Article

Association between Visceral Fat Content and Obesity-Related Indicators with Cognitive Impairment after Intracerebral Hemorrhage

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Abstract

Background: Intracerebral hemorrhage (ICH) is a major cause of morbidity and mortality, often leading to long-term cognitive impairment that significantly diminishes the quality of life. This study investigated the relationship between visceral fat content, obesity-related indicators, and cognitive dysfunction following ICH.

Methods: A total of 388 subjects with ICH who were admitted to the Neurosurgery Department of the Hospital and met the inclusion and exclusion criteria were included in this study. Obesity-related indicators, including body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR), were measured. L3 level images were obtained by abdominal computerized tomography (CT). The visceral fat content was estimated using IMAGE J software, and adiponectin levels were assessed via enzyme-linked immunosorbent assay (ELISA). The Mini-Mental State Examination (MMSE) was used to evaluate the cognitive level of patients within 2 weeks of onset, and the shortened version of the Montreal Cognitive Assessment (miniMoCA) was used to evaluate the cognitive level of patients 6 months after ICH. Univariate and multivariate analyses were used to analyze the correlations of BMI, WC, WHtR, abdominal fat, and adiponectin with cognitive impairment after ICH.

Results: BMI, WC, and WHtR were lower in the cognitive impairment group ($p < 0.01$). Overweight patients exhibited higher MMSE scores than normal-weight patients ($p < 0.05$) and higher miniMoCA scores than obese patients ($p = 0.014$). Abdominal obesity, assessed by WC and WHtR, was associated with higher MMSE scores ($p = 0.022$ and 0.003, respectively). Multivariate analysis indicated that WHtR was associated with cognitive impairment risk post-ICH (odds ratio (OR) = 0.233, 95% confidence interval (CI) (0.071, 0.762); $p = 0.016$). Although no overall association was found between adiponectin levels and cognitive impairment, subgroup analysis revealed lower adiponectin levels in overweight patients with cognitive impairment ($p = 0.040$).

Conclusion: WHtR is independently and inversely associated with cognitive impairment after ICH. There is no significant correlation between adiponectin with cognitive impairment after ICH, while subgroup analysis indicates that adiponectin levels are lower in overweight patients with cognitive impairment.

Keywords

intracerebral hemorrhage; cognitive impairment; obesity; visceral fat; adiponectin

Introduction

Post-stroke cognitive impairment (PSCI) refers to cognitive deficits that arise after a stroke, including memory loss, attention deficits, and impaired executive function [1,2]. Millions of stroke cases occur globally each year, and the resulting cognitive impairments place a significant burden on patients and their families. Intracerebral hemorrhage (ICH), a type of stroke caused by bleeding within the brain, is associated with a higher risk of cognitive impairment compared to ischemic stroke [1,3,4]. Spontaneous ICH, usually influenced by sporadic small vessel disease,

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results from the rupture of small vessels within the brain parenchyma [5]. Although ICH accounts for only 10–15% of all strokes, it has higher morbidity and mortality rates compared to ischemic stroke [5,6]. Despite the high prevalence of dementia following hemorrhagic stroke (5% to 44%) [7,8], the cognitive impairments associated with ICH and their underlying mechanisms have not received sufficient attention.

While many studies have focused on the neurological damage and inflammatory responses that follow ICH [9–11], the influence of metabolic factors, particularly visceral fat, on cognitive outcomes remains underexplored. Visceral fat, stored around internal organs within the abdominal cavity, is increasingly recognized as an active endocrine organ influencing various physiological processes [12,13]. High levels of visceral fat are closely associated with metabolic syndrome, including insulin resistance, hypertension, and dyslipidemia. These metabolic disturbances are also linked to poor cerebrovascular health outcomes [13]. Thus, visceral fat might participate in the regulation of brain health and cognitive functions through these metabolic disorders [14]. Furthermore, a study indicated that starting from a body mass index (BMI) of 20 kg/m^2, the risk of stroke increases by 5% for each additional unit, suggesting that the impact of visceral fat on post-stroke cognitive function may be reflected through BMI [15]. Excess visceral fat is also linked to chronic inflammation, oxidative stress, and vascular dysfunction, all of which can negatively impact cognitive processes [16]. However, the specific relationship between visceral fat and cognitive impairment after ICH remains unclear. Most existing studies have examined the effects of general obesity and metabolic syndrome on cognitive function without specifically addressing the role of visceral fat in ICH [17,18]. This gap highlights the need for targeted research to elucidate how visceral fat influences cognitive outcomes in ICH patients.

Furthermore, adipose tissue not only stores energy, but also serves as an endocrine organ, secreting numerous adipokines closely related to physiological activities [19]. Adiponectin (ANP) is a common adipokine, a glycoprotein composed of 244 amino acids, specifically expressed by adipose tissue, and plays anti-inflammation, anti-atherosclerosis, and insulin-sensitizing roles [19,20]. Low ANP levels have been associated with increased stroke risk [21]. In research by Chen *et al*. [22], patients with acute myocardial infarction and concurrent stroke had lower ANP levels than those with myocardial infarction alone. Additionally, ANP has been shown to reduce the risk of vascular dementia [23]. However, other researchers have proposed the "adiponectin paradox", where serum ANP levels are positively correlated with mortality in cardiovascular diseases like heart failure [24]. This paradox also exists in stroke patients [25,26]. Therefore, the correlation between ANP and cognitive impairment after ICH remains unclear.

Given these considerations, this study aimed to explore the relationship between visceral fat content, ANP levels, and cognitive impairment following ICH, providing a foundation for early identification and diagnosis of cognitive impairments in these patients.

Materials and Methods

Research Object

In this observational study, 388 subjects who were consecutively admitted to the neurosurgery department and met the inclusion and exclusion criteria were enrolled. This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Zhejiang Chinese Medical University (Approval No. (058)-01). All participants provided written informed consent, and the study adhered to the ethical principles of the Helsinki Declaration.

Inclusion criteria:

1. Clinical presentation consistent with the diagnosis of acute ICH, confirmed by head magnetic resonance imaging (MRI), following the Chinese Guidelines for Diagnosis and Treatment of Intracerebral Hemorrhage (2019) [27].

2. Admission within 72 hours of ICH onset.

3. Age $\geq$18 years.

4. Willingness to participate and provide informed consent.

Exclusion criteria:

1. Inability to cooperate with study procedures.

2. Severe dysfunction of the heart, lungs, liver, or kidneys, or presence of malignant tumors.

3. Presence of organic lesions in the central system.

4. Refusal to participate.

Demographic and Baseline Data

A neurosurgery specialist collected general clinical data, including gender, age, education, medical history (e.g., hypertension, diabetes, coronary heart disease, hy-

perlipidemia), drinking history, smoking history, and family history. Height, weight, and waist circumference were measured according to the "Human Body Measurement Method for Population Health Testing" standards. Height was measured with the subject standing barefoot, heels together, arms at the sides, and eyes forward. The measurement was recorded to the nearest 0.1 cm and averaged over three attempts. Weight was measured with the subject standing barefoot after voiding, recorded to the nearest 0.1 kg, and averaged over three attempts. Waist circumference was measured in the morning with the subject standing relaxed, feet apart, and breathing normally. The measurement was taken at the midpoint between the axillary midline and iliac crest, recorded to the nearest 0.1 cm, and averaged over three attempts.

Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) and categorized as normal (BMI $<$24 kg/m^2), overweight (BMI $<$28 kg/m^2), and obese (BMI $\geq$28 kg/m^2) based on Chinese guidelines [28]. The waist-to-height ratio (WHtR) was calculated as waist circumference (WC) (cm) divided by height (cm).

Laboratory Analysis

All subjects fasted for 10 hours prior to blood sample collection. Morning venous blood was drawn from the elbow and processed within 2 hours. Laboratory tests included fasting blood glucose, glycated hemoglobin, cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, and homocysteine. The levels of ANP and fatty acid binding protein 4 (FABP4) were measured using enzyme-linked immunosorbent assay (ELISA) kits from Wuhan Huamei Biotechnology Co., Ltd., with product numbers HME00280 and EH0752, respectively. After blood extraction, samples were centrifuged at 3000 rpm for 15 minutes using a low-temperature high-speed centrifuge. The supernatant was quickly extracted and divided into cryotubes, labeled, and stored at –80 °C. The procedure was performed following the manufacturer's instructions. The blood sample was diluted 1:500 with sample diluent before testing. A standard curve was drawn using Curve Expert software after detection. Each sample was set with 3 wells, and the average value was taken to obtain the final sample concentration.

Imaging Examinations

Head MRI

All participants underwent a comprehensive head MRI examination, with images covering the entire head. The obtained scanning sequences include T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI) sequence, apparent diffusion coefficient (ADC) sequence, and fluid-attenuated inversion recovery (FLAIR) sequence.

Abdominal Computerized Tomography (CT)

All subjects completed abdominal CT examination, taking L3 level CT images to evaluate the abdominal fat content [12,29,30]. The abdominal visceral fat content was estimated using IMAGE J software (Version: IMAGE J 1.53, Manufacturer: National Institutes of Health (NIH), Location: Bethesda, MD, USA), including total abdominal fat, visceral fat, and subcutaneous fat content. The visceral/subcutaneous fat ratio was calculated, and participants were categorized into high and low groups based on median values.

Neurological Function Assessment

Modified Rankin Scale (mRS)

The mRS measures the degree of disability or dependence in daily activities post-stroke [31]. Scores range from 0 to 6, with 0 indicating no symptoms, 1 indicating no significant disability despite symptoms, 2 indicating slight disability, 3 indicating moderate disability, 4 indicating moderately severe disability, 5 indicating severe disability, and 6 indicating death. Assessments were conducted at admission and follow-up to monitor recovery and outcome.

Shortened Version of Montreal Cognitive Assessment (miniMoCA)

To facilitate the cognitive assessment of subjects at 6 months after stroke and reduce the occurrence of patients being unable to come to the hospital for assessment during follow-up, this study used the miniMoCA scale to evaluate cognitive function at 6 months after ICH through telephone follow-up [16,17]. The miniMoCA test includes 12 points, including directional ability (6 points), language fluency (1 point), and delayed memory (5 points).

Mini-Mental State Examination (MMSE)

This study divided participants into cognitive impairment and non-cognitive impairment groups based on the MMSE score results within 2 weeks. Based on the education level of the subjects, MMSE ≤17 points (illiterate), ≤20 points (primary school), and ≤24 points (junior high school and above) are identified as cognitive impairment [32].

Fazekas Scale

The white matter condition of the brain was evaluated based on magnetic resonance FLAIR sequence, assessing the condition of paraventricular and deep white matter lesions, and finally summing up the scores to obtain the total score [33]. Paraventricular lesions were classified as no lesions, pencil-like or cap-shaped thin layer lesions, smooth halos, and irregular paraventricular hyperintensities extending to the deep white matter, with scores ranging from 0 to 3. Deep white matter lesions in the brain were classified as 0 to 3 points for no lesions, lesions appearing punctate, lesions beginning to fuse, and lesions extensively fusing. The total score was classified as mild (1–2 points), moderate (3–4 points), and severe (5–6 points).

Diagnostic Criteria

Hypertension: Patients who have not taken antihypertensive drugs have had their blood pressure measured three times in a quiet state, with systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or have a history of confirmed hypertension, or are currently using antihypertensive drugs.

Diabetes: Diabetes is diagnosed with typical diabetes symptoms plus random blood glucose ≥11.1 mmol/L, or fasting blood glucose ≥7.0 mmol/L, or oral glucose tolerance test (OGTT) 2-hour blood glucose ≥11.1 mmol/L, or glycosylated hemoglobin ≥6.5% according to the 2020 Guidelines for the Prevention and Treatment of diabetes in China [34]. Those without typical symptoms need to be retested every other day for confirmation. Or those with a history of previous diagnosis of diabetes, or currently using hypoglycemic drugs.

Hyperlipidemia: According to the revised 2016 edition of the Chinese Guidelines for the Prevention and Treatment of Adult Blood Lipid Abnormalities, a diagnosis of hyperlipidemia was made based on serum cholesterol ≥5.18 mmol/L, serum triglyceride content ≥1.70 mmol/L, or serum low-density lipoprotein ≥1.7 mmol/L, or a history of confirmed hyperlipidemia [35].

Smoking history: Defined as smoking ≥1 cigarette per day for over 1 year and continuing to smoke.

Drinking history: Defined according to the 2010 Guidelines for Diagnosis and Treatment of Alcoholic Liver Disease as consuming ≥50 mL of white alcohol at least once a week for more than 3 months [36].

Abdominal obesity: Defined as a waist circumference ≥90 cm for men or ≥85 cm for women [37] or a waist-to-height ratio ≥0.5 [38].

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 software (IBM, Armonk, NY, USA). Normality was tested using the Kolmogorov-Smirnov test. Normally distributed data were expressed as mean ± standard deviation and analyzed using independent *t*-tests. Non-normally distributed data were expressed as median (interquartile range) and analyzed using Mann-Whitney U, Kolmogorov-Smirnov Z, or Kruskal-Wallis H tests. Categorical data were presented as counts (n) and percentages (%) and analyzed using the chi-square test. Multivariate analysis was conducted using binary logistic regression. Statistical significance was set at $p < 0.05$.

Results

Clinical Features and Univariate Analysis of Cognitive Impairment after ICH

As shown in Table 1, in the univariate analysis of baseline characteristics between the cognitive impairment group and the non-cognitive impairment group after ICH, it was found that the cognitive impairment group had significantly higher median age (74.00 vs. 68.00, $p < 0.001$), systolic blood pressure (156.83 ± 19.50 vs. 149.53 ± 20.97, $p = 0.002$), lesion volume (1.00 vs. 0.85, $p < 0.001$), Fazekas score (4.00 vs. 3.00, $p < 0.001$), periventricular white matter lesions (PWML) (2.00 vs. 1.00, $p < 0.001$), deep white matter lesions (DWML) (3.00 vs. 1.50, $p < 0.001$), National Institute of Health Stroke Scale (NIHSS) at admission (3.00 vs. 2.00, $p < 0.001$), mRS at follow-up (3.00 vs. 1.00, $p < 0.001$), high-density lipoprotein (HDL) (1.08 vs. 1.02, $p < 0.001$), and homocysteine levels (13.40 vs. 11.45, $p < 0.001$) compared to the non-cognitive impairment group. Conversely, the cognitive impairment group had significantly lower MMSE at admission (18.00 vs. 26.50, $p <$

0.001), miniMoCA at follow-up (6.00 vs. 9.00, $p < 0.001$), glycated hemoglobin (6.20 vs. 6.50, $p < 0.001$), cholesterol (3.91 vs. 4.21, $p = 0.015$), triglycerides (1.15 vs. 1.40, $p < 0.001$), and low-density lipoprotein (LDL) (2.30 vs. 2.68, $p < 0.001$) compared to the non-cognitive impairment group. Additionally, the cognitive impairment group had a higher prevalence of hypertension (96.15% vs. 86.97%, $p = 0.009$) and a lower prevalence of diabetes (41.35% vs. 62.32%, $p < 0.001$). The Fazekas grading also indicated a higher proportion of moderate to severe cases in the cognitive impairment group ($p < 0.001$). These findings highlight significant differences in clinical characteristics between the cognitive impairment group and the non-cognitive impairment group, including age, blood pressure, lesion volume, Fazekas score, history of hypertension and diabetes, cognitive function scores, and blood biochemical markers.

Univariate Analysis of Visceral Fat Content and Cognitive Impairment Post-ICH

In the univariate analysis of the relationship between obesity indicators, abdominal fat types, and cognitive impairment after ICH, it was found that the cognitive impairment group had significantly lower mean BMI (23.47 ± 2.89 vs. 24.81 ± 3.04, $p < 0.001$), waist circumference (96.07 ± 11.87 vs. 99.93 ± 10.93, $p = 0.003$), and waist-to-height ratio (0.58 ± 0.02 vs. 0.60 ± 0.07, $p = 0.004$) compared to the non-cognitive impairment group. Additionally, the cognitive impairment group had significantly lower median total fat (294.17 vs. 341.56, $p = 0.038$), visceral fat (122.64 vs. 131.53, $p = 0.015$), and visceral/subcutaneous fat ratio (0.67 vs. 0.71, $p = 0.003$) than the non-cognitive impairment group. These results suggest that lower obesity indicators and visceral fat levels may be linked to a elevated risk of cognitive impairment after ICH (Table 2).

Analysis of the Relationship between Obesity Indicators and Cognitive Scores

Relationship between BMI Levels and Cognitive Scores

Participants were categorized into normal weight, overweight, and obese groups based on BMI. As illustrated in Fig. 1, there were significant differences in MMSE scores within 2 weeks of onset and miniMoCA scores at 6 months post-stroke among the three groups ($p < 0.05$). Pairwise comparisons revealed that the MMSE score was higher in the overweight group compared to the normal weight group (27.00 (24.00, 29.00) vs 26.00 (19.50, 28.00), $p < 0.05$). The miniMoCA score was also higher in the overweight group compared to the obese group (10.00 (8.00, 11.00) vs 8.00 (6.00, 10.00), $p = 0.014$).

Relationship between Waist Circumference (WC) and Cognitive Scores

Participants were divided into non-abdominal obesity group A and abdominal obesity group A based on WC. As shown in Fig. 2, there was a significant difference in MMSE scores within 2 weeks of onset between the two groups. The abdominal obesity group A had higher MMSE scores than the non-abdominal obesity group A (27.00 (23.00, 29.00) vs 25.00 (19.75, 27.00), $p = 0.022$). However, there was no significant difference in miniMoCA scores between the two groups at 6 months post-ICH ($p > 0.05$).

Relationship between Waist-to-Height Ratio (WHtR) and Cognitive Scores

Based on WHtR, participants were divided into non-abdominal obesity group B and abdominal obesity group B. As shown in Fig. 3, there was a statistically significant difference in MMSE scores between the two groups within 2 weeks of onset. The abdominal obesity group B had higher MMSE scores than non-abdominal obesity group B (27.00 (23.00, 29.00) vs 22.50 (15.00, 26.75), $p = 0.003$). No significant difference in miniMoCA was observed between the two groups at 6 months post-ICH ($p > 0.05$).

Logistic Regression Analysis of Visceral Fat Content and Cognitive Impairment after Stroke

A collinearity diagnosis among obesity indicators revealed no multicollinearity among BMI, WC, WHtR, visceral fat, and visceral/subcutaneous fat ratio. Binary logistic regression analysis was conducted on these variables. After adjusting age, admission systolic blood pressure, presence or absence of diabetes, white matter lesion degree (mild and moderate) and admission NIHSS score, as shown in Table 3, the WHtR was negatively correlated with the risk of ICH (OR = 0.233, 95% CI (0.071, 0.762); $p = 0.016$). There was no significant independent correlation between visceral fat content and visceral/subcutaneous fat ratio and ICH ($p > 0.05$).

Correlation Analysis between Adipokines and Cognitive Impairment after ICH

Participants were divided into high and low adiponectin (ANP) groups based on median levels. As shown in Table 4, patients in the low ANP group exhibited higher BMI, WC, and WHtR compared to those in the high ANP group (BMI: 25.49 ± 2.79 vs. 23.82 ± 3.18; WC: 101.74 ± 9.19 vs. 97.25 ± 12.17; WHtR: 0.61

Table 1. Baseline characteristics by cognitive impairment status.

Clinical feature	Cognitive impairment group (n = 104)	Non-cognitive impairment group (n = 284)	$t/Z/\chi^2$	*p*-value
Age (years)	74.00 (66.25, 84.00)	68.00 (63.00, 77.00)	–7.844	<0.001
Male, n (%)	68 (65.38)	180 (63.38)	0.133	0.716
Education (years)	9.00 (6.00, 12.00)	9.00 (9.00, 12.00)	–1.257	0.209
Systolic blood pressure (mmHg)	156.83 ± 19.50	149.53 ± 20.97	–3.153	0.002
Diastolic blood pressure (mmHg)	88.00 (81.00, 95.00)	88.00 (75.25, 99.00)	–1.065	0.287
Lesion volume	1.00 (0.40, 5.55)	0.85 (0.50, 2.98)	–6.450	<0.001
Fazekas score	4.00 (4.00, 6.00)	3.00 (2.00, 4.00)	–13.119	<0.001
PWML	2.00 (2.00, 3.00)	1.00 (1.00, 2.00)	–13.170	<0.001
DWML	3.00 (2.00, 3.00)	1.50 (1.00, 2.00)	–12.858	<0.001
Fazekas degree			37.935	<0.001
Normal	14 (13.46)	60 (21.13)		
Mild	12 (11.54)	92 (32.39)		
Moderate	36 (34.62)	90 (31.69)		
Severe	42 (40.38)	42 (14.79)		
Degree of vascular stenosis			1.700	0.192
Mild	55 (52.88)	129 (45.42)		
Moderate to severe	49 (47.12)	155 (54.58)		
Smoking history, n (%)	34 (32.69)	104 (36.62)	0.512	0.474
Drinking history, n (%)	13 (12.50)	56 (19.72)	2.713	0.100
History of hypertension, n (%)	100 (96.15)	247 (86.97)	6.791	0.009
History of diabetes, n (%)	43 (41.35)	177 (62.32)	13.645	<0.001
History of CHD, n (%)	16 (15.38)	30 (10.56)	1.693	0.193
Hyperlipidemia, n (%)	82 (78.85)	224 (78.87)	0.000	0.995
MMSE at admission	18.00 (14.00, 22.00)	26.50 (22.00, 28.00)	–13.605	<0.001
miniMoCA at follow-up	6.00 (4.00, 8.00)	9.00 (8.00, 11.00)	–11.189	<0.001
NIHSS at admission	3.00 (2.00, 5.00)	2.00 (1.00, 3.00)	–6.485	<0.001
mRS at follow-up	3.00 (2.00, 5.00)	1.00 (1.00, 2.00)	–12.857	<0.001
Fasting blood glucose (μmol/L)	5.40 (4.60, 6.70)	5.57 (4.76, 7.01)	–0.720	0.471
Glycated hemoglobin (%)	6.20 (5.71, 6.70)	6.50 (6.00, 7.50)	–4.773	<0.001
Cholesterol (μmol/L)	3.91 (3.15, 4.79)	4.21 (3.45, 4.94)	–2.423	0.015
Triglycerides (μmol/L)	1.15 (0.90, 1.63)	1.40 (1.03, 2.00)	–5.484	<0.001
HDL (μmol/L)	1.08 (0.88, 1.32)	1.02 (0.89, 1.02)	–3.559	<0.001
LDL (μmol/L)	2.30 (1.72, 3.10)	2.68 (2.00, 3.30)	–3.649	<0.001
Homocysteine (μmol/L)	13.40 (10.63, 17.25)	11.45 (9.50, 14.55)	–5.811	<0.001

Abbreviations: PWML, periventricular white matter lesions; DWML, deep white matter lesions; CHD, coronary heart disease; MMSE, Mini-Mental State Examination; NIHSS, National Institute of Health Stroke Scale; mRS, modified rankin scale; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

± 0.05 vs. 0.58 ± 0.07; $p < 0.05$). However, no significant differences were found between the two groups in MMSE at admission, miniMoCA score at follow-up, NIHSS at admission, and mRS scores at follow-up ($p > 0.05$). Stratified analysis by BMI level indicated that among overweight patients, there was a statistical difference in ANP levels between the cognitive impairment group and the non-cognitive impairment group, with the cognitive impairment group having lower ANP levels (16.56 (9.61, 26.17) vs 34.46 (24.05, 45.76), $p = 0.040$) (Table 5).

Discussion

In recent years, the issue of obesity has become increasingly prominent. The incidence rate of abdominal obesity has increased year by year since 1999. It is projected that by 2030, 55.6% of adult men and 80.0% of adult women will have abdominal obesity [39]. In China, the prevalence of overweight has increased from 18.9% in 2002 to 27.1% in 2012, an increase of 43.4%. Obese patients have increased from 2.9% in 2002 to 5.2% in 2012, an increase of 82.1% [40]. The issue of obesity is becoming in-

Table 2. Univariate analysis of obesity indicators, abdominal fat types, and cognitive impairment after ICH.

Variables	Cognitive impairment group (n = 104)	Non-cognitive impairment group (n = 284)	*t*/*Z*	*p*-value
BMI (kg/cm^2)	23.47 ± 2.89	24.81 ± 3.04	3.886	<0.001
WC (cm)	96.07 ± 11.87	99.93 ± 10.93	3.002	0.003
WHtR	0.58 ± 0.02	0.60 ± 0.07	2.869	0.004
Total fat (cm^2)	294.17 (237.37, 396.30)	341.56 (261.35, 404.23)	–2.071	0.038
Visceral fat (cm^2)	122.64 (84.40, 163.94)	131.53 (107.93, 169.34)	–2.434	0.015
Subcutaneous fat (cm^2)	178.34 (128.11, 236.69)	184.17 (141.59, 248.16)	–0.565	0.572
Visceral/subcutaneous fat ratio	0.67 (0.46, 0.87)	0.71 (0.51, 0.94)	–2.957	0.003

Abbreviations: ICH, intracerebral hemorrhage; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio.

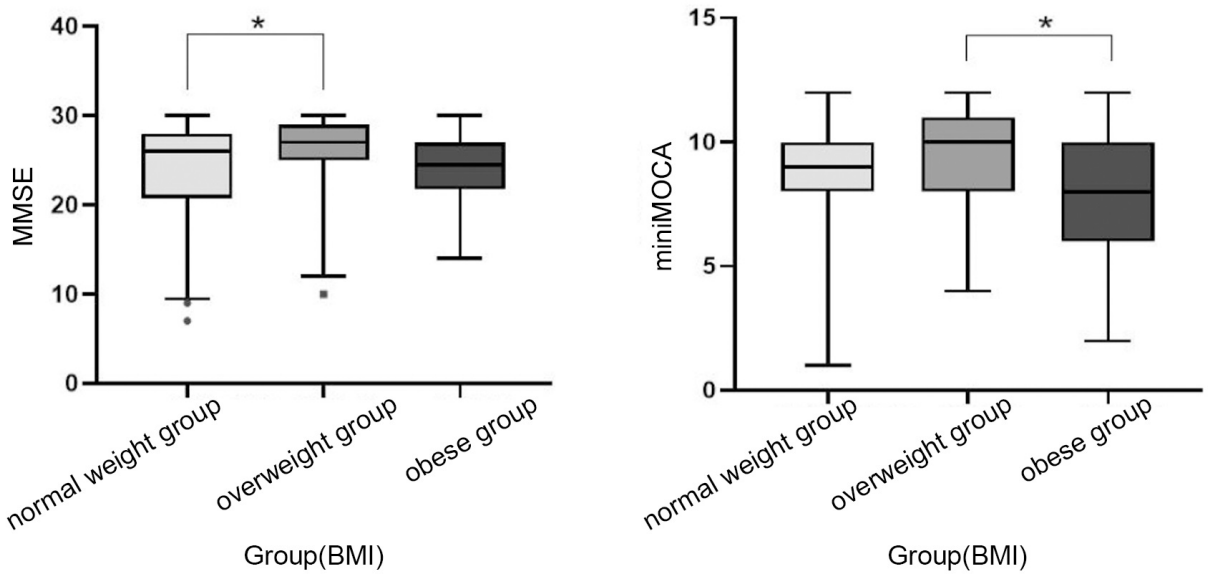

Fig. 1. Relationship between BMI levels and cognitive scores (Z). Normal weight group (n = 171), Overweight group (n = 139), Obesity group (n = 78). Data are presented as the median [P25, P75]. *$p < 0.05$. Abbreviations: BMI, body mass index; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

creasingly prominent, leading to a series of health problems. Most studies believed that obesity is related to hypertension, diabetes, coronary heart disease, and stroke [41,42]. The proportion of obesity is higher among stroke patients. A multicenter double-blind randomized trial in the United States reported that approximately 76% of stroke patients are overweight or obese, with approximately 70% of males and 81% of females [43]. In our study, 56% of stroke patients were either overweight or obese.

In addition, study has observed that 1.3% of patients with abdominal obesity still have a BMI within the normal range [44], suggesting that we should evaluate patients with systemic obesity and abdominal obesity as two different aspects. This study employed BMI and waist circumference (WC) to evaluate overall obesity and abdominal obesity, respectively. To correct for the effect of height on abdominal circumference, the ratio of abdominal circumference to height was used to further evaluate abdominal obesity [45]. In this study, 81.2% of patients with abdominal obesity were grouped according to their abdominal circumference level. According to the height ratio of abdominal circumference, 90.5% of patients had abdominal obesity.

Obesity has been considered a risk factor for cardiovascular and cerebrovascular diseases [41,46], heart failure [47], hypertension [48], and chronic kidney disease [49]. However, the concept of 'obesity paradox' has gained attention. Since Gruberg *et al.* [50] first identified this paradox in 2002 among coronary intervention patients, debate has persisted about the impact of obesity on cardiovascular and cerebrovascular outcomes. While a previous study

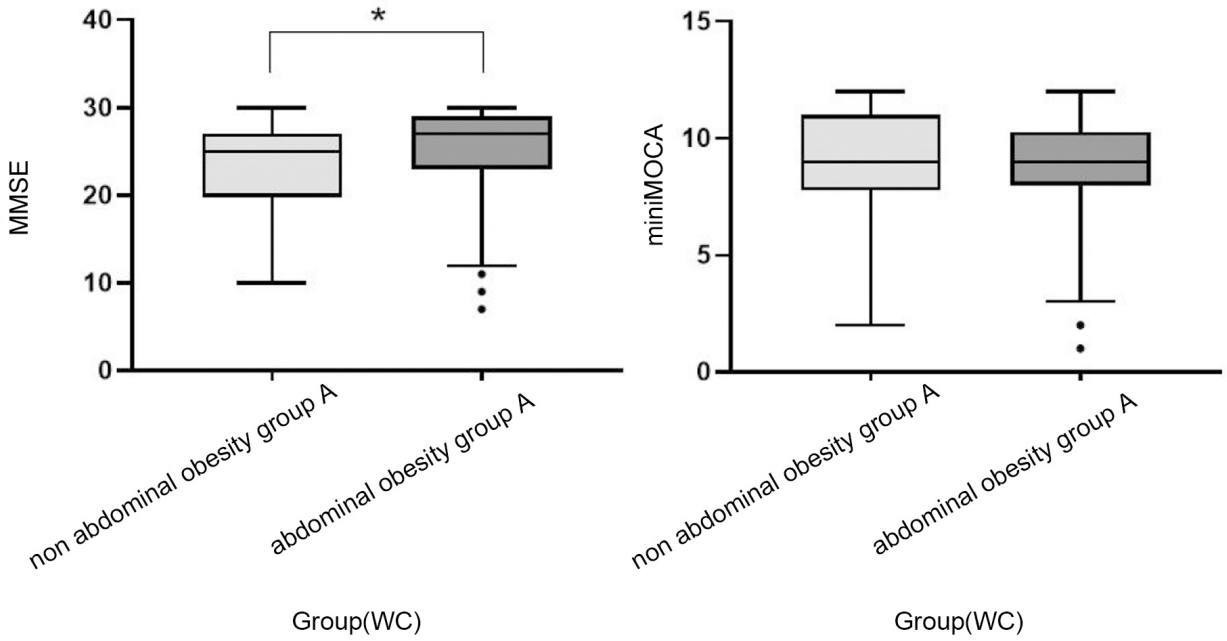

Fig. 2. Relationship between WC levels and cognitive scores. Non-abdominal obesity group A (n = 73), Abdominal obesity group A (n = 315). Data are presented as the median [P25, P75], *$p < 0.05$. Abbreviations: WC, waist circumference; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

suggested that obesity increased the risk of ischemic stroke [51], others argue that a higher BMI may be protective. The relationship between obesity and cognitive impairment is also controversial. Another study suggested that obesity and abdominal obesity were risk factors for cognitive impairment [52]. However, some results report that the impact of obesity and abdominal obesity on cognitive function needs to be analyzed differently based on gender and age levels. Liu *et al*. [53] observed that obesity is a risk factor for cognitive function in middle-aged and elderly men, but in normal weight elderly women, abdominal obesity actually reduces the risk of cognitive impairment. Stickel *et al*. [54] believed that there is no correlation between abdominal obesity and cognitive impairment.

In stroke, the association between obesity and cognitive outcome remains unclear. For example, Li *et al*. [55] identified metabolic syndrome as a significant risk factor for cognitive impairment in ischemic stroke patients (OR = 3.542). Pascoe *et al*. [56] believed that there is no correlation between BMI level and cognitive level in elderly stroke patients. This study observed statistical differences ($p < 0.05$) in the MMSE score within 2 weeks of onset and the miniMoCA score at 6 months after stroke among ischemic stroke patients with different BMI levels. Pairwise comparison showed that the MMSE score of overweight patients was higher than that of normal weight group patients ($p < 0.05$), and the miniMoCA score of overweight patients was higher than that of obese group patients ($p = 0.014$). Additionally, patients with abdominal obesity had higher MMSE scores than those without abdominal obesity ($p < 0.05$). The results of multivariate analysis suggested that there was an independent negative correlation between the abdominal height ratio (with or without abdominal obesity) and cognitive impairment after ICH. There are results reporting that in low-income elderly patients, for every 1cm increase in abdominal circumference, the risk of cognitive impairment decreases by 4% [57]. There is study reporting that low-income groups face serious social isolation problems, while elderly low-income patients will face a higher risk of social isolation [58]. This suggests that stroke patients with abdominal obesity may receive greater economic and familial support, potentially aiding their physical and cognitive rehabilitation. However, this study did not account for lifestyle, economic status, family dynamics, or social environment variables.

The relationship between visceral fat content and cognitive function remains controversial. While some studies suggest that visceral fat is a risk factor for cognitive im-

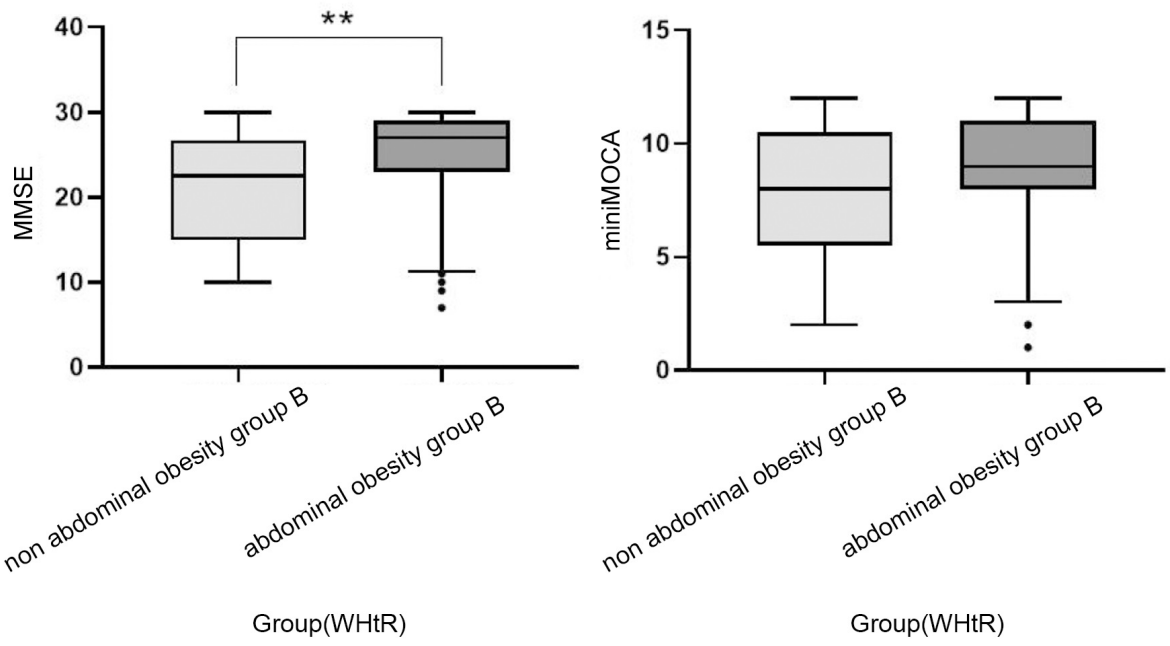

Fig. 3. Relationship between WHtR and cognitive scores (Z). Non-abdominal obesity group B (n = 37), Abdominal obesity group B (n = 351). Data are presented as median [P25, P75], $^{**}p < 0.01$. Abbreviations: WHtR, waist-to-height ratio; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

Table 3. Logistic analysis of visceral fat content and cognitive impairment after ICH.

Variables	B	S.E.	Wald	*p*-value	OR (95% CI)
WHtR	–1.46	0.60	5.81	0.016	0.233 (0.071, 0.762)
BMI	–0.10	0.09	1.19	0.275	0.904 (0.760, 1.076)
WC	–0.04	0.03	1.78	0.182	0.963 (0.903, 1.026)
Visceral fat	–0.01	0.01	1.00	0.317	0.993 (0.974, 1.011)
Visceral/subcutaneous fat ratio	–0.14	0.30	0.21	0.650	0.870 (0.484, 1.562)

Abbreviations: WHtR, waist-to-height ratio; BMI, body mass index; WC, waist circumference; B, regression coefficient; S.E., standard error; OR, odds ratio; CI, confidence interval.

pairment [14,52], another study reports the opposite, indicating that increased visceral fat may reduce the risk of mild cognitive impairment [59]. For instance, Anan *et al*. [60] observed that individuals with higher visceral fat had larger hippocampal volumes in a healthy population. In addition, Nishizawa *et al*. [61] observed that the higher the visceral fat content in older adults, the lower the risk of cognitive impairment. Conversely, some findings have found no significant association between visceral fat and cognitive function [53], consistent with our findings, which indicate no correlation between visceral fat content, the visceral/subcutaneous fat ratio, and cognitive impairment after ICH.

Adiponectin (ANP), a glycoprotein secreted by adipose tissue [14], has been reported to have a negative correlation with total fat content [62]. ANP is known for its insulin-sensitizing, anti-inflammatory, and anti-atherosclerotic properties and is closely linked to diabetes, coronary heart disease, and cerebrovascular diseases [22, 63–66]. The relationship between ANP and cognitive function in stroke patients is widely debated. While a previous study suggested no correlation between ANP and cognitive function [67], others report that reduced ANP levels are associated with cognitive decline [65,68]. For instance, Kamogawa *et al*. [25] observed that male patients with mild cognitive impairment had lower ANP levels. Our findings align with this, suggesting that overweight acute ischemic stroke patients in the cognitive impairment group

Table 4. Correlation analysis between adipokines and cognitive impairment after ICH.

Variables	Low adipokine group (n = 194)	High adipokine group (n = 194)	*t*/*Z*	*p*-value
Systolic blood pressure (mmHg)	151.05 ± 19.41	149.32 ± 24.19	0.775	0.439
Diastolic blood pressure (mmHg)	88.00 (76.00, 92.00)	87.50 (74.75, 100.50)	0.472	0.639
BMI (kg/cm^2)	25.49 ± 2.79	23.82 ± 3.18	5.484	<0.001
WC (cm)	101.74 ± 9.19	97.25 ± 12.17	4.090	<0.001
WHtR	0.61 ± 0.05	0.58 ± 0.07	4.845	<0.001
MMSE at admission	27.00 (25.00, 29.00)	27.00 (23.00, 29.00)	0.444	0.659
miniMoCA at follow-up	9.00 (7.00, 11.00)	9.00 (7.00, 10.00)	0.665	0.507
NIHSS at admission	2.00 (1.00, 5.00)	2.00 (1.00, 3.00)	0.670	0.504
mRS at follow-up	1.00 (1.00, 3.00)	1.00 (1.00, 2.00)	1.251	0.211

Abbreviations: BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio; MMSE, Mini-Mental State Examination; NIHSS, National Institute of Health stroke scale; mRS, modified rankin scale.

Table 5. Differences in ANP levels between overweight individuals with and without cognitive impairment.

Variables	Cognitively impairment group (n = 37)	Non-cognitively impairment group (n = 102)	*Z*-score	*p*-value
ANP	16.56 (9.61, 26.17)	34.46 (24.05, 45.76)	–15.093	0.040

Abbreviations: ANP, adiponectin.

had significantly lower ANP levels ($p = 0.040$). These findings suggest that ANP levels could serve as a predictive marker for cognitive impairment after ICH, especially in overweight stroke patients.

This study aimed to explore the relationship between visceral fat content, adipokines, and cognitive impairment after ICH. Our findings indicate that obesity indicators (BMI, waist circumference, and WHtR), total abdominal fat, and visceral fat content are associated with cognitive outcomes post-ICH. Overweight patients demonstrated higher cognitive scores than those of normal weight or obese individuals, suggesting that maintaining an appropriate BMI may reduce the incidence of ICH. Moreover, the WHtR (with or without abdominal obesity) was independently and negatively associated with ICH. ANP levels were inversely related to obesity indicators, with lower ANP levels observed in patients with higher BMI, waist circumference, and WHtR. Among overweight stroke patients, those with cognitive impairment had lower ANP levels, indicating that ANP may mediate the impact of obesity on cognitive outcomes post-ICH. Additionally, age and white matter lesions were identified as independent risk factors for cognitive impairment following ICH.

Although this study identifies a potential association between visceral fat content and cognitive impairment following ICH, we recognize that several limitations may influence the interpretation and generalizability of the results. First, while the findings are somewhat representative in a single-center study, the relatively small sample size limits the broader applicability of the results. Second, the retrospective design of this single-center study introduces a risk of selection bias, which may affect the external validity of the findings. Third, inflammation likely plays a critical role in cognitive impairment following ICH, but this study did not include inflammatory markers such as C-reactive protein or interleukins in its analysis, potentially limiting our understanding of the relationship between visceral fat and cognitive impairment. Fourth, the study employed the MMSE and miniMoCA to assess cognitive function, and although these tools are widely used, they may not be sufficient to comprehensively evaluate the different cognitive domains affected by ICH. Finally, although the multivariate analysis controlled for some confounding factors, other variables, such as pre-stroke cognitive status and blood pressure control, were not fully accounted for and may have influenced the results. Future research should address these limitations by incorporating larger sample sizes, multi-center designs, and the inclusion of inflammatory and other confounding factors to better understand the relationship between visceral fat and cognitive impairment following ICH.

Conclusion

In summary, this study found no independent correlation between visceral fat content, the visceral/subcutaneous fat ratio, and ICH. Similarly, no significant association was observed between ANP levels and ICH. However, subgroup analysis revealed that in overweight patients, the ANP level was lower in the cognitive impairment group. These findings suggest that while ANP is not directly associated with ICH overall, changes in ANP levels may be related to cog-

nitive impairment in specific populations. Clinically, although ANP and visceral fat measurements were not independent predictors of ICH, monitoring ANP levels in overweight patients could serve as a valuable tool for early identification of potential cognitive impairment, allowing for timely interventions. Further research is needed to explore the physiological mechanisms and potential clinical applications of ANP across different weight groups. Larger longitudinal studies are required to validate these findings and investigate the causal relationship between ANP levels and cognitive impairment, providing stronger guidance for clinical practice.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

YCW designed the research study; YCW and XTZ performed the research; XTZ and XZ collected and analyzed the data. YCW, XTZ and XZ were involved in drafting the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Zhejiang Chinese Medical University (Approval No. (058)-01). Each participant signed an informed consent form. And this study adhered to the ethical principles outlined in the Helsinki Declaration.

Acknowledgment

Not applicable.

Funding

This study is supported by The National Natural Science Foundation of China (81873186).

Conflict of Interest

The authors declare no conflicts of interest.

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