The Cross-Sectional Relationship Between Body Mass Index, Waist–Hip Ratio, and Cognitive Performance in Postmenopausal Women Enrolled in the Women's Health Initiative

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OBJECTIVES: To determine whether body mass index (BMI) is independently associated with cognitive function in postmenopausal women and the relationship between body fat distribution as estimated by waist-hip ratio (WHR).

DESIGN: Cross-sectional data analysis.

SETTING: Baseline data from the Women's Health Initiative (WHI) hormone trials.

PARTICIPANTS: Eight thousand seven hundred forty-five postmenopausal women aged 65 to 79 free of clinical evidence of dementia who completed the baseline evaluation in the WHI hormone trials.

MEASUREMENTS: Participants completed a Modified Mini-Mental State Examination (3MSE), health and lifestyle questionnaires, and standardized measurements of height, weight, body circumference, and blood pressure. Statistical analysis was performed of associations between 3MSE score, BMI, and WHR after controlling for known confounders.

RESULTS: With the exception of smoking and exercise, vascular disease risk factors, including hypertension, waist measurement, heart disease, and diabetes mellitus, were significantly associated with 3MSE score and were included as covariables in subsequent analyses. BMI was inversely related to 3MSE score; for every 1-unit increase in BMI, 3MSE score decreased 0.988 points ($P < .001$) after adjusting for age, education, and vascular disease risk factors. BMI had the most pronounced association with poorer cognitive functioning scores in women with smaller waist measurements. In women with the highest WHR, cognitive scores increased with BMI.

CONCLUSION: Higher BMI was associated with poorer cognitive function in women with smaller WHR. Higher WHR, estimating central fat mass, was associated with higher cognitive function in this cross-sectional study. Further research is needed to clarify the mechanism for this association. **J Am Geriatr Soc 58:1427–1432, 2010.**

Key words: obesity; cognition; dementia; waist–hip ratio; women

Dementia is a major public health concern because of its rapidly increasing rate of occurrence in aging populations. Dementia currently affects 1% to 6% of the population aged 65 and older, with the annual incidence rates doubling every 5 years between age 75 and 89.[1] It is estimated that, by 2030, approximately 50 million people, or 17% to 20% of the population, in the United States will be aged 65 and older.[2] Alzheimer's disease (AD) is the most common form of dementia in the United States and currently affects approximately 4 million persons in the United States.[3,4] Known risk factors for AD include family history and genetic predisposition, and some studies have suggested associations between AD and vascular disorders such as atherosclerosis,[5] hypertension, and coronary heart disease and diabetes mellitus. [6] Based on a recent meta-analysis of seven prospective studies, AD is 1.5 times as likely to

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DOI: 10.1111/j.1532-5415.2010.02969.x

0002-8614//$15.00

develop in women as in men.[7,8] Obesity and overweight increase the risk of vascular disorders and may also increase the risk of dementia. Furthermore, obesity is becoming a major public health concern.[9–13] Obesity has been suggested as a risk factor for AD in older women[14,15] and has been associated with poorer cognitive function in men[15–17] but not in women.[17–19] There is some evidence that obesity is protective against cognitive impairment in women, possibly due to endogenous estrogens.[20–22] This discrepancy between men and women in past studies may reflect sex-based differences in body weight and body fat distribution.

Early predictors of poor cognitive performance or cognitive decline may denote a population at risk for the development of dementia. Identifying populations at risk for dementia is becoming increasingly important as more information is available on possible preventative therapies to reduce or delay the incidence of dementia. This study explored the relationships between waist–hip ratio (WHR), BMI category, and cognition score in a geographically diverse cohort of older women without dementia. Because cognitive performance is predictive of subsequent dementia, the assessment of factors that may have a protective or detrimental effect on cognitive performance in a cohort of normal older women is an important area for investigation.

METHODS

The analyses used baseline data from a Women's Health Initiative (WHI) hormone trials cohort. The WHI is a large, multifaceted study focused on common causes of morbidity and mortality in postmenopausal women aged 50 to 79. The WHI Estrogen plus Progestin and Estrogen Alone randomized, placebo-controlled trials examined the risks and benefits of hormone therapies in women without and with hysterectomy, respectively. Detailed descriptions of eligibility criteria, recruitment methods, and study design have been published previously.[23–25] Briefly, 40 clinical centers throughout the United States enrolled participants between 1993 and 1998. Eligible women were postmenopausal, had no medical condition associated with a predicted survival of less than 3 years, and were likely to be residing in the same geographic area for at least 3 years. Exclusion criteria included attention to safety and adherence and retention concerns. Women who were taking hormones but who were interested in participating in the hormone trials were required to stop their hormones for at least 3 months before joining the study and had to be willing to be randomized to the hormone or placebo group.

Participants completed health questionnaires assessing previous hormone use; history of cardiovascular disease, diabetes mellitus, and stroke; lifestyle factors; and demographic data. WHI hormone study participants who were aged 65 and older also participated in baseline cognitive evaluation using the Modified Mini-Mental State Examination (3MSE), a 100-point validated test of global cognitive functioning.[26] The 3MSE's 46 items contribute to a total score from 0 to 100, with a higher scores reflecting better cognitive function. The test items measure temporal and spatial orientation, immediate and delayed recall, executive function, naming, verbal fluency, abstract reasoning, praxis, writing, and visuoconstructional abilities. The 3MSE has demonstrated good internal consistency and temporal reliability, sensitivity, and specificity for detecting cognitive impairment and dementia.[27–29] Trained technicians conducted standardized 3MSE assessments in a quiet, private area.

Standardized blood pressures were measured in the right arm after subjects had been seated quietly for at least 5 minutes. Hypertension was defined as blood pressure of 140 mmHg or greater systolic or 90 mmHg or greater diastolic or if the participant was taking antihypertensive agents. Weight and height measurements were obtained using a calibrated beam balance scale and a stadiometer anchored to the wall, with subjects wearing light street clothing and without shoes. Waist and hip measurements were obtained to the nearest 0.5 cm over nonbinding undergarments at the level of the umbilicus and the fullest hip circumference. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared. Women were classified into BMI categories that correspond to standard World Health Organization–designated categories for underweight, desirable weight, overweight, and obesity I, II, and III. In this classification, overweight is defined as a BMI of 25.0 kg/m^2 and obesity as a BMI of 30.0 kg/m^2, according to the World Health Organization criteria. All data were entered electronically into a centralized data base.

A majority of the study subjects were white (86.61%). Because ethnic minority women were not equally distributed between BMI categories, the analyses were restricted to white women. Means and distributions for age, 3MSE score, education, waist circumference, and other variables of interest (disease and lifestyle) were stratified according to BMI category. Means for variables of interest were also calculated after adjusting for age and education. Spearman rank correlation procedures were used to determine correlations between 3MSE score and BMI, waist circumference, age, education, systolic blood pressure, and smoking history. Odds ratios were calculated for atrial fibrillation, heart disease, hypertension, stroke, diabetes mellitus, and previous hormone use. Multivariate logistic regression analyses were used to determine whether BMI category predicts 3MSE score when controlled for age, education hypertension, stroke, smoking, diabetes mellitus, and heart disease. Because the 3MSE scores were skewed to the right in this cognitively intact cohort, each score was subtracted from 100, which skewed the data to the left, permitting the use of a generalized linear model (GLM) with discrete values. The Poisson distribution with an overdispersion parameter gamma was used, because transformed 3MSE scores had more variability than a pure Poisson process. Coefficients of the model are expressed in terms of the odds ratio and a 95% confidence interval. A log link function was used to model the transformed 3MSE scores. An ordinal logistic regression model was also used to validate the model independence of the results. This model (data not presented) led to the same conclusions. Linear regression contrasts within the GLM were used for trend tests, such as age, education, WHR, exercise, and 3MSE. Tests for trends in the continuous covariates across BMI categories used a linear contrast within an analysis of variance. Tests for trends on binary variables, such as hypertension, heart disease, stroke, transient ischemic attack, and diabetes mellitus, were based on linear contrasts within logistic

Table 1. Subject Characteristics According to Body Mass Index

Characteristic	<24.9 (Not Overweight) n = 2,263	25.0–29.9 (Overweight) n = 2,738	30.0–34.9 (Obese I) n = 1,659	35.0–39.9 (Obese II) n = 645	≥40.0 (Obese III) n = 256
Modified Mini-Mental State Examination score, mean ± SD	95.1 ± 0.1	95.0 ± 0.1	94.7 ± 0.1†	94.5 ± 0.2†	93.9 ± 0.3†
Age, mean ± SD	70.6 ± 0.1	70.3 ± 0.1*	69.9 ± 0.1*	69.4 ± 0.1*	68.7 ± 0.2*
Education, %		*	*	*	*
<HS diploma	4.9	5.5	7.4	9.0	6.6
Some college	58.5	63.8	67.0	67.6	66.4
≥College graduate	36.6	30.7	25.6	23.4	27.0
Waist, cm, mean ± SD	75.9 ± 0.2	87.1 ± 0.1*	97.6 ± 0.2*	106.7 ± 0.4*	113.4 ± 0.8*
Waist–hip ratio, mean ± SD	0.79 ± 0.01	0.83 ± 0.01*	0.86 ± 0.01*	0.86 ± 0.01*	0.85 ± 0.01*
Exercise, metabolic equivalents, mean ± SD	14.8 ± 0.3	11.9 ± 0.2*	8.9 ± 0.3*	7.2 ± 0.4*	6.4 ± 0.6*
Smoking, pack-years	24.5 ± 0.7	25.3 ± 0.7	27.1 ± 1.0	27.7 ± 1.7	28.6 ± 2.6
Hypertension, %	35.7	44.8*	54.0*	60.8*	63.7*
Heart disease, %‡	17.8	17.6	21.4*	24.3*	20.7
Diabetes mellitus, %	2.6	5.3*	8.4*	12.4*	18.0*

$P <$ * .05 † .10. Normal is the reference group.

‡ Heart or circulation problems, cardiac arrest, heart failure, cardiac catheterization, heart bypass, atrial fibrillation.

SD = standard deviation.

regression. SAS version 9.1.3 (SAS Institute, Inc, Cary, NC) was used for analyses.

RESULTS

A total of 8,745 postmenopausal women aged 65 to 79 completed 3MSE testing during baseline screening at 40 WHI clinical centers. Administration of the 3MSE was completed before randomization of women into the Estrogen Plus Progestin or the Estrogen Alone studies. None of the women were taking hormone therapy at the time of screening. Baseline characteristics of the women are classified according to BMI category in Table 1. Because few women (n = 70) had low body weight (BMI < 18.5 kg/m^2), observations on women with very low relative weights were combined with observations on women in the normal weight category.

Table 1 presents mean 3MSE score and as other selected variables for which previous associations with cognitive screening have been identified. As is apparent in Table 1, a large proportion of women (70.1%) were classified as overweight or obese. Overall, 3MSE scores decreased slightly with increasing BMI categories. Important covariables were also associated with BMI. Higher educational attainment was seen in women in the normal and low BMI categories than in women who were overweight or obese. Waist circumference and WHR increased with BMI, as did hypertension and diabetes mellitus, whereas physical activity levels were inversely related to BMI. Current smoking was more common in women with low body weight. Overall, only a minority of women were current smokers (15.5%), although many had been smokers previously (47.2%).

Multiple logistic regression techniques were used to determine the independent relationships between each covariable and 3MSE score after controlling for other confounders. The results of these analyses are presented in Table 2. Older women and women who exercised less tended to have lower 3MSE scores, whereas women with larger waist circumferences and higher levels of education tended to have higher 3MSE scores. Women who reported having had a stroke, heart disease, or diabetes mellitus or who were hypertensive had lower 3MSE scores. After adjusting for other variables, BMI was inversely associated with 3MSE score.

Table 3 presents mean 3MSE scores according to BMI category after adjusting for differences in 3MSE score due to age and educational attainment, both of which have important effects on 3MSE score. Overall, a test for trend was significant ($P < .001$), indicating that lower 3MSE scores are associated with higher BMI; for every 1.0-unit increase in BMI, 3MSE score was 0.988 points lower ($P < .001$)

Table 2. Multivariate Analyses of Body Mass Index (BMI), Activity, and Waist Circumference as Predictors of Modified Mini-Mental State Examination Score

Variable	Odds Ratio (95% Confidence Interval)	*P*-Value
BMI, kg/m^2	0.989 (0.985–0.995)	<.001
Activity level, metabolic equivalents/wk	0.999 (0.997–0.999)	.048
Waist circumference, cm	1.002 (1.001–1.005)	.01
Age	0.978 (0.973–0.983)	<.001
Education	1.142 (1.132–1.153)	<.001
Smoking	0.972 (0.938–1.007)	.12

Control variables: age, education, stroke, hypertension, diabetes mellitus, heart disease.

Table 3. Modified Mini-Mental State Examination Scores According to Body Mass Index Category

	Adjusted Mean ± Standard Deviation				
Adjusted for:	Not Overweight	Overweight	Obese I	Obese II	Obese III
Age	95.2 ± 0.09	94.9 ± 0.08	94.7 ± 0.10	94.5 ± 0.17	93.8 ± 0.26
Education	95.1 ± 0.09	95.0 ± 0.08	95.0 ± 0.10	95.0 ± 0.17	94.3 ± 0.26
Age+education	95.2 ± 0.09	95.1 ± 0.08	95.0 ± 0.10	95.0 ± 0.17	94.1 ± 0.26

after adjusting for age, education, and vascular disease risk factors.

When the relationships between 3MSE score, WHR, and BMI categories were explored, it was found that they were complex (Figure 1). The 3MSE scores for women with low WHRs (Figure 2) decreased as BMI category increased ($P < .001$), although this association reversed for women with the highest WHRs (Figure 2). In the highest WHR quartile, 3MSE score increased with increasing BMI category ($P = .01$).

BMI category had the most pronounced association with cognitive function scores in women with smaller waist measurements, suggesting that BMI is directly associated with cognitive function and not secondary to metabolic alterations associated with higher WHRs. Women with the highest WHRs had higher cognitive scores with higher BMI, suggesting that abdominal obesity may be associated with better cognitive functioning.

DISCUSSION

This cross-sectional analysis of associations between BMI category and cognitive function in older women found a complex relationship that WHR modified. In women with a low WHR, there was an inverse relationship between BMI category and 3MSE score after adjusting for demographic data and several weight-related comorbidities that was not observed in women with higher WHRs.

Previous studies of associations between obesity and cognitive function have yielded mixed findings. Obesity, especially midlife obesity, has been associated with greater risk of cognitive impairment and dementia in several studies.[30–32] In sex-specific studies, obesity has been suggested as protective of and a risk factor for AD in women.[14–22] It has been unclear whether either of the suggested effects of obesity on cognition has been a direct or indirect effect through higher endogenous estrogen levels improving cognition or the detrimental effects of vascular disease and inflammation associated with obesity causing greater risk of dementia. The present study suggests that body fat distribution is an important factor in obesity and its effects on cognitive function in older women.

Overall, obesity appears to be directly associated with cognitive function in postmenopausal older women. These data suggest that factors in addition to vascular disease, hypertension, diabetes mellitus, and inflammation, all of which have been associated with abdominal obesity, may mediate the detrimental effects of obesity on cognition. In the current study, central adiposity was associated with higher scores on the 3MSE at higher BMI categories, whereas lower BMI categories were associated with lower 3MSE scores, even after adjusting for confounders. Racial factors affecting the relationship cannot explain the associations, because the analyses was limited to white women. Several studies of exogenous estrogen therapy on dementia risk have not shown a protective effect.[33–35] One possibility is that the production of endogenous estrogen by abdominal adipocytes may play a protective role for cognition.[36–38]

Limitations

This was a cross-sectional analysis of a longitudinal cohort of women; thus, cause and effect cannot be concluded. The other major limitations of the cohort were that only white women were included in these analyses and that the dementia outcome probably combined participants with

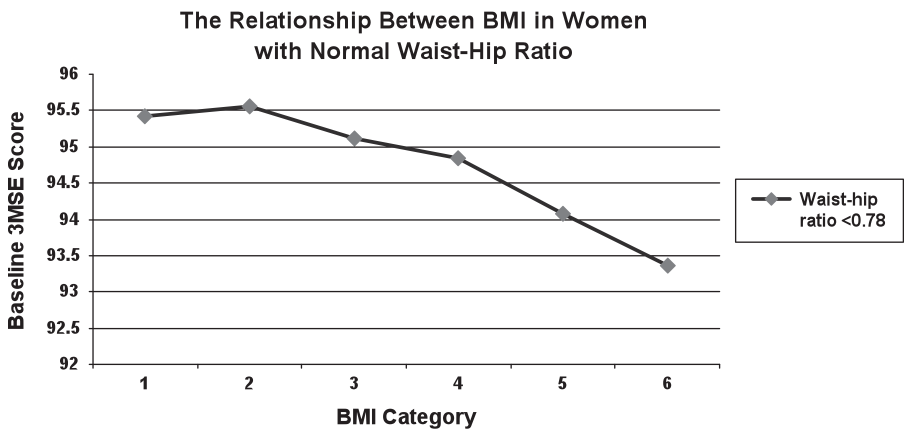

Figure 1. Relationship between body mass index (BMI) and baseline Modified Mini-Mental State Examination (3MSE) score. BMI was inversely related to cognitive function scores after adjusting for age, education, hypertension, heart disease, stroke, and diabetes mellitus.

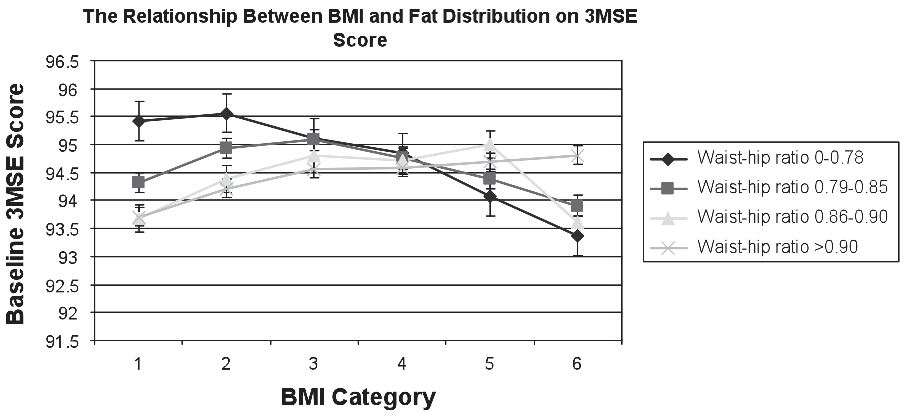

Figure 2. Relationship between the effect of body fat distribution and body mass index on cognitive scores.

dementia of differing etiology. The cognitive data in this analysis were limited to the 3MSE, a measure of global cognitive functioning, which screens for but does not extensively assess domain-specific cognitive functioning. Also, participants were healthy women who had relatively high levels of education and who were without dementia or cognitive impairment at baseline; thus participant 3MSE scores were clustered at a high level of cognitive functioning. Nonetheless, it was possible to detect an effect of BMI on cognitive functioning.

CONCLUSION

BMI category and WHR appear to be important factors in complex associations between obesity and cognitive function in older women. These findings suggest that greater central adiposity, estimated according to higher WHRs, is somehow associated with higher cognitive function scores in older, postmenopausal women. These findings do not negate other research demonstrating that obesity is a major risk factor for cardiovascular disease and other chronic diseases, including those such as hypertension and diabetes mellitus, which have been found to increase dementia risk.[39] Qualitative and quantitative nutritional analyses to further differentiate relationships between diet, physical activity, BMI, and cognitive functioning in older women are needed as well.

ACKNOWLEDGMENTS

Conflict of Interest: Diana R. Kerwin: honoraria, speaker forum, consultant to Pfizer Pharmaceuticals, Forest Laboratories, Novartis Pharmaceuticals.

Jennifer G Robinson: grants to institution: Abbott, Aegerion, Bristol-Myers Squibb, Daiichi-Sankyo, GlaxoSmith Kline, Hoffman La Roche, Merck, Merck Shering-Plough.

Funding Sources: This research was conducted while Diana Kerwin was a T. Franklin Williams Scholar supported by the Foundation for Health in Aging, the American Geriatrics Society, the Association of Subspecialty Professors and Atlantic Philanthropies, and a Dr. Judith Stitt Faculty Scholar supported by the Wisconsin Women's Health Foundation.

The WHI is funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health, U.S. Department of Health and Human Services. Wyeth Pharmaceuticals provided the study drug and the placebo to the WHI trial.

Author Contributions: As first/lead author, Kerwin was primarily responsible for the study concept, design, and preparation of the manuscript. Kerwin, Zhang, Kotchen, Hoffmann, and Espelan were involved in the study design and data analysis. All authors listed contributed to the interpretation of data and manuscript preparation. Acquisition of subjects and data was provided by the WHI and Clinical Sites as listed in the Author Section. This was a data analysis of an existing study (WHI), and Dr. Kerwin was not involved in recruitment of subjects. Kotchen, Robinson, and Coker were involved in acquisition of subjects and data for the WHI ongoing study.

Sponsor's Role: The sponsors had no role in the design, methods, recruitment, data collection, analysis, or preparation of this manuscript.

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