 (12.1-20.8)	1.42 (1.21-1.67)	1.20 (1.01-1.42)	1.18 (0.99-1.40)
Q2 (>20.8-22.9)	1	1	1
Q3 (>22.9-25.3)	0.92 (0.77-1.08)	1.02 (0.85-1.22)	1.02 (0.85-1.22)
Q4 (>25.3-42.8)	0.86 (0.72-1.02)	0.95 (0.79-1.14)	0.93 (0.77-1.12)

^a No covariate was included.

^b Adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physic exercise, hypertension, stroke, and depression.

Association between waist-to-hip ratio and cognitive impairment

We detected two-way interaction between BMI and WHR, and the result was significant ($P=0.002$). Further, the association between WHR and cognitive impairment was assessed under each BMI group. Under the lowest BMI group, the association between WHR and cognitive impairment was not statistically significant. The situation was similar in the 2nd and 3rd quartile of BMI. In the highest BMI group, each 0.1 higher WHR corresponded to a 1.39 folds higher risk of cognitive impairment in the basic model. The OR value remained significant after adjusting for more covariates in model 2 and model 3, which were 1.36 (95% CI, 1.10-1.69) and 1.37 (95% CI, 1.10-1.71), respectively (Table 3).

Table 3. Association of waist-to-hip ratio (per 0.1 increase) with cognitive impairment under different body mass index group

	Quartiles of body mass index			
	Q1	Q2	Q3	Q4
Subjects (<i>n</i>)	2244	2266	2311	2266
Waist-to-hip ratio				
Range	0.61-1.26	0.46-1.29	0.49-1.49	0.58-1.38
Mean	0.87±0.07	0.89±0.06	0.91±0.06	0.93±0.06
Model 1 ^a	1.13 (0.98-1.31)	1.12 (0.93-1.35)	1.38 (1.14-1.65)	1.39 (1.13-1.70)
Model 2 ^b	1.01 (0.86-1.18)	0.93 (0.75-1.13)	1.13 (0.94-1.41)	1.36 (1.10-1.69)
Model 3 ^c	0.99 (0.83-1.17)	0.92 (0.75-1.13)	1.14 (0.93-1.40)	1.37 (1.10-1.71)

^a Adjusted for body mass index.

^b Based on model 1, model 2 was further adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physic exercise, hypertension, stroke, and depression.

Discussion

1
2
3
4 In this cross-sectional study of 9087 Chinese elderly aged 60 years and older, we
5
6 investigated the associations between BMI, WHR and cognitive impairment risk. We found
7
8 that each 0.1 unit increase in WHR corresponded to 1.37 (1.10-1.71) elevated cognitive
9
10 impairment risk in high BMI ($>25.3 \text{ kg/m}^2$) group in the fully adjusted model (model 3).
11
12

13 In our study, compared with Q2 BMI ($>20.8\text{-}22.9 \text{ kg/m}^2$), Q1 BMI ($\leq 20.8 \text{ kg/m}^2$) was a
14
15 risk factor for cognitive impairment, while Q4 BMI tended to be a protective factor, though
16
17 not statistically significant. In previous studies, some have shown that high BMI tended to be
18
19 a risk factor for cognitive decline [10-12], while others observed protective effect of high
20
21 BMI on cognitive function [4 5 8 9]. The inconsistency suggests the relationship between
22
23 BMI and cognitive function is complex.
24
25
26

27
28 Zhou et al. [20] suggested that subjects who were both with obesity and dementia had a
29
30 high mortality rate, which might very likely remove those with high BMI and dementia, and
31
32 leave moderate or severe dementia subjects with low BMI, thus enforce the association
33
34 between BMI and dementia. Assuming the survivor bias existed, the observed association
35
36 between high BMI and cognition impairment would be biased towards the null, and such bias
37
38 would be even more serious in cross-sectional study if it exists. Nevertheless, the hypothesis
39
40 is not enough to explain the relationship between low BMI and cognitive impairment.
41
42
43 Furthermore, several cohort studies reported that both persons with low BMI and persons
44
45 with high BMI have lower cognitive functions in later life [21-25].
46
47
48
49

50 Among the participants of this study, the mean value of WHR tended to increase within
51
52 higher BMI group. We observed a strong positive association between WHR and cognitive
53
54 impairment risk under Q4 BMI ($>25.3 \text{ kg/m}^2$) group, but no significant association was found
55
56
57

1
2
3 among other BMI group (Q1-Q3). The association remained after adjusting for covariates.
4
5
6 Our results revealed that elderly with higher WHR in the highest BMI group have an elevated
7
8 risk of cognitive impairment, which suggested targeted prevention and screening for this
9
10 high-risk group. It is reported that adipokines might be a link between obesity and dementia.
11
12 Adipokines include hundreds of polypeptides secreted by the cells of white adipose tissue.
13
14 The action of adipokines could be altered during neurodegenerative events and might
15
16 feedback to contribute to neurodegeneration [26]. It is noteworthy to mention that previous
17
18 studies have reported high fat diet exacerbates cognitive decline [27 28]. Amyloid deposition,
19
20 and cerebral microvasculature dysfunction are the most discussed reasons in relevant studies
21
22 [27-30]. These findings suggest further studies are needed to explore the mechanisms that
23
24 underlie the association between obesity and cognitive impairment.
25
26
27
28
29

30 Some limitations of the present study should be noted. One limitation is that, high fat diet,
31
32 which is an important influence factor for cognitive function as mentioned above, was not
33
34 included in this study. It is probable that high fat diet leads to central obesity with high BMI
35
36 and WHR among Chinese elderly. Further studies are needed to explore the relationship
37
38 within diet, WHR and cognitive impairment. Besides, caution would be needed when
39
40 generalizing the present findings, as our results were based on cross-sectional study.
41
42
43
44

45 **Conclusions**

46
47 Higher WHR significantly increase risk for cognitive impairment among the elderly with
48
49 BMI > 25.3 kg/m². The results of this study suggest that it is of benefit for the elderly with
50
51 high BMI to control WHR.
52
53

54
55 **Acknowledgments:** We acknowledge the invaluable contributions made by all the
56
57

1
2
3 interviewers of the Zhejiang Ageing and Health Cohort Study.
4
5

6 **Contributors:** JL, RY, TZ, QC, XY, YZ, FL, XW, FH, and C.Y. participated in the design
7
8 of the study, collection of data, data cleaning. TZ, RY, YZ, FL, XW, and CY conducted the
9
10 statistical analyses. TZ wrote the manuscript. RY, QC, XY, and JL contributed to the
11
12 interpretation of the results and revised the manuscript critically. All authors approved the
13
14 final version of the manuscript.
15
16

17
18 **Funding:** This work was supported by Zhejiang Provincial Medical and Health Science
19
20 and Technology Project (2015KYB081) and Science and Technology Bureau of Yuhuan
21
22 (201731).
23
24

25 **Competing interests:** None declared.
26
27

28 **Patient consent:** Obtained.
29
30

31 **Data sharing statement:** Data are not publicly available due to local ethical restrictions.
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Herrera AC, Prince M, Knapp M, et al. World Alzheimer Report 2016: Improving healthcare for people with dementia. Coverage, quality and costs now and in the future. 2016
2. Chan KY, Wang W, Wu JJ, et al. Epidemiology of Alzheimer's disease and other forms of dementia in China, 1990-2010: a systematic review and analysis. *Lancet (London, England)* 2013;**381**(9882):2016 doi: 10.1016/S0140-6736(13)60221-4[published Online First: Epub Date] .
3. Nie H, Xu Y, Liu B, et al. The prevalence of mild cognitive impairment about elderly population in China: a meta-analysis. *International journal of geriatric psychiatry* 2011;**26**(6):558–63 doi: 10.1002/gps.2579[published Online First: Epub Date] .
4. Qizilbash N, Gregson J, Johnson ME, et al. BMI and risk of dementia in two million people over two decades: a retrospective cohort study. *Lancet Diabetes & Endocrinology* 2015;**3**(6):431-36 doi: 10.1016/S2213-8587(15)00033-9[published Online First: Epub Date] .
5. Tolppanen AM, Ngandu T, K  reholt I, et al. Midlife and late-life body mass index and late-life dementia: results from a prospective population-based cohort. *Journal of Alzheimers Disease* 2014;**38**(1):201 doi: 10.3233/JAD-130698[published Online First: Epub Date] .
6. Nguyen NT, Magno CP, Lane KT, et al. Association of Hypertension, Diabetes, Dyslipidemia, and Metabolic Syndrome with Obesity: Findings from the National Health and Nutrition Examination Survey, 1999 to 2004. *Journal of the American College of Surgeons* 2008;**207**(6):928-34 doi: 10.1016/j.jamcollsurg.2008.08.022[published Online First: Epub Date] .
7. Pierce BL, Kalra T, Argos M, et al. A prospective study of body mass index and mortality in Bangladesh. *International journal of epidemiology* 2010;**39**(4):1037-45 doi: 10.1093/ije/dyp364[published Online First: Epub Date] .
8. Tikhonoff V, Casiglia E, Guidotti F, et al. Body fat and the cognitive pattern: A population - based study. *Obesity* 2015;**23**(7):1502-10 doi: 10.1002/oby.21114.[published Online First: Epub Date] .
9. Kim S, Kim Y, Park SM. Body Mass Index and Decline of Cognitive Function. *Plos One* 2016;**11**(2):e0148908 doi: 10.1371/journal.pone.0148908.[published Online First: Epub Date] .
10. Gunstad J, Lhotsky A, Wendell CR, et al. Longitudinal Examination of Obesity and Cognitive Function: Results from the Baltimore Longitudinal Study of Aging. *Neuroepidemiology* 2010;**34**(4):222-29 doi: 10.1159/000297742.[published Online First: Epub Date] .
11. Gallucci M, Mazzuco S, Ongaro F, et al. Body mass index, lifestyles, physical performance and cognitive decline: The "Treviso Longeva (Trelong)" study. *Journal of Nutrition Health & Aging* 2013;**17**(4):378-84 doi: 10.1007/s12603-012-0397-1.[published Online First: Epub Date] .
12. Besser LM, Gill DP, Monsell SE, et al. Body mass index, weight change, and clinical progression in mild cognitive impairment and Alzheimer disease. *Alzheimer disease and associated disorders* 2014;**28**(1):36-43 doi: 10.1097/WAD.000000000000005[published Online First: Epub Date] .
13. Smith E, Hay P, Campbell L, et al. A review of the relationship between obesity and cognition across the lifespan: Implications for novel approaches to prevention and treatment. *Obesity Reviews* 2011;**12**(9):740-55 doi: 10.1111/j.1467-789X.2011.00920.x[published Online First: Epub Date] .
14. Benito-Leon J, Mitchell AJ, Hernandez-Gallego J, et al. Obesity and impaired cognitive functioning in the elderly: a population-based cross-sectional study (NEDICES). *Eur J Neurol* 2013;**20**(6):899-906, e76-7 doi: 10.1111/ene.12083[published Online First: Epub Date] .
15. Turcato E, Bosello O, Di FV, et al. Waist circumference and abdominal sagittal diameter as surrogates of body fat distribution in the elderly: their relation with cardiovascular risk factors. *International Journal*

- of Obesity & Related Metabolic Disorders Journal of the International Association for the Study of Obesity 2000;**24**(8):1005 doi: 10.1038/sj.ijo.0801352[published Online First: Epub Date]].
16. Villareal DT, Apovian CM, Kushner RF, et al. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. American Journal of Clinical Nutrition 2005;**82**(5):923-34 doi: 10.1038/oby.2005.228[published Online First: Epub Date]].
17. Zhengyu W, mingyuan Z. Application of Chinese version of Mini-Mental State examination (MMSE). Shanghai Archives of Psychiatry 1989(3):108-11
18. Li F, He F, Chen T, et al. Reproductive History and Risk of Cognitive Impairment in Elderly Women: A Cross-Sectional Study in Eastern China. Journal of Alzheimer's Disease 2016;**49**(1):139-47 doi: 10.3233/JAD-150444.[published Online First: Epub Date]].
19. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;**16**(9):606-13 doi: 10.1046/j.1525-1497.2001.016009606.x[published Online First: Epub Date]].
20. Zhou Y, Flaherty JH, Huang CQ, et al. Association between body mass index and cognitive function among Chinese nonagenarians/centenarians. Dementia & Geriatric Cognitive Disorders 2010;**30**(6):517 doi: 10.1159/000322110.[published Online First: Epub Date]].
21. Sabia S, Nabi H, Kivimaki M, et al. Health behaviors from early to late midlife as predictors of cognitive function: The Whitehall II study. American journal of epidemiology 2009;**170**(4):428-37 doi: 10.1093/aje/kwp161.[published Online First: Epub Date]].
22. Dahl AK, Hassing LB, Fransson EI, et al. Body mass index across midlife and cognitive change in late life. International journal of obesity 2013;**37**(2):296-302 doi: 10.1038/ijo.2012.37.[published Online First: Epub Date]].
23. Sturman MT, de Leon CF, Bienias JL, et al. Body mass index and cognitive decline in a biracial community population. Neurology 2008;**70**(5):360-7 doi: 10.1212/01.wnl.0000285081.04409.bb[published Online First: Epub Date]].
24. Arvanitakis Z, Capuano AW, Bennett DA, et al. Body mass index and decline in cognitive function in older black and white persons. Journals of Gerontology 2017 doi: 10.1093/gerona/glx152[published Online First: Epub Date]].
25. Wang F, Zhao M, Han Z, et al. Association of body mass index with amnesic and non-amnesic mild cognitive impairment risk in elderly. BMC Psychiatry 2017;**17**(1):334 doi: 10.1186/s12888-017-1493-x[published Online First: Epub Date]].
26. Kiliaan AJ, Arnoldussen IA, Gustafson DR. Adipokines: a link between obesity and dementia? Lancet Neurology 2014;**13**(9):913-23 doi: 10.1016/S1474-4422(14)70085-7[published Online First: Epub Date]].
27. Theriault P, ElAli A, Rivest S. High fat diet exacerbates Alzheimer's disease-related pathology in APPswe/PS1 mice. Oncotarget 2016;**7**(42):67808-27 doi: 10.18632/oncotarget.12179[published Online First: Epub Date]].
28. Lin B, Yu H, Koki T, et al. High - Fat - Diet Intake Enhances Cerebral Amyloid Angiopathy and Cognitive Impairment in a Mouse Model of Alzheimer's Disease, Independently of Metabolic Disorders. Journal of the American Heart Association Cardiovascular & Cerebrovascular Disease 2016;**5**(6):e003154 doi: 10.1161/JAHA.115.003154.[published Online First: Epub Date]].
29. Pimentel-Coelho PM, Rivest S. The early contribution of cerebrovascular factors to the pathogenesis of Alzheimer's disease. The European journal of neuroscience 2012;**35**(12):1917-37 doi: 10.1111/j.1460-9568.2012.08126.x[published Online First: Epub Date]].

- 1
2
3 30. Zlokovic BV. Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders.
4 Nature reviews Neuroscience 2011;**12**(12):723-38 doi: 10.1038/nrn3114[published Online First: Epub
5 Date]].
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract (Page 1-3)	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale (Page 4-5)	2	Explain the scientific background and rationale for the investigation being reported
Objectives (Page 5)	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design (Page 5)	4	Present key elements of study design early in the paper
Setting (Page 5)	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants (Page 5)	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables (Page 5-6)	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement (Page 5-6)	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods (Page 7)	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses

Continued on next page

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data (Page 7-9)	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data (Page 7-9)	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results (Page 9-10)	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results (Page 10-11)	18	Summarise key results with reference to study objectives
Limitations (Page 12)	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation (Page 11-12)	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability (Page 12)	21	Discuss the generalisability (external validity) of the study results

Other information

Funding (Page 13)	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
----------------------	----	---

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Body Mass Index, Waist-to-Hip Ratio and Cognitive Function among Chinese Elderly: A Cross-Sectional Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-022055.R1
Article Type:	Research
Date Submitted by the Author:	05-May-2018
Complete List of Authors:	Zhang, Tao; Zhejiang Provincial Center for Disease Control and Prevention Yan, Rui; Zhejiang Provincial Center for Disease Control and Prevention Chen, Qifeng; Shaoxing Center for Disease Control and Prevention Ying, Xuhua; Yuhuan Center for Disease Control and Prevention Zhai, Yujia; Zhejiang Provincial Center for Disease Control and Prevention Li, Fudong; Zhejiang Provincial Center for Disease Control and Prevention Wang, Xinyi; Zhejiang Provincial Center for Disease Control and Prevention He, Fan; Zhejiang Provincial Center for Disease Control and Prevention Ye, Chiyu; Zhejiang Provincial Center for Disease Control and Prevention Lin, Junfen; Zhejiang Provincial Center for Disease Control and Prevention
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	cognitive impairment, body mass index, abdominal obesity, elderly, Chinese

SCHOLARONE™
Manuscripts

1
2
3 **Body Mass Index, Waist-to-Hip Ratio and Cognitive Function among Chinese Elderly:**
4 **A Cross-Sectional Study**
5

6 Tao Zhang ^{a,1}, Rui Yan ^{a,1}, Qifeng Chen ^{b,1}, Xuhua Ying ^c, Yujia Zhai ^a, Fudong Li ^a, Xinyi
7 Wang ^a, Fan He ^a, Chiyu Ye ^a, Junfen Lin ^{a,*}
8
9

10 ^a *Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, Zhejiang, China*
11
12

13 ^b *Shaoxing Center for Disease Control and Prevention, Shaoxing, Zhejiang, China*
14
15

16 ^c *Yuhuan Center for Disease Control and Prevention, Taizhou, Zhejiang, China*
17

18 ¹ These authors contributed equally to this work
19

20 **Correspondence to:** Junfen Lin, No.3399, Binsheng Rd., Binjiang District, Hangzhou,
21
22

23 P.R.China; +86-571-87115131; zjlinjunfen@163.com
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Objectives: To investigate the associations between body mass index (BMI), waist-to-hip ratio (WHR) and cognitive function among Chinese elderly.

Design: Cross-sectional study.

Setting: Community.

Participants: Data was obtained from the baseline survey of a community-based cohort in Zhejiang Province, and enrolled 9 326 persons aged 60 years and older.

Primary outcome measures: We investigated the association between BMI and cognition, and then explored the association between WHR and cognition across different quartiles of BMI.

Results: A sample of 9 087 persons was used in this study, including 4 375 men and 4 712 women. Higher WHR increased cognitive impairment risk in those with BMI > 25.3 kg/m² (OR (per 0.1 increase), 1.39, 95% CI, 1.13-1.70). No statistically significant association was found in other BMI categories.

Conclusions: Higher WHR could increase risk for cognitive impairment among elderly with BMI > 25.3 kg/m². Our results suggest that it could be of benefit for the elderly with high BMI to control WHR.

Strengths and limitations of this study:

1. The strength of this study was the in-depth analysis of the association between waist-to-hip ratio and cognitive impairment across different body mass index categories.
2. High fat diet, which is an important influence factor for cognitive function as mentioned above, was not included in this study.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

3. Since this was a cross-sectional study, caution would be needed when generalizing the present findings.

Keywords: cognitive function, body mass index, abdominal obesity, elderly, Chinese

For peer review only

Introduction

Cognitive impairment is an important health issue in the elderly. According to Alzheimer's Disease International (ADI) [1], an estimated 46.8 million people currently have dementia in the world, the most well-known form of cognitive impairment, and this number will rise to 131.5 million in 2050. ADI estimated over 9.5 million people with dementia in China, which was 20% of the total number of people in the world with dementia. By 2030, the number of people living with dementia in China is expected to rise to over 16 million. The incidence of dementia in people aged 60 years and older, is 9.87 cases per 1000 person-years in China [2], and the situation of cognitive impairment would be more serious [3].

Obesity was normally recognized as an influence factor of dementia [4 5]. The possible reasons included inflammation and β -amyloid metabolism, which had been observed connection with obesity [6]. However, studies on association between BMI and cognitive impairment in the elderly have shown conflicting results: both positive and negative association have been reported [7-11]. There is a limitation of BMI when comparing individuals with same weight and height but different body fat mass. BMI is affected by both fat and fat-free mass, which may have opposite effects on health [12]. The use of BMI as a surrogate for obesity may be particularly problematic in the elderly due to the effect of aging on fat distribution [13]. WHR, as a proxy for body fat distribution, would be a complementary indicator in health-related studies for the elderly. It has been reported that high WHR was associated with adverse health outcomes independent of BMI [14 15]. Actually, high WHR could increase death even with normal BMI [16 17]. Therefore, it would

1
2
3
4 be necessary to evaluate the effect of WHR when BMI was within a certain range.

5
6 However, to our knowledge, studies evaluating the association between BMI-specific
7
8 WHR and cognitive impairment in a large Chinese elderly population were lacking. To help
9
10 shed light on this area, we investigated the associations between BMI, WHR and cognitive
11
12 impairment among Chinese aged 60 years and older.
13

14 15 **Materials and Methods**

16 17 **Study Population**

18
19 The present study used data collected from the baseline survey of a community-based
20
21 cohort study focusing on aging and health problems among the elderly in Zhejiang Province,
22
23 China since 2014. In brief, 6 out of 90 counties were randomly selected from Zhejiang
24
25 Province, with at least 1 500 participants were randomly recruited in each county for
26
27 participation in 2014. Inclusion criteria were as following: 1) permanent residents who lived
28
29 for over 6 months in the past year; 2) aged 60 years and above. Exclusion criterion was
30
31 inability to complete interview due to physical disability. Finally, 9 326 subjects were
32
33 enrolled, with a response rate of 76%. During the baseline survey, we performed
34
35 questionnaire-based interview, physical examinations and laboratory tests for each participant.
36
37 Informed consent was obtained from all participants, and the study was approved by the
38
39 Ethics Committee of Zhejiang Provincial Center for Disease Control and Prevention. A
40
41 sample of 9 087 of 9 326 participants was included in this study. The remained 239 were
42
43 excluded because of missing values in age, Chinese language version of the Mini-Mental
44
45 State Examination (MMSE) score, or BMI.
46
47
48
49
50
51
52
53

54 55 **Cognitive Function**

1
2
3
4 Cognitive function was determined by MMSE, which included 30 items. The maximum
5
6 score of MMSE is 30, and higher scores indicate better cognitive function. According to
7
8 Wang et al., The questionnaire of MMSE has good reliability and validity as an instrument to
9
10 detect cognitive impairment among Chinese [18]. The cut-off score of cognitive impairment
11
12 is education-specific: 17/18 for illiteracy, 20/21 for people with primary education level,
13
14
15 24/25 for people with higher than primary education level [19].
16
17

18 **Body Mass Index (BMI)**

19
20 BMI (kg/m^2) was calculated as the body weight (by kilograms) divided by the square of
21
22 the body height (by meters). Body weight and height was measured by digital weight and
23
24 height scale. All the participants were asked to remove shoes, heavy clothing, and hats prior
25
26 to height and weight measurements, and have the participants stand straight with heels
27
28 together, legs straight, and looking straight ahead.
29
30
31

32 **Waist-to-hip Ratio (WHR)**

33
34
35 Waist circumference was measured midway between the lower rib margin and iliac crest,
36
37 with a soft cloth tape measure. Hip circumference was measured at the level of the widest
38
39 circumference over the greater trochanters, with a soft cloth tape measure. In the baseline
40
41 survey, waist circumference and hip circumference were measured twice, and the difference
42
43 of two measured values were restricted in ± 2 centimeters. Waist-hip ratio was calculated as
44
45 waist circumference divided by hip circumference. In this study, waist circumference and hip
46
47 circumference were calculated as mean of two measured values.
48
49
50

51 **Covariates**

52
53
54 Covariates were collected by face-to-face interview with questionnaire, including: age,
55
56
57

1
2
3 race, education level (self-reported), marital status (self-reported), economic status
4
5 (self-reported), smoking (self-reported), alcohol drinking (self-reported), physical exercise
6
7 (activities which were carried out to sustain or improve health and fitness in one's spare time),
8
9 hypertension (diagnosed by doctors), diabetes (diagnosed by doctors), coronary heart disease
10
11 (diagnosed by doctors), and depressive symptom. Depressive symptom was determined using
12
13 the Patient Health Questionnaire- 9 scale (PHQ-9). Those scored 5 or above were defined as
14
15 depression [20].
16
17
18
19

20 21 **Statistical Analysis**

22
23 Descriptive statistics were applied to illustrate the socio-demographic and health
24
25 characteristics of the enrolled participants. Differences of the characteristics across different
26
27 cognitive status groups were assessed by *t*-test for continuous variables, and by Chi-square
28
29 test for categorical variables. Logistic regressions were used to examine the association
30
31 between BMI, WHR and cognitive impairment. BMI was evaluated as categorical variable,
32
33 divided by quartiles. WHR was evaluated under different BMI levels. Both BMI and WHR
34
35 were assessed by 3 logistic models. In the basic model (model 1), no covariate was included
36
37 when assessing the association between BMI and cognitive impairment, and BMI was
38
39 adjusted when assessing the association between WHR and cognitive impairment. Model 2
40
41 was based on model 1, with adjusting for additional socio-demographics variables (age, sex,
42
43 nation, education, marital status, and family economics). Model 3 was based on model 2,
44
45 with additional adjustments of lifestyles (smoking, drinking, and physic exercise) and health
46
47 variables (hypertension, stroke, and depression).
48
49
50
51
52
53

54 All statistical analyses were performed by SAS 9.4 (SAS Institute Inc., Cary, NC), and
55
56

two tailed P -value <0.05 was considered statistically significant.

Patient and Public Involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results

Socio-demographics and health Characteristics

Of the 9 087 subjects, 1 339 (14.7%) were defined as cognitive impairment by MMSE. The mean age of all the subjects was 69.8 (± 8.3). More than a half (51.9%) was female. Among the subjects with cognitive impairment, the mean MMSE score was 13.6 (± 5.1), while the mean score was 25.8 (± 3.1) in normal cognition group. The mean values of BMI and WHR were 22.7 \pm 3.6, 0.9 \pm 0.1, respectively in the cognitive impairment group, and the mean values were 23.3 \pm 3.3, 0.9 \pm 0.1, respectively in normal cognition group. Differences of BMI and WHR between the two groups were both significant statistically. The subjects with cognitive impairment tended to be older, female, minority ethnic group, without physical exercise, with hypertension, with stroke, with depression. Also, cognitive impairment was associated with education, marital status, family economics, smoking, and drinking. More details were shown in Table 1.

Table 1. Socio-demographics and health characteristics of 9087 participants by cognitive status

Characteristics	Normal cognition ($n=7748$)	Cognitive impairment ($n=1339$)	Overall	P
Age, years(mean, SD)	68.8 \pm 7.8	75.4 \pm 8.5	69.8 \pm 8.3	<0.001

1					
2					
3	Sex				<0.001
4	Male	3877(50.0)	498(37.2)	4375(48.1)	
5	Female	3871(50.0)	841(62.8)	4712(51.9)	
6					
7	Nation				<0.001
8	Han	7489(96.7)	1213(90.6)	8702(95.8)	
9	Minority	259(3.3)	126(9.4)	385(4.2)	
10	Education				<0.001
11	Illiteracy	3703(47.8)	893(66.7)	4596(50.6)	
12	Primary school	3461(44.7)	379(28.3)	3840(42.3)	
13	Middle school or higher	584(7.5)	67(5.0)	651(7.2)	
14					
15	Marital status				<0.001
16	Single	104(1.4)	38(2.8)	142(1.6)	
17	Married	6060(78.4)	776(58.0)	6836(75.4)	
18	Widowed/Divorced	1566(20.3)	525(39.2)	2091(23.1)	
19					
20	Family economics				<0.001
21	Rich	796(10.3)	77(5.8)	873(9.6)	
22	Median	6135(79.2)	984(73.5)	7119(78.4)	
23	Poor	817(10.5)	277(20.7)	1094(12.0)	
24					
25	Smoking				<0.001
26	Current smokers	1749(22.6)	173(12.9)	1922(21.2)	
27	Ex-smokers	768(9.9)	121(9.0)	889(9.8)	
28	Never smokers	5231(67.5)	1045(78.0)	6276(69.1)	
29					
30	Drinking				<0.001
31	Current drinkers	2079(26.8)	204(15.2)	2283(25.1)	
32	Ex-drinkers	662(8.5)	158(11.8)	820(9.0)	
33	Never drinkers	5007(64.6)	977(73.0)	5984(65.9)	
34					
35	Physical exercise	1499(19.4)	190(14.2)	1689(18.6)	<0.001
36	Hypertension	3462(44.7)	648(48.4)	4110(45.2)	0.011
37	Diabetes	667(8.6)	113(8.4)	780(8.6)	0.838
38	Coronary heart disease	230(3.0)	48(3.6)	278(3.1)	0.227
39	Stroke	204(2.6)	91(6.8)	295(3.2)	<0.001
40	Depression	664(8.6)	275(20.5)	939(10.3)	<0.001
41	Body mass index	23.3±3.3	22.7±3.6	23.2±3.4	<0.001
42	Waist-to-Hip ratio	0.9±0.1	0.9±0.1	0.9±0.1	0.026
43	MMSE score	25.8±3.1	13.6±5.1	24.0±5.6	<0.001
44					
45					

Association between BMI and cognitive impairment

The mean MMSE scores were calculated by quartiles of BMI. The highest quartile of BMI had the highest mean MMSE score (24.36±5.28), and the lowest quartile had the lowest mean value (23.33±5.94). Compared with the 2nd quartile of BMI, the odds ratio (OR) of the

lowest quartile was 1.42 (95% confidence interval (CI), 1.21-1.67), the OR of the highest quartile was 0.86 (95% CI, 0.72-1.02), and the 3rd quartile had an OR value of 0.92 (95% CI, 0.77-1.08). In model 3, the OR of Q1 BMI was close to being statistically significant, and these results were essentially unchanged after adjustment for more covariates (Table 2).

Table 2. Association between body mass index and cognitive impairment

Quartiles of body mass index, kg/m ²	Odds ratio (95% confidence interval)		
	Model 1 ^a (n=9087)	Model 2 ^b (n=9068)	Model 3 ^c (n=9068)
12.1-20.8	1.42 (1.21-1.67)	1.20 (1.01-1.42)	1.18 (0.99-1.40)
>20.8-22.9	1	1	1
>22.9-25.3	0.92 (0.77-1.08)	1.02 (0.85-1.22)	1.02 (0.85-1.22)
>25.3-42.8	0.86 (0.72-1.02)	0.95 (0.79-1.14)	0.93 (0.77-1.12)

^a No covariate was included.

^b Adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physical exercise, hypertension, stroke, and depression.

Association between waist-to-hip ratio and cognitive impairment

We detected two-way interaction between BMI and WHR, and the result was significant ($P=0.002$). Further, the association between WHR and cognitive impairment was assessed under each BMI group. Under the lowest BMI group, the association between WHR and cognitive impairment was not statistically significant. The situation was similar in the 2nd and 3rd quartile of BMI. In the highest BMI group, each 0.1 higher WHR corresponded to a 1.39 folds higher risk of cognitive impairment in the basic model. The OR value remained significant after adjusting for more covariates in model 2 and model 3, which were 1.36 (95% CI, 1.10-1.69) and 1.37 (95% CI, 1.10-1.71), respectively (Table 3).

Table 3. Association of waist-to-hip ratio (per 0.1 increase) with cognitive impairment

under different body mass index group

	Quartiles of body mass index, kg/m ²			
	12.1-20.8	>20.8-22.9	>22.9-25.3	>25.3-42.8
Subjects (<i>n</i>)	2244	2266	2311	2266
Waist-to-hip ratio				
Range	0.61-1.26	0.46-1.29	0.49-1.49	0.58-1.38
Mean	0.87±0.07	0.89±0.06	0.91±0.06	0.93±0.06
Model 1 ^a	1.13 (0.98-1.31)	1.12 (0.93-1.35)	1.38 (1.14-1.65)	1.39 (1.13-1.70)
Model 2 ^b	1.01 (0.86-1.18)	0.93 (0.75-1.13)	1.13 (0.94-1.41)	1.36 (1.10-1.69)
Model 3 ^c	0.99 (0.83-1.17)	0.92 (0.75-1.13)	1.14 (0.93-1.40)	1.37 (1.10-1.71)

^a Adjusted for body mass index.

^b Based on model 1, model 2 was further adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physical exercise, hypertension, stroke, and depression.

Association between waist circumference and cognitive impairment

Similarly, we assessed the association of waist circumference with cognitive impairment within various BMI levels. When BMI, age, sex, nation, education, marital status, family economics, smoking, drinking, physical exercise, hypertension, stroke, and depression were controlled, each 1 unit higher waist circumference corresponded to a 1.02 folds higher risk of cognitive impairment among the elderly with BMI >22.9 kg/m² (Table 4).

Table 4. Association of waist circumference with cognitive impairment under different body mass index group

	Quartiles of body mass index, kg/m ²			
	12.1-20.8	>20.8-22.9	>22.9-25.3	>25.3-42.8
Subjects (<i>n</i>)	2244	2266	2311	2266
Model 1 ^a	1.03(1.01-1.05)	1.03(1.01-1.05)	1.04(1.02-1.06)	1.03(1.01-1.04)
Model 2 ^b	1.02(1.001-1.04)	1.02(0.995-1.03)	1.03(1.01-1.05)	1.02(1.01-1.04)
Model 3 ^c	1.01(0.996-1.03)	1.01(0.993-1.03)	1.02(1.004-1.05)	1.02(1.01-1.04)

^a Adjusted for body mass index.

^b Based on model 1, model 2 was further adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physical exercise, hypertension, stroke, and depression.

Discussion

In this cross-sectional study of 9087 Chinese elderly aged 60 years and older, we investigated the associations between BMI, WHR and cognitive impairment risk. We found that each 0.1 unit increase in WHR corresponded to 1.37 (1.10-1.71) evaluated cognitive impairment risk in high BMI ($>25.3 \text{ kg/m}^2$) group in the fully adjusted model (model 3).

In our study, compared with Q2 BMI ($>20.8\text{-}22.9 \text{ kg/m}^2$), Q1 BMI ($\leq 20.8 \text{ kg/m}^2$) was a risk factor for cognitive impairment, while Q4 BMI tended to be a protective factor, though not statistically significant. In previous studies, some have shown that high BMI tended to be a risk factor for cognitive decline [9-11], while others observed negative association between high BMI and cognitive function [4 5 7 8]. The inconsistency suggests the relationship between BMI and cognitive function is complex.

Zhou et al. [21] suggested that subjects who were both with obesity and dementia had a high mortality rate, which might very likely remove those with high BMI and dementia, and leave moderate or severe dementia subjects with low BMI, thus enforce the association between BMI and dementia. Assuming the survivor bias existed, the observed association between high BMI and cognition impairment would be biased towards the null, and such bias would be even more serious in cross-sectional study if it exists. Nevertheless, the hypothesis is not enough to explain the relationship between low BMI and cognitive impairment. Furthermore, several cohort studies reported that both persons with low BMI and persons with high BMI have lower cognitive functions in later life [22-26].

Among the participants of this study, the mean value of WHR tended to increase within higher BMI group. We observed a strong positive association between WHR and cognitive

1
2
3 impairment risk under Q4 BMI ($>25.3 \text{ kg/m}^2$) group. The association remained after
4
5 adjusting for covariates. Similar results were observed when evaluating association between
6
7 waist circumference and cognitive impairment. These findings led us to speculate that body
8
9 fat and muscle had reverse effect on cognition. Adipokines might be a link between body fat
10
11 and dementia. Adipokines include hundreds of polypeptides secreted by the cells of white
12
13 adipose tissue. The action of adipokines could be altered during neurodegenerative events and
14
15 might feedback to contribute to neurodegeneration [27]. Age-related reduction of muscle
16
17 mass and strength were a major public health concern in older persons. The association
18
19 between muscle and cognition could mainly derived from muscle strength. Boyle et al. [28]
20
21 found muscle strength decreased risk of AD, and Chen et al. [29] had similar findings.
22
23
24
25
26
27

28 It is noteworthy to mention that previous studies have reported high fat diet exacerbates
29
30 cognitive decline [30 31]. Amyloid deposition, and cerebral microvasculature dysfunction are
31
32 the most discussed mechanisms in relevant studies [30-33]. These findings suggest further
33
34 studies are needed to explore the mechanisms that underlie the association between obesity
35
36 and cognitive impairment.
37
38
39

40 Some limitations of the present study should be noted. One limitation is that, high fat diet,
41
42 which is an important influence factor for cognitive function as mentioned above, was not
43
44 included in this study. It is probable that high fat diet leads to central obesity with high BMI
45
46 and WHR among Chinese elderly. Further studies are needed to explore the relationship
47
48 within diet, WHR and cognitive impairment. Besides, caution would be needed when
49
50 generalizing the present findings, as our results were based on cross-sectional study.
51
52
53
54

55 **Conclusions**

56
57

1
2
3 Higher WHR significantly increase risk for cognitive impairment among the elderly with
4 BMI > 25.3 kg/m². The results of this study suggest that it is of benefit for the elderly with
5
6 high BMI to control WHR.
7
8
9

10
11 **Acknowledgments:** We acknowledge the invaluable contributions made by all the
12
13 interviewers of the Zhejiang Ageing and Health Cohort Study.
14

15
16 **Contributors:** JL, RY, TZ, QC, XY, YZ, FL, XW, FH, and C.Y. participated in the design
17
18 of the study, collection of data, data cleaning. TZ, RY, YZ, FL, XW, and CY conducted the
19
20 statistical analyses. TZ wrote the manuscript. RY, QC, XY, and JL contributed to the
21
22 interpretation of the results and revised the manuscript critically. All authors approved the
23
24 final version of the manuscript.
25
26

27
28 **Funding:** This work was supported by Zhejiang Provincial Medical and Health Science
29
30 and Technology Project (2015KYB081) and Science and Technology Bureau of Yuhuan
31
32 (201731).
33
34

35 **Competing interests:** None declared.
36

37 **Patient consent:** Obtained.
38
39

40 **Data sharing statement:** Data are not publicly available due to local ethical restrictions.
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Herrera AC, Prince M, Knapp M, et al. World Alzheimer Report 2016: Improving healthcare for people with dementia. Coverage, quality and costs now and in the future. 2016
2. Chan KY, Wang W, Wu JJ, et al. Epidemiology of Alzheimer's disease and other forms of dementia in China, 1990-2010: a systematic review and analysis. *Lancet (London, England)* 2013;**381**(9882):2016 doi: 10.1016/S0140-6736(13)60221-4.
3. Nie H, Xu Y, Liu B, et al. The prevalence of mild cognitive impairment about elderly population in China: a meta-analysis. *International journal of geriatric psychiatry* 2011;**26**(6):558–63 doi: 10.1002/gps.2579.
4. Qizilbash N, Gregson J, Johnson ME, et al. BMI and risk of dementia in two million people over two decades: a retrospective cohort study. *Lancet Diabetes & Endocrinology* 2015;**3**(6):431-36 doi: 10.1016/S2213-8587(15)00033-9.
5. Tolppanen AM, Ngandu T, K  reholt I, et al. Midlife and late-life body mass index and late-life dementia: results from a prospective population-based cohort. *Journal of Alzheimers Disease* 2014;**38**(1):201 doi: 10.3233/JAD-130698.
6. Monda V, Marra ML, Perrella R, et al. Obesity and brain illness: from cognitive and psychological evidences to obesity paradox. *Diabetes Metabolic Syndrome & Obesity Targets & Therapy* 2017;**10**(1):473.
7. Tikhonoff V, Casiglia E, Guidotti F, et al. Body fat and the cognitive pattern: A population-based study. *Obesity* 2015;**23**(7):1502-10 doi: 10.1002/oby.21114.
8. Kim S, Kim Y, Park SM. Body Mass Index and Decline of Cognitive Function. *Plos One* 2016;**11**(2):e0148908 doi: 10.1371/journal.pone.0148908.
9. Gunstad J, Lhotsky A, Wendell CR, et al. Longitudinal Examination of Obesity and Cognitive Function: Results from the Baltimore Longitudinal Study of Aging. *Neuroepidemiology* 2010;**34**(4):222-29 doi: 10.1159/000297742.
10. Gallucci M, Mazzuco S, Ongaro F, et al. Body mass index, lifestyles, physical performance and cognitive decline: The "Treviso Longeva (Trelong)" study. *Journal of Nutrition Health & Aging* 2013;**17**(4):378-84 doi: 10.1007/s12603-012-0397-1.
11. Besser LM, Gill DP, Monsell SE, et al. Body mass index, weight change, and clinical progression in mild cognitive impairment and Alzheimer disease. *Alzheimer disease and associated disorders* 2014;**28**(1):36-43 doi: 10.1097/WAD.0000000000000005.
12. Smith E, Hay P, Campbell L, et al. A review of the relationship between obesity and cognition across the lifespan: Implications for novel approaches to prevention and treatment. *Obesity Reviews* 2011;**12**(9):740-55 doi: 10.1111/j.1467-789X.2011.00920.x.
13. Benito-Leon J, Mitchell AJ, Hernandez-Gallego J, et al. Obesity and impaired cognitive functioning in the elderly: a population-based cross-sectional study (NEDICES). *Eur J Neurol* 2013;**20**(6):899-906, e76-7 doi: 10.1111/ene.12083.
14. Turcato E, Bosello O, Di FV, et al. Waist circumference and abdominal sagittal diameter as surrogates of body fat distribution in the elderly: their relation with cardiovascular risk factors. *International Journal of Obesity & Related Metabolic Disorders* *Journal of the International Association for the Study of Obesity* 2000;**24**(8):1005 doi: 10.1038/sj.ijo.0801352.
15. Villareal DT, Apovian CM, Kushner RF, et al. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *American Journal of Clinical Nutrition* 2005;**82**(5):923-34 doi: 10.1038/oby.2005.228.
16. Sharma S, Batsis JA, Coutinho T, et al. Normal-Weight Central Obesity and Mortality Risk in Older Adults

- 1
2
3 With Coronary Artery Disease. *Mayo Clinic Proceedings* 2016;**91**(3):343.
- 4 17. Sahakyan KR, Somers VK, Rodriguezscudero JP, et al. Normal-Weight Central Obesity: Implications for Total
5 and Cardiovascular Mortality. *Annals of Internal Medicine* 2015;**163**(11):827-35.
- 6 18. Zhengyu W, mingyuan Z. Application of Chinese version of Mini-Mental State examination (MMSE).
7 *Shanghai Archives of Psychiatry* 1989(3):108-11.
- 8 19. Li F, He F, Chen T, et al. Reproductive History and Risk of Cognitive Impairment in Elderly Women: A
9 Cross-Sectional Study in Eastern China. *Journal of Alzheimer's Disease* 2016;**49**(1):139-47 doi:
10 10.3233/JAD-150444.
- 11 20. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern*
12 *Med* 2001;**16**(9):606-13 doi: 10.1046/j.1525-1497.2001.016009606.x.
- 13 21. Zhou Y, Flaherty JH, Huang CQ, et al. Association between body mass index and cognitive function among
14 Chinese nonagenarians/centenarians. *Dementia & Geriatric Cognitive Disorders* 2010;**30**(6):517 doi:
15 10.1159/000322110.
- 16 22. Sabia S, Nabi H, Kivimaki M, et al. Health behaviors from early to late midlife as predictors of cognitive
17 function: The Whitehall II study. *American journal of epidemiology* 2009;**170**(4):428-37 doi:
18 10.1093/aje/kwp161.
- 19 23. Dahl AK, Hassing LB, Fransson EI, et al. Body mass index across midlife and cognitive change in late life.
20 *International journal of obesity* 2013;**37**(2):296-302 doi: 10.1038/ijo.2012.37.
- 21 24. Sturman MT, de Leon CF, Bienias JL, et al. Body mass index and cognitive decline in a biracial community
22 population. *Neurology* 2008;**70**(5):360-7 doi: 10.1212/01.wnl.0000285081.04409.bb.
- 23 25. Arvanitakis Z, Capuano AW, Bennett DA, et al. Body mass index and decline in cognitive function in older
24 black and white persons. *Journals of Gerontology* 2017 doi: 10.1093/gerona/glx152.
- 25 26. Wang F, Zhao M, Han Z, et al. Association of body mass index with amnesic and non-amnesic mild
26 cognitive impairment risk in elderly. *BMC Psychiatry* 2017;**17**(1):334 doi: 10.1186/s12888-017-1493-x.
- 27 27. Kiliaan AJ, Arnoldussen IA, Gustafson DR. Adipokines: a link between obesity and dementia? *Lancet*
28 *Neurology* 2014;**13**(9):913-23 doi: 10.1016/S1474-4422(14)70085-7.
- 29 28. Boyle PA, Buchman AS, Wilson RS, et al. Association of Muscle Strength with the Risk of Alzheimer's Disease
30 and the Rate of Cognitive Decline in Community-Dwelling Older Persons. *Archives of Neurology*
31 2009;**66**(11):1339
- 32 29. Chen WL, Peng TC, Sun YS, et al. Examining the Association Between Quadriceps Strength and Cognitive
33 Performance in the Elderly. *Medicine* 2015;**94**(32):e1335
- 34 30. Theriault P, ElAli A, Rivest S. High fat diet exacerbates Alzheimer's disease-related pathology in APPswe/PS1
35 mice. *Oncotarget* 2016;**7**(42):67808-27 doi: 10.18632/oncotarget.12179.
- 36 31. Lin B, Yu H, Koki T, et al. High-Fat-Diet Intake Enhances Cerebral Amyloid Angiopathy and Cognitive
37 Impairment in a Mouse Model of Alzheimer's Disease, Independently of Metabolic Disorders. *Journal*
38 *of the American Heart Association Cardiovascular & Cerebrovascular Disease* 2016;**5**(6):e003154 doi:
39 10.1161/JAHA.115.003154.
- 40 32. Pimentel-Coelho PM, Rivest S. The early contribution of cerebrovascular factors to the pathogenesis of
41 Alzheimer's disease. *The European journal of neuroscience* 2012;**35**(12):1917-37 doi:
42 10.1111/j.1460-9568.2012.08126.x.
- 43 33. Zlokovic BV. Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders.
44 *Nature reviews Neuroscience* 2011;**12**(12):723-38 doi: 10.1038/nrn3114.
- 45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract (Page 1-3)	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale (Page 4-5)	2	Explain the scientific background and rationale for the investigation being reported
Objectives (Page 5)	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design (Page 5)	4	Present key elements of study design early in the paper
Setting (Page 5)	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants (Page 5)	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables (Page 5-6)	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement (Page 5-6)	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods (Page 7)	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses

Continued on next page

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data (Page 5-9)	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data (Page 8-9)	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results (Page 8-11)	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results (Page 11-12)	18	Summarise key results with reference to study objectives
Limitations (Page 13)	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation (Page 11-13)	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability (Page 13)	21	Discuss the generalisability (external validity) of the study results

Other information

Funding (Page 14)	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
----------------------	----	---

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Body Mass Index, Waist-to-Hip Ratio and Cognitive Function among Chinese Elderly: A Cross-Sectional Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-022055.R2
Article Type:	Research
Date Submitted by the Author:	07-Sep-2018
Complete List of Authors:	Zhang, Tao; Zhejiang Provincial Center for Disease Control and Prevention Yan, Rui; Zhejiang Provincial Center for Disease Control and Prevention Chen, Qifeng; Shaoxing Center for Disease Control and Prevention Ying, Xuhua; Yuhuan Center for Disease Control and Prevention Zhai, Yujia; Zhejiang Provincial Center for Disease Control and Prevention Li, Fudong; Zhejiang Provincial Center for Disease Control and Prevention Wang, Xinyi; Zhejiang Provincial Center for Disease Control and Prevention He, Fan; Zhejiang Provincial Center for Disease Control and Prevention Ye, Chiyu; Zhejiang Provincial Center for Disease Control and Prevention Lin, Junfen; Zhejiang Provincial Center for Disease Control and Prevention
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	cognitive impairment, body mass index, abdominal obesity, elderly, Chinese

SCHOLARONE™
Manuscripts

1
2
3 **Body Mass Index, Waist-to-Hip Ratio and Cognitive Function among Chinese Elderly:**
4 **A Cross-Sectional Study**
5

6 Tao Zhang ^{a,1}, Rui Yan ^{a,1}, Qifeng Chen ^{b,1}, Xuhua Ying ^c, Yujia Zhai ^a, Fudong Li ^a, Xinyi
7 Wang ^a, Fan He ^a, Chiyu Ye ^a, Junfen Lin ^{a,*}
8
9

10 ^a *Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, Zhejiang, China*
11

12 ^b *Shaoxing Center for Disease Control and Prevention, Shaoxing, Zhejiang, China*
13

14 ^c *Yuhuan Center for Disease Control and Prevention, Taizhou, Zhejiang, China*
15

16 ¹ These authors contributed equally to this work
17

18 **Correspondence to:** Junfen Lin, No.3399, Binsheng Rd., Binjiang District, Hangzhou,
19

20 P.R.China; +86-571-87115131; zjlinjunfen@163.com
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Objectives: To investigate the associations between body mass index (BMI), waist-to-hip ratio (WHR) and cognitive function among Chinese elderly.

Design: Cross-sectional study.

Setting: Community.

Participants: Data were obtained from the baseline survey of a community-based cohort in Zhejiang Province, and 9 326 persons aged 60 years and older were enrolled.

Primary outcome measures: We investigated the association between BMI and cognition, and then explored the association between WHR and cognition across different quartiles of BMI.

Results: A sample of 9 087 persons was used in this study, including 4 375 men and 4 712 women. Higher WHR increased cognitive impairment risk in those with BMI > 25.3 kg/m² (OR (per 0.1 increase), 1.39; 95% CI, 1.13-1.70). No statistically significant association was found in other BMI categories.

Conclusions: Higher WHR could increase the risk for cognitive impairment among elderly with BMI > 25.3 kg/m². Our results suggest that it could be of benefit to the elderly with high BMI to control WHR.

Strengths and limitations of this study:

1. The strength of this study was the in-depth analysis of the association between waist-to-hip ratio and cognitive impairment across different body mass index categories.
2. High-fat diet, which is an important influence factor for cognitive function, was not included in this study.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

3. Since this was a cross-sectional study, caution would be needed when generalizing the present findings.

Keywords: cognitive function, body mass index, abdominal obesity, elderly, Chinese

For peer review only

Introduction

Cognitive impairment is an important health issue in the elderly. According to Alzheimer's Disease International (ADI) [1], an estimated 46.8 million people currently have dementia in the world, the most well-known form of cognitive impairment, and this number will rise to 131.5 million in 2050. ADI estimated over 9.5 million people with dementia in China, which was 20% of the total number of dementia cases in the world. By 2030, the number of people living with dementia in China is expected to rise to over 16 million. The incidence of dementia in people aged 60 years and older is 9.87 cases per 1000 person-years in China [2], and the situation of cognitive impairment would be more serious [3].

Obesity was normally recognized as an influence factor of dementia [4 5]. The possible reasons included inflammation and β -amyloid metabolism, which had been observed connection with obesity [6]. However, studies on association between BMI and cognitive impairment in the elderly have shown conflicting results: both positive and negative association have been reported [7-11]. There is a limitation of BMI when comparing individuals with the same weight and height but different body fat mass. BMI is affected by both fat and fat-free mass, which may have opposite effects on health [12]. Using BMI as a surrogate for obesity may be particularly problematic in the elderly due to the effect of aging on fat distribution [13]. Waist-to-hip ratio (WHR), as a proxy for body fat distribution, would be a complementary indicator in health-related studies for the elderly. It has been reported that high WHR was associated with adverse health outcomes independent of BMI [14 15]. Actually, high WHR could increase death even with normal BMI [16 17]. Therefore, it would be necessary to evaluate the effect of WHR when BMI was within a certain range.

1
2
3 However, to our knowledge, studies evaluating the association between BMI-specific
4 WHR and cognitive impairment in a large Chinese elderly population were lacking. To help
5
6 shed light on this area, we investigated the associations between BMI, WHR and cognitive
7
8 impairment among Chinese aged 60 years and older.
9
10

11 **Materials and Methods**

12 **Study Population**

13
14
15 The present study used data collected from the baseline survey of a community-based
16
17 cohort study focusing on aging and health problems among the elderly in Zhejiang Province,
18
19 China since 2014. In brief, 6 out of 90 counties were randomly selected from Zhejiang
20
21 Province, with at least 1 500 participants were randomly recruited in each county for
22
23 participation in 2014. Inclusion criteria were as following: 1) permanent residents who lived
24
25 for over 6 months in the past year; 2) aged 60 years and above. Exclusion criterion was an
26
27 inability to complete the interview due to physical disability. Finally, 9 326 subjects were
28
29 enrolled, with a response rate of 76%. During the baseline survey, we performed
30
31 questionnaire-based interview, physical examinations and laboratory tests for each participant.
32
33 Informed consent was obtained from each participant, and the study was approved by the
34
35 Ethics Committee of Zhejiang Provincial Center for Disease Control and Prevention. A total
36
37 of 239 participants were excluded because of missing values in age, Chinese language
38
39 version of the Mini-Mental State Examination (MMSE) score, or BMI, leaving 9 087
40
41 available for analyses.
42
43
44
45
46
47
48
49
50

51 **Cognitive Function**

52
53
54 Cognitive function was determined by MMSE, which included 30 items. The maximum
55
56

1
2
3 score of MMSE is 30, and higher scores indicate better cognitive function. According to
4
5
6 Wang et al., the questionnaire of MMSE has good reliability and validity as an instrument to
7
8 detect cognitive impairment among Chinese [18]. The cut-off score of cognitive impairment
9
10 is education-specific: 17/18 for illiteracy, 20/21 for people with primary education level,
11
12
13 24/25 for people with higher than primary education level [19].
14

15 **Body Mass Index (BMI)**

16
17
18 BMI (kg/m^2) was calculated as a person's body weight (in kilograms) divided by the
19
20 square of the body height (in meters). Body weight and height were measured by digital
21
22 weight and height scale, respectively. All the participants were asked to remove shoes, heavy
23
24 clothing, and hats prior to height and weight measurements, and had the participants stand
25
26 straight with heels together, legs straight, and looking straight ahead.
27
28
29

30 **WHR**

31
32
33 Waist circumference was measured midway between the lower rib margin and the iliac
34
35 crest, with a soft cloth tape measure. Hip circumference was measured at the level of the
36
37 widest circumference over the greater trochanters, with a soft cloth tape measure. In the
38
39 baseline survey, waist circumference and hip circumference were measured twice, and the
40
41 difference of two measured values was restricted in ± 2 centimeters. WHR was calculated as a
42
43 person's waist circumference divided by the hip circumference. In this study, waist
44
45 circumference and hip circumference were calculated as the mean of two measured values.
46
47
48
49

50 **Covariates**

51
52 Covariates were collected by face-to-face interview with questionnaire, including: age,
53
54 race, education level (self-reported), marital status (self-reported), economic status
55
56
57

1
2
3 (self-reported), smoking (self-reported), alcohol drinking (self-reported), physical exercise
4
5
6 (activities which were carried out to sustain or improve health and fitness in one's spare time),
7
8 hypertension (diagnosed by doctors), diabetes (diagnosed by doctors), coronary heart disease
9
10 (diagnosed by doctors), and depressive symptom. Depressive symptom was determined using
11
12 the Patient Health Questionnaire- 9 scale (PHQ-9). Those scored 5 or above were defined as
13
14 depression [20].
15
16

17 18 **Statistical Analysis** 19

20
21 Descriptive statistics were applied to illustrate the socio-demographic and health
22
23 characteristics of the enrolled participants. Differences of the characteristics across different
24
25 cognitive status groups were assessed by *t*-test for continuous variables, and by Chi-square
26
27 test for categorical variables. Logistic regressions were used to examine the associations
28
29 between BMI, WHR and cognitive impairment. BMI was evaluated as a categorical variable,
30
31 divided by quartiles. WHR was evaluated under different BMI levels. Both BMI and WHR
32
33 were assessed by 3 logistic models. In the basic model (model 1), no covariate was included
34
35 when assessing the association between BMI and cognitive impairment, and BMI was
36
37 adjusted when assessing the association between WHR and cognitive impairment. Model 2
38
39 was based on model 1, with additional adjusting for socio-demographic variables (age, sex,
40
41 nation, education, marital status, and family economics). Model 3 was based on model 2,
42
43 with additional adjustments of lifestyles (smoking, drinking, and physic exercise) and health
44
45 variables (hypertension, stroke, and depression).
46
47
48
49
50
51

52 All statistical analyses were performed by SAS 9.4 (SAS Institute Inc., Cary, NC), and
53
54 two-tailed *P*-value <0.05 was considered statistically significant.
55
56

Patient and Public Involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Results

Socio-demographics and health Characteristics

Of the 9 087 subjects, 1 339 (14.7%) were defined as cognitive impairment by MMSE. The mean age of all subjects was 69.8 (± 8.3). More than a half (51.9%) were female. Among the subjects with cognitive impairment, the mean MMSE score was 13.6 (± 5.1), while the mean score was 25.8 (± 3.1) in normal cognition group. The mean values of BMI and WHR were 22.7 \pm 3.6, 0.9 \pm 0.1, respectively in the cognitive impairment group, and the mean values were 23.3 \pm 3.3, 0.9 \pm 0.1, respectively in normal cognition group. Differences of BMI and WHR between the two groups were both statistically significant. The subjects with cognitive impairment tended to be older, female, minority ethnic group, without physical exercise, with hypertension, with stroke, with depression. Also, cognitive impairment was associated with education, marital status, family economics, smoking, and drinking. More details are shown in Table 1.

Table 1. Socio-demographics and health characteristics of 9087 participants by cognitive status

Characteristics	Normal cognition (n=7748)	Cognitive impairment (n=1339)	Overall	<i>P</i>
Age, years(mean, SD)	68.8 \pm 7.8	75.4 \pm 8.5	69.8 \pm 8.3	<0.001
Sex				<0.001
Male	3877(50.0)	498(37.2)	4375(48.1)	

1					
2					
3	Female	3871(50.0)	841(62.8)	4712(51.9)	
4	Nation				<0.001
5	Han	7489(96.7)	1213(90.6)	8702(95.8)	
6	Minority	259(3.3)	126(9.4)	385(4.2)	
7					
8	Education				<0.001
9	Illiteracy	3703(47.8)	893(66.7)	4596(50.6)	
10	Primary school	3461(44.7)	379(28.3)	3840(42.3)	
11	Middle school or higher	584(7.5)	67(5.0)	651(7.2)	
12					
13	Marital status				<0.001
14	Single	104(1.4)	38(2.8)	142(1.6)	
15	Married	6060(78.4)	776(58.0)	6836(75.4)	
16	Windowed/Divorced	1566(20.3)	525(39.2)	2091(23.1)	
17					
18	Family economics				<0.001
19	Rich	796(10.3)	77(5.8)	873(9.6)	
20	Median	6135(79.2)	984(73.5)	7119(78.4)	
21	Poor	817(10.5)	277(20.7)	1094(12.0)	
22					
23	Smoking				<0.001
24	Current smokers	1749(22.6)	173(12.9)	1922(21.2)	
25	Ex-smokers	768(9.9)	121(9.0)	889(9.8)	
26	Never smokers	5231(67.5)	1045(78.0)	6276(69.1)	
27					
28	Drinking				<0.001
29	Current drinkers	2079(26.8)	204(15.2)	2283(25.1)	
30	Ex-drinkers	662(8.5)	158(11.8)	820(9.0)	
31	Never drinkers	5007(64.6)	977(73.0)	5984(65.9)	
32	Physical exercise	1499(19.4)	190(14.2)	1689(18.6)	<0.001
33	Hypertension	3462(44.7)	648(48.4)	4110(45.2)	0.011
34	Diabetes	667(8.6)	113(8.4)	780(8.6)	0.838
35	Coronary heart disease	230(3.0)	48(3.6)	278(3.1)	0.227
36	Stroke	204(2.6)	91(6.8)	295(3.2)	<0.001
37	Depression	664(8.6)	275(20.5)	939(10.3)	<0.001
38	Body mass index	23.3±3.3	22.7±3.6	23.2±3.4	<0.001
39	Waist-to-Hip ratio	0.9±0.1	0.9±0.1	0.9±0.1	0.026
40	MMSE score	25.8±3.1	13.6±5.1	24.0±5.6	<0.001
41					
42					
43					
44					

Association between BMI and cognitive impairment

The mean MMSE scores were calculated by quartiles of BMI. Subjects in the highest BMI quartile category had the highest mean MMSE score (24.36±5.28), and those in the lowest quartile category had the lowest mean MMSE value (23.33±5.94). Compared with the 2nd quartile of BMI, the odds ratio (OR) of the lowest quartile was 1.42 (95% confidence

interval (CI), 1.21-1.67), the OR of the highest quartile was 0.86 (95% CI, 0.72-1.02), and the 3rd quartile had an OR value of 0.92 (95% CI, 0.77-1.08). In model 3, the OR of Q1 BMI was close to being statistically significant, and these results were essentially unchanged after adjustment for more covariates (Table 2).

Table 2. Association between body mass index and cognitive impairment

Quartiles of body mass index, kg/m ²	Odds ratio (95% confidence interval)		
	Model 1 ^a (n=9087)	Model 2 ^b (n=9068)	Model 3 ^c (n=9068)
12.1-20.8	1.42 (1.21-1.67)	1.20 (1.01-1.42)	1.18 (0.99-1.40)
>20.8-22.9	1	1	1
>22.9-25.3	0.92 (0.77-1.08)	1.02 (0.85-1.22)	1.02 (0.85-1.22)
>25.3-42.8	0.86 (0.72-1.02)	0.95 (0.79-1.14)	0.93 (0.77-1.12)

^a No covariate was included.

^b Adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physical exercise, hypertension, stroke, and depression.

Association between waist-to-hip ratio and cognitive impairment

We detected two-way interaction between BMI and WHR, and the result was statistically significant ($P=0.002$). Further, the association between WHR and cognitive impairment was assessed under each BMI group. Under the lowest BMI group, the association between WHR and cognitive impairment was not statistically significant. Similar results were found in the 2nd and 3rd quartile of BMI. In the highest BMI group, each 0.1 higher WHR corresponded to a 1.39 folds higher risk of cognitive impairment in the basic model. The OR value remained significant after adjusting for more covariates in model 2 and model 3, which were 1.36 (95% CI, 1.10-1.69) and 1.37 (95% CI, 1.10-1.71), respectively (Table 3).

Table 3. Association of waist-to-hip ratio (per 0.1 increase) with cognitive impairment under different body mass index group

	Quartiles of body mass index, kg/m ²			
	12.1-20.8	>20.8-22.9	>22.9-25.3	>25.3-42.8
Subjects (<i>n</i>)	2244	2266	2311	2266
Waist-to-hip ratio				
Range	0.61-1.26	0.46-1.29	0.49-1.49	0.58-1.38
Mean	0.87±0.07	0.89±0.06	0.91±0.06	0.93±0.06
Model 1 ^a	1.13 (0.98-1.31)	1.12 (0.93-1.35)	1.38 (1.14-1.65)	1.39 (1.13-1.70)
Model 2 ^b	1.01 (0.86-1.18)	0.93 (0.75-1.13)	1.13 (0.94-1.41)	1.36 (1.10-1.69)
Model 3 ^c	0.99 (0.83-1.17)	0.92 (0.75-1.13)	1.14 (0.93-1.40)	1.37 (1.10-1.71)

^a Adjusted for body mass index.

^b Based on model 1, model 2 was further adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physical exercise, hypertension, stroke, and depression.

Association between waist circumference and cognitive impairment

Similarly, we assessed the associations between waist circumference and cognitive impairment within various BMI levels. When BMI, age, sex, nation, education, marital status, family economics, smoking, drinking, physic exercise, hypertension, stroke, and depression were controlled, each 1 unit higher waist circumference corresponded to a 1.02 folds higher risk of cognitive impairment among the elderly with BMI >22.9 kg/m² (Table 4).

Table 4. Association of waist circumference with cognitive impairment under different body mass index group

	Quartiles of body mass index, kg/m ²			
	12.1-20.8	>20.8-22.9	>22.9-25.3	>25.3-42.8
Subjects (<i>n</i>)	2244	2266	2311	2266
Model 1 ^a	1.03(1.01-1.05)	1.03(1.01-1.05)	1.04(1.02-1.06)	1.03(1.01-1.04)
Model 2 ^b	1.02(1.001-1.04)	1.02(0.995-1.03)	1.03(1.01-1.05)	1.02(1.01-1.04)
Model 3 ^c	1.01(0.996-1.03)	1.01(0.993-1.03)	1.02(1.004-1.05)	1.02(1.01-1.04)

^a Adjusted for body mass index.

^b Based on model 1, model 2 was further adjusted for age, sex, nation, education, marital status, and family economics.

^c Based on model 2, model 3 was further adjusted for smoking, drinking, physical exercise, hypertension, stroke, and depression.

Discussion

In this cross-sectional study of 9087 Chinese elderly aged 60 years and older, we investigated the associations between BMI, WHR and cognitive impairment risk. We found that each 0.1 unit increase in WHR corresponded to 1.37 (1.10-1.71) evaluated cognitive impairment risk in high BMI ($>25.3 \text{ kg/m}^2$) group in the fully adjusted model (model 3).

In our study, compared with Q2 BMI ($>20.8\text{-}22.9 \text{ kg/m}^2$), Q1 BMI ($\leq 20.8 \text{ kg/m}^2$) was a risk factor for cognitive impairment, while Q4 BMI tended to be a protective factor, though not statistically significant. In previous studies, some reported that high BMI tended to be a risk factor for cognitive decline [9-11], while others observed a negative association between high BMI and cognitive function [4 5 7 8]. The inconsistency suggests the complex relationship between BMI and cognitive function.

Zhou et al. [21] suggested that subjects who were both with obesity and dementia had a high mortality rate, which might very likely remove those with high BMI and dementia, and leave moderate or severe dementia subjects with low BMI, thus enforce the association between BMI and dementia. Assuming the survivor bias existed, the observed association between high BMI and cognition impairment would be biased towards the null, and such bias would be even more serious in cross-sectional study if it exists. Nevertheless, the hypothesis is not enough to explain the relationship between low BMI and cognitive impairment. Furthermore, several cohort studies reported that both persons with low BMI and persons with high BMI had lower cognitive functions in later life [22-26].

Among the participants of this study, the mean value of WHR tended to increase within higher BMI group. We observed a strong positive association between WHR and cognitive

1
2
3 impairment risk under Q4 BMI ($>25.3 \text{ kg/m}^2$) group. The association remained after
4
5 adjusting for covariates. Similar results were observed when evaluating the association
6
7 between waist circumference and cognitive impairment. These findings led us to speculate
8
9 that body fat and muscle had a reverse effect on cognition. Adipokines might be a link
10
11 between body fat and dementia. Adipokines include hundreds of polypeptides secreted by the
12
13 cells of white adipose tissue. The action of adipokines could be altered during
14
15 neurodegenerative events and might feedback to contribute to neurodegeneration [27].
16
17
18 Age-related reduction of muscle mass and strength is a major public health concern in older
19
20 persons. The association between muscle and cognition could mainly be derived from muscle
21
22 strength. Boyle et al. [28] found that high muscle strength decreased the risk of AD, and Chen
23
24 et al. [29] had similar findings.
25
26
27
28
29

30 It is noteworthy to mention that previous studies have reported high-fat diet exacerbates
31
32 cognitive decline [30-31]. Amyloid deposition and cerebral microvasculature dysfunction are
33
34 the most discussed mechanisms in relevant studies [30-33]. These findings suggest further
35
36 studies are needed to explore the mechanisms that underlie the association between obesity
37
38 and cognitive impairment.
39
40
41

42 Some limitations of the present study should be noted. One limitation is that, high-fat diet,
43
44 which is an important influence factor for cognitive function as mentioned above, was not
45
46 included in this study. It is probable that high-fat diet leads to central obesity with high BMI
47
48 and WHR among Chinese elderly. Further studies are needed to explore the relationship
49
50 within diet, WHR, and cognitive impairment. Besides, caution would be needed when
51
52 generalizing the present findings, as our results were based on a cross-sectional study.
53
54
55
56
57

Conclusions

Higher WHR significantly increases the risk for cognitive impairment among the elderly with BMI > 25.3 kg/m². The results of this study suggest that it is of benefit to the elderly with high BMI to control WHR.

Acknowledgments: We acknowledge the invaluable contributions made by all the interviewers of the Zhejiang Ageing and Health Cohort Study.

Contributors: JL, RY, TZ, QC, XY, YZ, FL, XW, FH, and C.Y. participated in the design of the study, collection of data, data cleaning. TZ, RY, YZ, FL, XW, and CY conducted the statistical analyses. TZ wrote the manuscript. RY, QC, XY, and JL contributed to the interpretation of the results and revised the manuscript critically. All authors approved the final version of the manuscript.

Funding: This work was supported by Zhejiang Provincial Medical and Health Science and Technology Project (2015KYB081, 2017KY285) and Science and Technology Bureau of Yuhuan (201731).

Competing interests: None declared.

Patient consent: Obtained.

Data sharing statement: Data are not publicly available due to local ethical restrictions.

References

1. Herrera AC, Prince M, Knapp M, et al. World Alzheimer Report 2016: Improving healthcare for people with dementia. Coverage, quality and costs now and in the future. 2016
2. Chan KY, Wang W, Wu JJ, et al. Epidemiology of Alzheimer's disease and other forms of dementia in China, 1990-2010: a systematic review and analysis. *Lancet (London, England)* 2013;**381**(9882):2016 doi: 10.1016/S0140-6736(13)60221-4.
3. Nie H, Xu Y, Liu B, et al. The prevalence of mild cognitive impairment about elderly population in China: a meta-analysis. *International journal of geriatric psychiatry* 2011;**26**(6):558–63 doi: 10.1002/gps.2579.
4. Qizilbash N, Gregson J, Johnson ME, et al. BMI and risk of dementia in two million people over two decades: a retrospective cohort study. *Lancet Diabetes & Endocrinology* 2015;**3**(6):431-36 doi: 10.1016/S2213-8587(15)00033-9.
5. Tolppanen AM, Ngandu T, K areholt I, et al. Midlife and late-life body mass index and late-life dementia: results from a prospective population-based cohort. *Journal of Alzheimers Disease* 2014;**38**(1):201 doi: 10.3233/JAD-130698.
6. Monda V, Marra ML, Perrella R, et al. Obesity and brain illness: from cognitive and psychological evidences to obesity paradox. *Diabetes Metabolic Syndrome & Obesity Targets & Therapy* 2017;**10**(1):473.
7. Tikhonoff V, Casiglia E, Guidotti F, et al. Body fat and the cognitive pattern: A population-based study. *Obesity* 2015;**23**(7):1502-10 doi: 10.1002/oby.21114.
8. Kim S, Kim Y, Park SM. Body Mass Index and Decline of Cognitive Function. *Plos One* 2016;**11**(2):e0148908 doi: 10.1371/journal.pone.0148908.
9. Gunstad J, Lhotsky A, Wendell CR, et al. Longitudinal Examination of Obesity and Cognitive Function: Results from the Baltimore Longitudinal Study of Aging. *Neuroepidemiology* 2010;**34**(4):222-29 doi: 10.1159/000297742.
10. Gallucci M, Mazzuco S, Ongaro F, et al. Body mass index, lifestyles, physical performance and cognitive decline: The "Treviso Longeva (Trelong)" study. *Journal of Nutrition Health & Aging* 2013;**17**(4):378-84 doi: 10.1007/s12603-012-0397-1.
11. Besser LM, Gill DP, Monsell SE, et al. Body mass index, weight change, and clinical progression in mild cognitive impairment and Alzheimer disease. *Alzheimer disease and associated disorders* 2014;**28**(1):36-43 doi: 10.1097/WAD.0000000000000005.
12. Smith E, Hay P, Campbell L, et al. A review of the relationship between obesity and cognition across the lifespan: Implications for novel approaches to prevention and treatment. *Obesity Reviews* 2011;**12**(9):740-55 doi: 10.1111/j.1467-789X.2011.00920.x.
13. Benito-Leon J, Mitchell AJ, Hernandez-Gallego J, et al. Obesity and impaired cognitive functioning in the elderly: a population-based cross-sectional study (NEDICES). *Eur J Neurol* 2013;**20**(6):899-906, e76-7 doi: 10.1111/ene.12083.
14. Turcato E, Bosello O, Di FV, et al. Waist circumference and abdominal sagittal diameter as surrogates of body fat distribution in the elderly: their relation with cardiovascular risk factors. *International Journal of Obesity & Related Metabolic Disorders* *Journal of the International Association for the Study of Obesity* 2000;**24**(8):1005 doi: 10.1038/sj.ijo.0801352.
15. Villareal DT, Apovian CM, Kushner RF, et al. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *American Journal of Clinical Nutrition* 2005;**82**(5):923-34 doi: 10.1038/oby.2005.228.
16. Sharma S, Batsis JA, Coutinho T, et al. Normal-Weight Central Obesity and Mortality Risk in Older Adults

- 1
2
3 With Coronary Artery Disease. *Mayo Clinic Proceedings* 2016;**91**(3):343.
- 4 17. Sahakyan KR, Somers VK, Rodriguezscudero JP, et al. Normal-Weight Central Obesity: Implications for Total
5 and Cardiovascular Mortality. *Annals of Internal Medicine* 2015;**163**(11):827-35.
- 6 18. Zhengyu W, mingyuan Z. Application of Chinese version of Mini-Mental State examination (MMSE).
7 *Shanghai Archives of Psychiatry* 1989(3):108-11.
- 8 19. Li F, He F, Chen T, et al. Reproductive History and Risk of Cognitive Impairment in Elderly Women: A
9 Cross-Sectional Study in Eastern China. *Journal of Alzheimer's Disease* 2016;**49**(1):139-47 doi:
10 10.3233/JAD-150444.
- 11 20. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern*
12 *Med* 2001;**16**(9):606-13 doi: 10.1046/j.1525-1497.2001.016009606.x.
- 13 21. Zhou Y, Flaherty JH, Huang CQ, et al. Association between body mass index and cognitive function among
14 Chinese nonagenarians/centenarians. *Dementia & Geriatric Cognitive Disorders* 2010;**30**(6):517 doi:
15 10.1159/000322110.
- 16 22. Sabia S, Nabi H, Kivimaki M, et al. Health behaviors from early to late midlife as predictors of cognitive
17 function: The Whitehall II study. *American journal of epidemiology* 2009;**170**(4):428-37 doi:
18 10.1093/aje/kwp161.
- 19 23. Dahl AK, Hassing LB, Fransson EI, et al. Body mass index across midlife and cognitive change in late life.
20 *International journal of obesity* 2013;**37**(2):296-302 doi: 10.1038/ijo.2012.37.
- 21 24. Sturman MT, de Leon CF, Bienias JL, et al. Body mass index and cognitive decline in a biracial community
22 population. *Neurology* 2008;**70**(5):360-7 doi: 10.1212/01.wnl.0000285081.04409.bb.
- 23 25. Arvanitakis Z, Capuano AW, Bennett DA, et al. Body mass index and decline in cognitive function in older
24 black and white persons. *Journals of Gerontology* 2017 doi: 10.1093/gerona/glx152.
- 25 26. Wang F, Zhao M, Han Z, et al. Association of body mass index with amnesic and non-amnesic mild
26 cognitive impairment risk in elderly. *BMC Psychiatry* 2017;**17**(1):334 doi: 10.1186/s12888-017-1493-x.
- 27 27. Kiliaan AJ, Arnoldussen IA, Gustafson DR. Adipokines: a link between obesity and dementia? *Lancet*
28 *Neurology* 2014;**13**(9):913-23 doi: 10.1016/S1474-4422(14)70085-7.
- 29 28. Boyle PA, Buchman AS, Wilson RS, et al. Association of Muscle Strength with the Risk of Alzheimer's Disease
30 and the Rate of Cognitive Decline in Community-Dwelling Older Persons. *Archives of Neurology*
31 2009;**66**(11):1339
- 32 29. Chen WL, Peng TC, Sun YS, et al. Examining the Association Between Quadriceps Strength and Cognitive
33 Performance in the Elderly. *Medicine* 2015;**94**(32):e1335
- 34 30. Theriault P, ElAli A, Rivest S. High fat diet exacerbates Alzheimer's disease-related pathology in APPswe/PS1
35 mice. *Oncotarget* 2016;**7**(42):67808-27 doi: 10.18632/oncotarget.12179.
- 36 31. Lin B, Yu H, Koki T, et al. High-Fat-Diet Intake Enhances Cerebral Amyloid Angiopathy and Cognitive
37 Impairment in a Mouse Model of Alzheimer's Disease, Independently of Metabolic Disorders. *Journal*
38 *of the American Heart Association Cardiovascular & Cerebrovascular Disease* 2016;**5**(6):e003154 doi:
39 10.1161/JAHA.115.003154.
- 40 32. Pimentel-Coelho PM, Rivest S. The early contribution of cerebrovascular factors to the pathogenesis of
41 Alzheimer's disease. *The European journal of neuroscience* 2012;**35**(12):1917-37 doi:
42 10.1111/j.1460-9568.2012.08126.x.
- 43 33. Zlokovic BV. Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders.
44 *Nature reviews Neuroscience* 2011;**12**(12):723-38 doi: 10.1038/nrn3114.
- 45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract (Page 1-3)	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale (Page 4-5)	2	Explain the scientific background and rationale for the investigation being reported
Objectives (Page 5)	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design (Page 5)	4	Present key elements of study design early in the paper
Setting (Page 5)	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants (Page 5)	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables (Page 5-6)	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement (Page 5-6)	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods (Page 7)	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses

Continued on next page

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data (Page 5-9)	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data (Page 8-9)	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results (Page 8-11)	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results (Page 11-12)	18	Summarise key results with reference to study objectives
Limitations (Page 13)	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation (Page 11-13)	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability (Page 13)	21	Discuss the generalisability (external validity) of the study results

Other information

Funding (Page 14)	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
----------------------	----	---

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.