Effect of body mass index on outcome after aneurysmal subarachnoid hemorrhage treated with clipping versus coiling

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OBJECTIVE It has been suggested that increased body mass index (BMI) may confer a protective effect on patients who suffer from aneurysmal subarachnoid hemorrhage (aSAH). Whether the modality of aneurysm occlusion influences the effect of BMI on patient outcomes is not well understood. The authors aimed to compare the effect of BMI on outcomes for patients with aSAH treated with surgical clipping versus endovascular coiling.

METHODS The authors retrospectively reviewed the outcomes for patients admitted to their institution for the management of aSAH treated with either clipping or coiling. BMI at the time of admission was recorded and used to assign patients to a group according to low or high BMI. Cutoff values for BMI were determined by classification and regression tree analysis. Predictors of poor functional outcome (defined as modified Rankin Scale score > 2 measured $\geq$ 90 days after the ictus) and posttreatment cerebral hypodensities detected during admission were then determined separately for patients treated with clipping or coiling using stepwise multivariate logistic regression analysis.

RESULTS Of the 469 patients admitted to the authors' institution with aSAH who met the study's inclusion criteria, 144 were treated with clipping and 325 were treated with coiling. In the clipping group, the frequency of poor functional outcome was higher in patients with BMI $\geq$ 32.3 kg/m² (47.6% vs 19.0%; $p = 0.007$). In contrast, in the coiling group, patients with BMI $\geq$ 32.3 kg/m² had a lower frequency of poor functional outcome at $\geq$ 90 days (5.8% vs 30.9%; $p < 0.001$). On multivariate analysis, high BMI was independently associated with an increased (OR 3.92, 95% CI 1.20–13.41; $p = 0.024$) and decreased (OR 0.13, 95% CI 0.03–0.40; $p < 0.001$) likelihood of poor functional outcome for patients treated with clipping and coiling, respectively. For patients in the surgical group, BMI $\geq$ 28.4 kg/m² was independently associated with incidence of cerebral hypodensities during admission (OR 2.44, 95% CI 1.16–5.25; $p = 0.018$) on multivariate analysis. For patients treated with coiling, BMI $\geq$ 33.2 kg/m² was independently associated with reduced odds of hypodensities (OR 0.45, 95% CI 0.21–0.89; $p = 0.021$).

CONCLUSIONS The results of this study suggest that BMI may differentially affect functional outcomes after aSAH, depending on treatment modality. These findings may aid in treatment selection for patients with aSAH.

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KEY WORDS body mass index; cerebral infarction; subarachnoid hemorrhage; vascular disorders

PREVIOUS work has suggested the possibility of a protective effect of increased body mass index (BMI) on patients suffering from aneurysmal subarachnoid hemorrhage (aSAH).^{13,38} This finding, however, has not been consistently observed in other studies;^{9,17,28,29,33} in fact, certain studies have observed a negative effect of increased BMI on patient outcomes.^{15,27}

Ruptured aneurysms are typically secured with either surgical clipping or endovascular coiling. The physiological effects of elevated BMI may confer higher levels of procedural risk and subsequent complications, particularly for patients undergoing open intracranial surgery.^{3,26,30} Whether BMI affects the clinical course of patients with aSAH in a treatment modality-dependent manner is not

ABBREVIATIONS aSAH = aneurysmal subarachnoid hemorrhage; BMI = body mass index; CART = classification and regression tree; DCI = delayed cerebral ischemia; mRS = modified Rankin Scale; WFNS = World Federation of Neurosurgical Societies.

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well understood. Herein, we compared the effect of BMI on patient functional outcomes after aSAH treated with either surgical clipping or endovascular coiling.

Methods

Patient Selection

After approval from our institutional review board, we retrospectively reviewed the clinical course and outcome of patients admitted to our institution for management of aSAH between 2002 and 2016. Patients were included for analysis if they were treated with either surgical clipping or endovascular coiling. Patients were subsequently classified for analysis according to treatment modality. Patients treated with both endovascular coiling and surgical clipping were included in the surgical group ($n = 4$). Patients without sufficient information to calculate BMI were excluded ($n = 5$ from the clipping group, $n = 6$ from the coiling group).

Treatment Selection Criteria for Clipping Versus Coiling

During the study period, the decision to perform surgical clipping versus endovascular coiling was based primarily on aneurysm-related factors (geometry and location), with increasing preference for endovascular coiling over time if the aneurysm in question was deemed suitable to safe endovascular treatment. Among patient-related factors, endovascular treatment was strongly favored in patients ≥ 70 years of age.

Patient Outcomes

The primary outcome of interest was patient functional outcome as assessed by the modified Rankin Scale (mRS). mRS scores were dichotomized according to values ≤ 2 or > 2 , indicating good and poor outcomes, respectively. Outcomes were determined at the last follow-up visit with a neurosurgeon, cerebrovascular neurologist, physical medicine and rehabilitation physician specializing in brain rehabilitation, or allied health staff member trained in determination of the mRS score. We also noted those patients with follow-up after the ictus of at least 90 days. There were 362 (77.2%) patients with follow-up of at least 90 days, with a mean follow-up of 362.6 days (SD 461.5). A secondary outcome of interest was the detection of hypodensities suggestive of cerebral infarction visualized on postprocedural CT scans obtained at any point after treatment that were not present on images obtained at the time of admission. Images were reviewed by the first author (L.R.), who was blinded to patient BMI at the time of imaging evaluation. Hypodensities in a vascular distribution that persisted or became more evident over time were considered more likely to represent infarction and were categorized as such. The interpretation of the reading radiologist was also taken into consideration for each case. An additional secondary outcome was all-cause mortality during the follow-up period.

Patient Characteristics and Covariates of Interest

The primary variable of interest was patient BMI, determined according to a patient's height and weight in cen-

timeters and kilograms, respectively, upon admission for aSAH. BMI was considered as a categorical variable, with patients segregated according to whether their BMI was above or below a cutoff value. Cutoff values for BMI were determined through the use of Classification and Regression Tree (CART) analysis. For an independent continuous variable, in this case BMI, CART analysis determines a value above and below which the greatest differences are observed in a dependent variable, in this case poor functional outcome (mRS score > 2). Specific cutoff values were determined separately for the clipping and coiling groups. CART was also used to determine a cutoff value for BMI above and below which was observed the greatest difference in detection of cerebral hypodensities after clipping and coiling. We also performed an analysis in which the cutoff for BMI was set at 30.0 kg/m^2 , which is the standard cutoff for obesity as established by the WHO.³⁷

Additional covariates included patient age, sex, presence of comorbid hypertension, smoking status at time of aSAH, presenting World Federation of Neurosurgical Societies (WFNS) grade and modified Fisher grade, presence of intracerebral hemorrhage on initial CT scan, need for external ventricular drainage, aneurysm size and location, incidence of intraoperative aneurysmal rupture, usage of temporary clipping, longest duration of temporary clipping, arterial sacrifice or occlusion secondary to aneurysm clipping, blood loss during aneurysm surgery, procedural duration of aneurysm surgery, incidence of delayed cerebral ischemia (DCI), and early cerebral hypodensities $> 10 \text{ ml}^3$ after clipping.

WFNS grades and modified Fisher grades were dichotomized into good and severe grades, with grades $> \text{III}$ and II and > 3 and 2 denoting severe grades for WFNS and modified Fisher scales, respectively. The incidence of intraoperative aneurysm rupture and usage of temporary clipping was determined via review of the operative record. Duration of temporary clipping was obtained via review of anesthetic records documenting the duration of each period of temporary clipping. Information on procedural blood loss and duration was also obtained through review of the anesthetic record.

DCI was defined as focal neurological deterioration that did not manifest immediately after aneurysm occlusion and that was not attributable to a cause immediately evident on clinical assessment or on CT or MR images, as previously described.³⁴ Early hypodensities after clipping were defined as hypodensities visualized on postoperative CT scans that were not present on preoperative images. The mean time to first postoperative scan was 1.6 days (SD 2.2). The cutoff of 10 ml^3 was chosen on the basis of previous work suggesting that infarctions of this size are associated with poor functional outcome after clipping of ruptured aneurysms.⁴ Hypodensity volumes were determined using the $xyz/2$ method, with x , y , and z representing the maximal dimensions of the infarct in 3 orthogonal planes.

Statistical Analysis

Descriptive statistics for continuous and categorical variables were reported as a mean with standard deviation

and range, and as frequency and percentage, respectively. Differences in patient baseline characteristics, treatment, and functional outcomes between patients with low and high BMI were determined through the use of the unpaired Student t-test and Pearson's χ^2 test, when appropriate. Predictors of poor functional outcome were identified by univariate logistic regression analysis and determined separately for patients treated with clipping and coiling. Covariates associated with poor functional outcome with a p value ≤ 0.100 were included in a stepwise multivariate logistic regression model to identify independent predictors of poor functional outcome. Predictors of cerebral hypodensities detected during admission were also determined using univariate and stepwise multivariate logistic regression in a similar fashion. C-statistics were recorded to provide a measure of the predictive capacity of multivariate models. All statistical tests were 2-sided with an alpha level set at 0.05 for statistical significance. Statistical analyses were performed using commercially available software (JMP 10.0.0; SAS Institute, Inc.).

Results

Effect of BMI on Patient Characteristics and Outcomes for Patients Treated With Clipping Versus Coiling

One hundred forty-four patients who presented to our institution and were treated with surgical clipping met our inclusion criteria for analysis. The cutoff for BMI, above and below which maximal differences in the incidence of poor functional outcome were observed, was 32.3 kg/m². One hundred nine patients treated with surgical clipping had a BMI < 32.3 kg/m² (low BMI), and 35 patients had a BMI $\geq$ 32.3 kg/m² (high BMI). The mean values for BMI of these groups were 25.7 and 37.1 kg/m², respectively.

Baseline characteristics of patients with low and high BMI are detailed in Table 1. There were no differences in the incidence of WFNS Grades IV–V (16.5% vs 20.0%; $p = 0.636$) and modified Fisher Grades 3–4 (67.0% vs 74.3%; $p = 0.417$) at presentation for patients with low and high BMI. There was also no difference in the incidence of intracerebral hemorrhage (21.1% vs 28.6%; $p = 0.360$). No significant difference in the incidence of early cerebral hypodensities > 10 ml³ after clipping was observed between patients with low and high BMI (21.0% vs 30.3%; $p = 0.280$).

There was a slight trend toward a higher overall incidence of cerebral hypodensities during admission in patients with high BMI (51.8% vs 67.6%; $p = 0.106$), although this difference was not significant. The incidence of poor functional outcome at last follow-up was lower for patients with low BMI relative to those with high BMI (17.4% vs 37.1%; $p = 0.015$). When analysis was limited to patients with last follow-up occurring at least 90 days after the initial ictus, this relationship persisted (19.0% vs 47.6%; $p = 0.007$; Table 1). There was a trend toward an increased rate of mortality during follow-up for patients with high BMI (5.5% vs 14.3%; $p = 0.089$), although this was not statistically significant.

Three hundred twenty-five patients who presented to our institution with aSAH were treated with endovascular coiling. The cutoff value for BMI (determined by CART

analysis) that yielded the greatest differences in the incidence of poor functional outcome for this group was 32.5 kg/m². There were 253 patients with a BMI < 32.5 kg/m² (low BMI) and 72 patients with a BMI $\geq$ 32.5 kg/m² (high BMI), with an average BMI of 25.8 and 37.8 kg/m² for these groups, respectively. Baseline characteristics of these groups are shown in Table 2.

Comparable to the surgical clipping group, most patient variables between the low- and high-BMI groups were similar, with a few exceptions. There were trends toward a higher frequency of female patients (62.1% vs 73.6%; $p = 0.070$) and modified Fisher Grades 3–4 in the high-BMI group (70.7% vs 81.9%; $p = 0.058$). More aneurysms were located in the anterior circulation in the low-BMI group compared with those in the high-BMI group (79.1% vs 66.7%; $p = 0.029$). There was also a trend toward a lower incidence of cerebral hypodensities among patients with high BMI (31.6% vs 20.8%; $p = 0.076$).

In contrast to the surgical group, patients with high BMI who were treated with coiling had a lower incidence of poor functional outcome (27.3% with low BMI vs 12.5% with high BMI; $p = 0.001$). A similar relationship was observed when analysis was limited to patients with at least 90 days of follow-up (30.9% with low BMI vs 5.8% with high BMI; $p < 0.001$; Table 2). There was also a lower mortality rate among patients with high BMI (16.2% vs 2.8%; $p = 0.003$).

Predictors of Poor Functional Outcome for Patients Treated With Clipping Versus Coiling

Predictors of poor functional outcome among patients with ≥ 90 days of follow-up were first determined for patients treated with clipping. On univariate analysis, BMI ≥ 32.3 kg/m² was associated with an increased odds of poor functional outcome (OR 3.88, 95% CI 1.39–10.96; $p = 0.010$). Active smoking (OR 3.25, 95% CI 1.22–9.76; $p = 0.017$), presence of intracerebral hemorrhage on admission (OR 5.69, 95% CI 2.12–15.83; $p < 0.001$), need for external ventricular drainage (OR 2.52, 95% CI 1.01–6.53; $p = 0.048$), and hypodensities detected during admission (OR 5.25, 95% CI 1.79–19.32; $p = 0.002$) were also associated with poor functional outcome.

There was a trend toward increased odds of poor functional outcome with DCI (OR 2.25, 95% CI 0.90–5.82; $p = 0.082$), although this relationship was not significant (Table 3). On multivariate analysis, BMI ≥ 32.3 kg/m² (OR 3.92, 95% CI 1.20–13.41; $p = 0.024$), intracerebral hemorrhage (OR 6.18, 95% CI 1.94–21.94; $p = 0.002$), external ventricular drainage (OR 3.46, 95% CI 1.16–11.54; $p = 0.026$), and cerebral hypodensities detected during admission (OR 3.44, 95% CI 1.03–13.84; $p = 0.045$) were found to be independent predictors of poor functional outcome (Table 4).

For patients treated with coiling, a BMI ≥ 32.5 kg/m² was found to be associated with reduced odds of poor functional outcome at ≥ 90 days after the ictus (OR 0.14, 95% CI 0.03–0.39; $p < 0.001$). Increasing age (unit OR 1.04, 95% CI 1.02–1.07; $p < 0.001$), severe WFNS grades (OR 4.99, 95% CI 2.74–9.19; $p < 0.001$) and modified Fisher grades (OR 6.96, 95% CI 2.92–20.59; $p < 0.001$), intracerebral hemorrhage (OR 2.46, 95% CI 1.10–5.38; p

TABLE 1. Comparison of characteristics and clinical outcomes between patients with low and high BMI whose aneurysms were treated with clipping

Variable	BMI <32.3 kg/m ²	BMI ≥32.3 kg/m ²	Total	p Value
No. of patients	109	35	144	
Age, yrs				
Mean (SD)	54.0 (12.0)	54.1 (12.3)	54.0 (12.1)	
Range	19–85	26–74	19–85	0.949
Sex, no. (%)				
Male	39 (35.8)	11 (31.4)	50 (34.7)	
Female	70 (64.2)	24 (68.6)	94 (65.3)	0.638
BMI, kg/m ²				
Mean (SD)	25.7 (3.6)	37.1 (5.6)	28.5 (6.4)	
Range	16.3–32.1	32.3–60.9	16.3–60.9	NA
Hypertension, no. (%)				
No	57 (52.3)	16 (45.7)	73 (50.7)	
Yes	52 (47.7)	19 (54.3)	71 (49.3)	0.498
Smoker, no. (%)				
No	45 (41.3)	18 (51.4)	63 (43.8)	
Yes	64 (58.7)	17 (48.6)	81 (56.3)	0.293
WFNS grade, no. (%)				
I–III	91 (83.5)	28 (80.0)	119 (82.6)	
IV–V	18 (16.5)	7 (20.0)	25 (17.4)	0.636
Modified Fisher grade, no. (%)				
1–2	36 (33.0)	9 (25.7)	45 (31.3)	
3–4	73 (67.0)	26 (74.3)	99 (68.7)	0.417
Intracerebral hemorrhage, no. (%)				
No	86 (78.9)	25 (71.4)	111 (77.1)	
Yes	23 (21.1)	10 (28.6)	33 (22.9)	0.360
External ventricular drainage, no. (%)				
No	68 (62.4)	18 (51.4)	86 (59.7)	
Yes	41 (37.6)	17 (48.6)	58 (40.3)	0.250
Aneurysm size, mm				
Mean (SD)	7.5 (6.3)	8.6 (4.9)	7.8 (6.0)	
Range	1.5–40.0	1.5–25.0	1.5–40.0	0.372
Aneurysm location, no. (%)				
Anterior circulation	99 (90.8)	33 (94.3)	132 (91.7)	
Posterior circulation	10 (9.2)	2 (5.7)	12 (8.3)	0.519
Early infarction >10 ml ³ , no. (%)				
No	75 (79.0)	23 (69.7)	98 (76.6)	
Yes	20 (21.0)	10 (30.3)	30 (23.4)	0.280
DCI, no. (%)				
No	68 (62.4)	22 (62.9)	90 (62.5)	
Yes	41 (37.6)	13 (37.1)	54 (37.5)	0.960
Hypodensity during admission, no. (%)				
No	52 (48.2)	11 (32.4)	63 (44.4)	
Yes	56 (51.8)	23 (67.6)	79 (55.6)	0.106
mRS score >2 at last FU, no. (%)				
No	90 (82.6)	22 (62.9)	112 (77.8)	
Yes	19 (17.4)	13 (37.1)	32 (22.2)	0.015
mRS score >2 at ≥90 days after ictus, no. (%)				
No	64 (81.0)	11 (52.4)	75 (75.0)	
Yes	15 (19.0)	10 (47.6)	25 (25.0)	0.007

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TABLE 1. Comparison of characteristics and clinical outcomes between patients with low and high BMI whose aneurysms were treated with clipping

Variable	BMI <32.3 kg/m ²	BMI ≥32.3 kg/m ²	Total	p Value
Mortality during FU, no. (%)				
No	103 (94.5)	30 (85.7)	133 (92.4)	
Yes	6 (5.5)	5 (14.3)	11 (7.6)	0.089

FU = follow-up; NA = not applicable; no statistical test was performed for this variable between the groups.

= 0.030), external ventricular drainage (OR 5.73, 95% CI 3.08–11.21; $p < 0.001$), DCI (OR 3.73, 95% CI 2.09–6.70; $p < 0.001$), and cerebral hypodensities (OR 6.66, 95% CI 3.67–12.36; $p < 0.001$) were associated with poor functional outcome (Table 3).

On multivariate analysis, a BMI ≥ 32.5 kg/m² was independently associated with reduced odds of poor functional outcome (OR 0.13, 95% CI 0.03–0.40; $p < 0.001$). Increasing age (unit OR 1.04, 95% CI 1.01–1.07; $p = 0.004$), WFNS Grades IV–V (OR 2.30, 95% CI 1.04–5.15; $p = 0.040$), modified Fisher Grades 3–4 (OR 3.17, 95% CI 1.16–10.24; $p = 0.023$), external ventricular drainage (OR 2.77, 95% CI 1.24–6.34; $p = 0.013$), and cerebral hypodensities (OR 4.64, 95% CI 2.32–9.50; $p < 0.001$) were independently associated with poor functional outcome.

Effect of BMI on Intra- and Postoperative Outcomes After Clipping

We next assessed the effect of BMI on treatment outcomes after surgical clipping. CART analysis was again used to define a cutoff value for BMI. In this case, the presence of cerebral hypodensities after clipping was chosen as the dependent variable, and the cutoff for BMI that yielded the greatest differences in incidence of hypodensities was 28.4 kg/m². There were 78 patients with a BMI < 28.4 kg/m² and 66 patients with a BMI ≥ 28.4 kg/m², with mean values for BMI of 24.1 and 33.7 kg/m², respectively. Baseline characteristics between these groups were compared, the results of which are shown in Table 5.

Of note, patients with high BMI had a greater incidence of intracerebral hemorrhage on presentation (14.1% vs 33.3%; $p = 0.006$). Patients with high BMI were also more likely to require the use of temporary clipping during surgical treatment (69.2% vs 87.8%; $p = 0.007$). There was no difference in duration of the longest period of temporary clipping between patients with low and high BMI (9.7 vs 10.0 min; $p = 0.176$). Patients with high BMI were found to have cerebral hypodensities during admission with higher frequency (43.6% vs 70.3%; $p = 0.001$; Table 5).

Predictors of Cerebral Hypodensities After Clipping and Coiling

Predictors of cerebral hypodensities were then identified through univariate logistic regression analysis. BMI ≥ 28.4 kg/m² was found to be associated with increased odds of detection of hypodensities (OR 3.07, 95% CI 1.54–6.26; $p = 0.002$). Smoking (OR 2.14, 95% CI 1.09–4.24; $p = 0.027$), modified Fisher Grades 3–4 (OR 3.36, 95% CI 1.62–7.16; $p = 0.001$), intracerebral hemorrhage (OR 4.93,

95% CI 2.00–14.07; $p < 0.001$), increasing aneurysm size (unit OR 1.07, 95% CI 1.00–1.15; $p = 0.036$), and DCI (OR 2.72, 95% CI 1.34–5.69; $p = 0.005$) were also found to predict the incidence of cerebral hypodensities after clipping (Table 6). On multivariate analysis, BMI ≥ 28.4 kg/m² (OR 2.44, 95% CI 1.16–5.25; $p = 0.018$), modified Fisher Grades 3–4 (OR 3.22, 95% CI 1.48–7.27; $p = 0.003$), and intracerebral hemorrhage (OR 4.01, 95% CI 1.53–11.97; $p = 0.004$) were found to be independently associated with the incidence of hypodensities (Table 7).

We also investigated predictors of hypodensities after coiling on univariate and multivariate analysis. CART analysis was again used to define a cutoff value for BMI, which in this instance yielded a cutoff value of ≥ 33.2 kg/m². Two hundred fifty-seven patients had a BMI < 33.2 kg/m², and 68 patients had a BMI ≥ 33.2 kg/m². BMI ≥ 33.2 kg/m² was found to be associated with reduced odds of cerebral hypodensities (OR 0.50, 95% CI 0.25–0.95; $p = 0.033$). History of hypertension (OR 1.67, 95% CI 1.03–2.73; $p = 0.039$), WFNS Grades IV–V (OR 2.40, 95% CI 1.41–4.07; $p = 0.001$), modified Fisher Grades 3–4 (OR 2.69, 95% CI 1.47–5.23; $p = 0.001$), intracerebral hemorrhage (OR 2.89, 95% CI 1.33–6.33; $p = 0.007$), external ventricular drainage (OR 2.31, 95% CI 1.42–3.80; $p < 0.001$), and DCI (OR 5.41, 95% CI 3.24–9.18; $p < 0.001$) were associated with increased odds of detecting cerebral hypodensities (Table 6). On multivariate analysis, BMI ≥ 33.2 kg/m² was independently associated with reduced odds of hypodensity (OR 0.45, 95% CI 0.21–0.89; $p = 0.021$). Modified Fisher Grades 3–4 (OR 2.34, 95% CI 1.22–4.71; $p = 0.009$) and DCI (OR 5.00, 95% CI 2.95–8.58; $p < 0.001$) were also independently associated with increased odds of hypodensities (Table 7).

Effect of BMI Meeting WHO Criteria for Obesity on Incidence of Cerebral Hypodensities and Poor Functional Outcome

Given the ubiquitous use of WHO criteria for defining obesity in clinical practice,³⁷ we also assessed the association of a BMI ≥ 30.0 kg/m² with the incidence of cerebral hypodensities after procedural intervention and poor functional outcome at last follow-up. For patients treated with clipping, on univariate analysis, a BMI ≥ 30.0 kg/m² was associated with an increased odds of the presence of a hypodensity appearing after surgery (OR 2.76, 95% CI 1.32–6.04; $p = 0.007$) and poor functional outcome (OR 2.61, 95% CI 1.16–5.90; $p = 0.020$). On multivariate analysis, BMI ≥ 30.0 kg/m² was independently associated with an increased odds of infarction (OR 2.68, 95% CI

TABLE 2. Comparison of characteristics and clinical outcomes between patients with low and high BMI whose aneurysms were treated with coiling

Variable	BMI <32.5 kg/m ²	BMI ≥32.5 kg/m ²	Total	p Value
No. of patients	253	72	325	
Age, yrs				
Mean (SD)	56.5 (13.4)	54.4 (11.7)	56.0 (13.1)	
Range	21–89	32–82	21–89	0.224
Sex, no. (%)				
Male	96 (37.9)	19 (26.4)	115 (35.4)	
Female	157 (62.1)	53 (73.6)	210 (64.6)	0.070
BMI, kg/m ²				
Mean (SD)	25.8 (3.6)	37.8 (4.7)	28.5 (6.3)	
Range	16.4–32.5	32.5–56.4	16.4–56.4	NA
Hypertension				
No	121 (47.8)	31 (43.1)	152 (46.8)	
Yes	132 (52.2)	41 (56.9)	173 (53.2)	0.474
Smoker, no. (%)				
No	137 (54.2)	39 (54.2)	176 (54.2)	
Yes	116 (45.8)	33 (45.8)	149 (45.8)	0.998
WFNS grade, no. (%)				
I–III	187 (73.9)	58 (80.6)	245 (75.4)	
IV–V	66 (26.1)	14 (19.4)	80 (24.6)	0.248
Modified Fisher grade, no. (%)				
1–2	74 (29.3)	13 (18.1)	87 (26.8)	
3–4	179 (70.7)	59 (81.9)	238 (73.2)	0.058
Intracerebral hemorrhage, no. (%)				
No	231 (91.3)	65 (90.3)	296 (91.1)	
Yes	22 (8.7)	7 (9.7)	29 (8.9)	0.788
External ventricular drainage, no. (%)				
No	128 (50.6)	39 (54.2)	167 (51.4)	
Yes	125 (49.4)	33 (45.8)	158 (48.6)	0.592
Aneurysm size, mm				
Mean (SD)	6.6 (3.9)	6.4 (3.7)	6.6 (3.9)	
Range	1.0–24.0	1.4–21.0	1.0–24.0	0.670
Aneurysm location, no. (%)				
Anterior circulation	200 (79.1)	48 (66.7)	248 (76.3)	
Posterior circulation	53 (20.9)	24 (33.3)	77 (23.7)	0.029
DCI, no. (%)				
No	174 (68.8)	52 (72.2)	226 (69.5)	
Yes	79 (31.2)	20 (27.8)	99 (30.5)	0.574
Hypodensity during admission, no. (%)				
No	173 (68.4)	57 (79.2)	230 (70.8)	
Yes	80 (31.6)	15 (20.8)	95 (29.2)	0.076
mRS score >2 at last FU, no. (%)				
No	184 (72.7)	63 (87.5)	247 (76.0)	
Yes	69 (27.3)	9 (12.5)	78 (24.0)	0.001
mRS score >2 at ≥90 days after ictus, no. (%)				
No	145 (69.1)	49 (94.2)	194 (74.1)	
Yes	65 (30.9)	3 (5.8)	68 (25.9)	<0.001
Mortality during FU, no. (%)				
No	212 (83.8)	70 (97.2)	282 (86.8)	
Yes	41 (16.2)	2 (2.8)	43 (13.2)	0.003

NA = not applicable; no statistical test was performed for this variable between the groups.

TABLE 3. Results of univariate logistic regression analysis indicating predictors of poor functional outcome (mRS score > 2 at ≥ 90 days after ictus)

Variable	OR (95% CI)	p Value
Clipping		
Age	1.00 (0.96–1.04)*	0.999
Female	0.77 (0.29–2.14)	0.610
BMI ≥32.3 kg/m ²	3.88 (1.39–10.96)	0.010
Hypertension	1.93 (0.77–5.07)	0.163
Smoker	3.25 (1.22–9.76)	0.017
WFNS Grades IV–V	2.24 (0.78–6.26)	0.131
Modified Fisher Grades 3–4	1.88 (0.67–6.19)	0.240
Intracerebral hemorrhage	5.69 (2.12–15.83)	<0.001
External ventricular drainage	2.52 (1.01–6.53)	0.048
Aneurysm size	1.03 (0.96–1.11)*	0.372
Anterior circulation	0.64 (0.15–3.22)	0.556
DCI	2.25 (0.90–5.82)	0.082
Hypodensity during admission	5.25 (1.79–19.32)	0.002
Early infarction >10 ml ³	2.05 (0.72–5.65)	0.176
Coiling		
Age	1.04 (1.02–1.07)*	<0.001
Female	0.70 (0.40–1.25)	0.227
BMI ≥32.5 kg/m ²	0.14 (0.03–0.39)	<0.001
Hypertension	1.26 (0.73–2.22)	0.408
Smoker	0.81 (0.46–1.42)	0.461
WFNS Grades IV–V	4.99 (2.74–9.19)	<0.001
Modified Fisher Grades 3–4	6.96 (2.92–20.59)	<0.001
Intracerebral hemorrhage	2.46 (1.10–5.38)	0.030
External ventricular drainage	5.73 (3.08–11.21)	<0.001
Aneurysm size	1.05 (0.97–1.12)*	0.216
Anterior circulation	0.89 (0.45–1.68)	0.716
DCI	3.73 (2.09–6.70)	<0.001
Hypodensity during admission	6.66 (3.67–12.36)	<0.001

* Unit odds ratio, indicating the increase in odds ratio for every 1-unit increase in variable.

1.21–6.20; $p = 0.015$); however, this was no longer significantly associated with poor functional outcome (OR 2.16, 95% CI 0.89–5.26; $p = 0.087$; Table 8).

For patients treated with coiling, BMI ≥ 30.0 kg/m² was associated with reduced odds of poor functional outcome (OR 0.53, 95% CI 0.29–0.94; $p = 0.030$); however, this was not significantly associated with the incidence of a cerebral hypodensity (OR 0.74, 95% CI 0.44–1.24; $p = 0.263$). On multivariate analysis, BMI ≥ 30.0 kg/m² was not significantly associated with poor functional outcome (OR 0.56, 95% CI 0.28–1.07; $p = 0.078$) or the incidence of hypodensities (OR 0.72, 95% CI 0.40–1.25; $p = 0.245$; Table 8).

Discussion

Herein, we compared the effect of BMI on functional outcome after aSAH in patients treated with surgical clip-

TABLE 4. Results of multivariate stepwise logistic regression analysis indicating predictors of poor functional outcome (mRS score > 2 at ≥ 90 days after ictus)

Variable	OR (95% CI)	p Value	C-Statistic
Clipping			
BMI ≥ 32.3 kg/m ²	3.92 (1.20–13.41)	0.024	
Intracerebral hemorrhage	6.18 (1.94–21.94)	0.002	
External ventricular drainage	3.46 (1.16–11.54)	0.026	
Hypodensity during admission	3.44 (1.03–13.84)	0.045	0.82
Coiling			
Age	1.04 (1.01–1.07)*	0.004	
BMI ≥ 32.5 kg/m ²	0.13 (0.03–0.40)	<0.001	
WFNS Grades IV–V	2.30 (1.04–5.15)	0.040	
Modified Fisher Grades 3–4	3.17 (1.16–10.24)	0.023	
External ventricular drainage	2.77 (1.24–6.34)	0.013	
Hypodensity during admission	4.64 (2.32–9.50)	<0.001	0.86

* Unit odds ratio, indicating the increase in odds ratio for every 1-unit increase in age.

ping versus endovascular coiling. Elevated BMI was found to be associated with increased and decreased odds of poor functional outcome for patients treated with clipping and coiling, respectively, suggesting that the effect of BMI on patient outcomes may depend on treatment modality. Similarly, increased BMI was independently associated with increased and decreased odds of detecting cerebral hypodensities after treatment with clipping and coiling, respectively, providing a potential mechanism for the effect of BMI on patient outcomes.

The effect of BMI on outcomes after aSAH has been investigated previously, with conflicting results.^{9,13,15,17,28,29,33,38} The inconsistent effect across multiple studies may be partially explained by differences in the frequency of treatment with clipping versus coiling. Five separate studies investigating this topic either provided information on treatment modality for study subjects^{13,15,27,29} or performed subgroup analyses for patients treated with clipping versus coiling.⁹ In an analysis of patients enrolled in clinical trials examining the effect of tirilazad administration on outcomes after aSAH, Schultheiss and colleagues observed no relationship between BMI and patient outcome.²⁹ Of note, however, of 3576 patients enrolled in 4 separate trials, 3208 (89.7%) were treated with surgical clipping.^{11,18,23,24}

In a study by Juvela and colleagues, increased BMI was independently associated with increased odds of cerebral infarction; 97.1% of patients (170 of 175 patients) in their study were treated with open surgery.¹⁵ In contrast, the most beneficial effect of elevated BMI was observed in a study by Hughes and colleagues (data from which are included in the present study), in which 68.3% of patients were treated with endovascular coiling. In a pooled analysis of patients treated with clipping and coiling, patients

TABLE 5. Comparison of treatment outcomes during and after clipping between patients with low and high BMI

Variable	BMI <28.4 kg/m ²	BMI ≥28.4 kg/m ²	Total	p Value
No. of patients	78	66	144	
Age, yrs				
Mean (SD)	53.6 (12.6)	54.5 (11.5)	54.0 (12.1)	
Range	19–85	26–82	19–85	0.629
Sex, no. (%)				
Male	23 (29.5)	27 (40.9)	50 (34.7)	
Female	55 (70.5)	39 (59.1)	94 (65.3)	0.151
BMI, kg/m ²				
Mean (SD)	24.1 (2.8)	33.7 (5.5)	28.5 (6.4)	
Range	16.3–28.3	28.4–60.9	16.3–60.9	NA
Hypertension, no. (%)				
No	41 (52.6)	32 (48.5)	73 (50.7)	
Yes	37 (47.4)	34 (51.5)	71 (49.3)	0.626
Smoker, no. (%)				
No	33 (42.3)	30 (45.5)	63 (43.8)	
Yes	45 (57.7)	36 (54.5)	81 (56.3)	0.705
WFNS grade, no. (%)				
I–III	66 (84.6)	53 (80.3)	119 (82.6)	
IV–V	12 (15.4)	13 (19.7)	25 (17.4)	0.496
Modified Fisher grade, no. (%)				
1–2	28 (35.9)	17 (25.8)	45 (31.3)	
3–4	50 (64.1)	49 (74.2)	99 (68.7)	0.191
Intracerebral hemorrhage, no. (%)				
No	67 (85.9)	44 (66.7)	111 (77.1)	
Yes	11 (14.1)	22 (33.3)	33 (22.9)	0.006
External ventricular drainage, no. (%)				
No	48 (61.5)	38 (57.6)	86 (59.7)	
Yes	30 (38.5)	28 (42.4)	58 (40.3)	0.629
Aneurysm size, mm				
Mean (SD)	7.4 (5.8)	8.3 (6.3)	7.8 (6.0)	
Range			1.5–40.0	0.393
Aneurysm location, no. (%)				
Anterior circulation	71 (91.0)	61 (92.4)	132 (91.7)	
Posterior circulation	7 (9.0)	5 (7.6)	12 (8.3)	0.762
Intraop rupture, no. (%)				
No	55 (70.5)	39 (59.1)	94 (65.3)	
Yes	23 (29.5)	27 (40.9)	50 (34.7)	0.151
Temporary clipping, no. (%)				
No	24 (30.8)	8 (12.2)	32 (22.2)	
Yes	54 (69.2)	58 (87.8)	112 (77.8)	0.007
Longest temporary clipping, mins				
Mean (SD)	9.7 (10.4)	10.0 (10.9)	9.9 (10.6)	
Range	1–52	1–54	1–54	0.176
Arterial occlusion, no. (%)				
No	73 (93.6)	64 (97.0)	137 (95.1)	
Yes	5 (6.4)	2 (3.0)	7 (4.9)	0.347
Procedural blood loss, ml				
Mean (SD)	334.6 (281.8)	392.7 (327.6)	361.4 (304.0)	
Range	50–2000	50–1800	50–2000	0.279

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TABLE 5. Comparison of treatment outcomes during and after clipping between patients with low and high BMI

Variable	BMI <28.4 kg/m ²	BMI ≥28.4 kg/m ²	Total	p Value
Procedural time, mins				
Mean (SD)	279.0 (76.3)	291.5 (75.5)	284.8 (75.9)	
Range	138–491	171–559	138–559	0.328
Early cerebral hypodensity >10 ml ³ , no. (%)				
No	11 (16.9)	19 (30.2)	30 (23.4)	
Yes	54 (83.1)	44 (69.8)	98 (76.6)	0.077
Delayed cerebral ischemia, no. (%)				
No	49 (62.8)	41 (62.1)	90 (62.5)	
Yes	29 (37.2)	25 (37.9)	54 (37.5)	0.931
Hypodensity during admission, no. (%)*				
No	44 (56.4)	19 (29.7)	63 (44.4)	
Yes	34 (43.6)	45 (70.3)	79 (55.6)	0.001

NA = not applicable; no statistical test was performed for this variable between the groups.

* Due to lack of postprocedural head CT imaging, information on the incidence of cerebral infarction was not available for 2 patients.

with higher BMI were found to have lower short- and long-term mortality rates, although there was no difference in functional outcomes.¹³ On the other hand, despite a comparable coiling rate of 59.4%, Platz and colleagues found no association of BMI with outcome. In addition, among patients with a poor WFNS grade (> III) at presentation, obesity was associated with reduced odds of favorable outcomes.²⁷

A recent study by Dasenbrock and colleagues attempted to directly address the possibility of treatment-dependent effects of BMI on outcome after aSAH. Using data from 18,281 admissions for aSAH contained within the Nationwide Inpatient Sample, in a subgroup analysis of patients treated with coiling, obese (but not morbidly obese) patients had reduced rates of certain in-hospital complications. In addition, obese patients had reduced odds of discharge to a location other than home and a trend toward reduced odds of poor neurological outcome relative to patients of normal weight. No effect of BMI was observed on patients treated with clipping, however.⁹ Ultimately, further work is needed to clarify whether there is a treatment-dependent effect of BMI on outcomes after aSAH.

Treatment-specific effects of BMI on patient outcomes may be mediated by a differential effect on the risk of cerebral hypodensities (potentially representing cerebral infarction) detected after treatment of aSAH. Within our patient cohort, cerebral hypodensities were detected in 37.1% of all patients (174 of 469). The incidence of hypodensities in patients treated surgically was 55.6% (79 of 142 patients), which is a surprisingly high number. Although efforts were made to differentiate transient postoperative swelling secondary to intraoperative retraction from persistent hypodensities more likely to represent cerebral infarction, this distinction was at times not easily made, particularly in the setting of limited postoperative imaging obtained on an as-needed basis.

On review of the literature, previous large-scale studies examining the incidence of cerebral infarction after aSAH (defined as hypodensities visualized on CT images)

observed a putative infarction rate during admission ranging from 29.8% to 61.3% (mean 44.0%, *n* = 4),^{4,12,14,21} with a mean rate among surgically treated patients of 44.7% (SD 14.2%). In addition, similar to our study, the rate of postprocedural infarction was typically higher among patients treated with clipping,^{4,14,21} with 1 exception.¹² These data suggest that the true rate of cerebral infarction in our patient cohort is probably comparable to that observed in other institutions around the country and validates our use of cerebral hypodensities as a secondary outcome.

Regarding the relationship between BMI and risk of infarction, we observed an independent association of high BMI with the incidence of cerebral hypodensities in patients treated with clipping, an association that has been observed previously.^{15,16} In contrast, increased BMI was associated with reduced odds of hypodensities in patients treated with coiling. An explanation for the discrepant effects of BMI depending on treatment modality is not immediately clear. Obesity, particularly central obesity characterized by high levels of abdominal adiposity, is associated with reduced venous return and consequent increases and decreases in intracranial and cerebral perfusion pressures, respectively.^{6–8,31} Obese patients may thus be less likely able to tolerate the necessary retraction to approach ruptured saccular aneurysms, particularly in the setting of an already tense and swollen brain, potentially increasing their risk for cerebral infarction. In a nonsurgical setting, obesity may increase the risk of ischemic stroke.^{22,25,32,35} Paradoxically, however, obesity may portend better recovery from brain infarction,^{1,2,19,20} although this concept is controversial.^{5,10} Whether obesity confers a protective effect after aSAH treated endovascularly or has a negative effect on recovery after clipping requires further investigation.

Limitations of the Study

Our study has limitations. First, compared with a study that used a large national database and did not find a significant treatment-dependent effect of BMI on functional

TABLE 6. Results of univariate logistic regression analysis indicating predictors of cerebral hypodensities during admission after clipping and coiling

Variable	OR (95% CI)	p Value
Clipping		
Age	1.01 (0.98–1.04)*	0.535
Female	0.54 (0.26–1.10)	0.090
BMI ≥ 28.4 kg/m ²	3.07 (1.54–6.26)	0.002
Hypertension	1.13 (0.58–2.19)	0.721
Smoker	2.14 (1.09–4.24)	0.027
WFNS Grades IV–V	2.36 (0.95–6.46)	0.065
Modified Fisher Grades 3–4	3.36 (1.62–7.16)	0.001
Intracerebral hemorrhage	4.93 (2.00–14.07)	<0.001
External ventricular drainage	1.56 (0.79–3.11)	0.200
Aneurysm size	1.07 (1.00–1.15)*	0.036
Anterior circulation	2.72 (0.82–10.63)	0.104
Intraoperative rupture	1.02 (0.51–2.06)	0.948
Temporary clipping	1.86 (0.84–4.17)	0.125
Longest temporary clipping	1.01 (0.98–1.05)	0.451
Arterial occlusion	2.06 (0.43–14.73)	0.379
Procedural blood loss	1.00 (1.00–1.00)	0.234
Procedural time	1.09 (0.96–1.25)	0.202
DCI	2.72 (1.34–5.69)	0.005
Coiling		
Age	1.01 (0.99–1.03)	0.184
Female	1.27 (0.77–2.13)	0.354
BMI ≥ 33.2 kg/m ²	0.50 (0.25–0.95)	0.033
Hypertension	1.67 (1.03–2.73)	0.039
Smoker	1.09 (0.67–1.76)	0.724
WFNS Grades IV–V	2.40 (1.41–4.07)	0.001
Modified Fisher Grades 3–4	2.69 (1.47–5.23)	0.001
Intracerebral hemorrhage	2.89 (1.33–6.33)	0.007
External ventricular drainage	2.31 (1.42–3.80)	<0.001
Aneurysm size	1.03 (0.97–1.10)	0.350
Anterior circulation	1.04 (0.59–1.81)	0.888
DCI	5.41 (3.24–9.18)	<0.001

* Unit odds ratio, indicating the increase in odds ratio for every 1-unit increase in age and aneurysm size, 50-ml increase in procedural blood loss, and 30-minute increase in procedural time.

TABLE 7. Results of multivariate stepwise logistic regression analysis indicating predictors of cerebral hypodensities after clipping and coiling

Variable	OR (95% CI)	p Value	C-Statistic
Clipping			
BMI ≥ 28.4 kg/m ²	2.44 (1.16–5.25)	0.018	
Modified Fisher Grades 3–4	3.22 (1.48–7.27)	0.003	
Intracerebral hemorrhage	4.01 (1.53–11.97)	0.004	0.75
Coiling			
BMI ≥ 33.2 kg/m ²	0.45 (0.21–0.89)	0.021	
Modified Fisher Grades 3–4	2.34 (1.22–4.71)	0.009	
DCI	5.00 (2.95–8.58)	<0.001	0.74

prespecified protocol. As such, it is possible that clinically silent hypodensities were missed. In addition, although efforts were made to use a consistent methodology for distinguishing between hypodensities likely to represent infarction and those secondary to transient postoperative swelling, it is possible that certain hypodensities were mis-categorized; thus our results on predictors of postintervention hypodensities should be interpreted with caution.

Cutoff values for BMI used to segregate patients were determined by CART analysis as opposed to established cutoffs for defining obesity. Whereas CART analysis detects natural cutoffs that are more sensitive for the detection of an effect compared with arbitrarily defined thresholds, the cutoff values at which the greatest effect of BMI was observed may be specific to our particular patient cohort, potentially limiting the generalizability of our results. In addition, multivariate models including the variable defined by CART are heavily weighted in favor of that variable (in this case, BMI), which may have affected whether other covariates were found or not found to be independently associated with outcomes of interest. We did perform an analysis in which the cutoff for BMI was set at 30.0 kg/m², which is the threshold for obesity according to WHO criteria.³⁷ Although the relationship of BMI to outcomes of interest held on univariate analysis for both patients who underwent clipping and coiling (with the exception of the association of BMI with postoperative cerebral hypodensities in patients who underwent coiling; Table 8), the associations were not as robust and lost statistical significance in all but 1 instance on multivariate analysis. It is possible that our study was underpowered to detect an effect of BMI when dichotomized according to pre-established thresholds; larger-scale, multi-institutional studies may be needed to better define the relationship of BMI to outcomes after SAH.

Among patients whose aneurysms were clipped, neither age nor WFNS Grades IV–V were associated with poor outcome on univariate analysis. This may be due to the eschewing of surgical clipping in older patients with poor grades for whom the likelihood of morbidity from open surgery was deemed to be unacceptably high. Differences in selection criteria for clipping versus coiling may have introduced differences in baseline characteristics between

outcomes after aSAH,⁹ the sample size of our study is relatively small; thus our results should be interpreted with caution. Of note, however, Dasenbrock and colleagues⁹ did not have information on functional outcomes and had to rely on the Nationwide Inpatient Sample (NIS)-SAH outcome measure, an indirect assessment shown to be grossly correlated with an mRS score > 3 at discharge.³⁶ We were instead able to analyze functional outcomes evaluated by specialists and measured upon postdischarge follow-up.

Our study is also limited by the single-institutional, retrospective methodology. This is particularly relevant for the detection of cerebral infarction. CT scans on which hypodensities were visualized were obtained at the discretion of the patient provider team and not according to a

TABLE 8. Multivariate analysis assessing association of obesity (according to WHO criteria) with poor functional outcome (mRS score > 2 at ≥ 90 days after ictus) and incidence of cerebral hypodensities

Variable	OR (95% CI)	p Value	C-Statistic
mRS score >2			
Clipping			
BMI ≥30.0 kg/m ²	2.16 (0.89–5.26)	0.087	
Intracerebral hemorrhage	3.52 (1.40–9.00)	0.008	
External ventricular drainage	2.16 (0.91–5.26)	0.082	
Hypodensity during admission	2.98 (1.11–8.96)	0.030	0.77
Coiling			
Age	1.04 (1.01–1.06)*	0.002	
BMI ≥30.0 kg/m ²	0.56 (0.28–1.07)	0.078	
WFNS Grades IV–V	2.82 (1.45–5.55)	0.002	
Modified Fisher Grades 3–4	2.21 (0.94–5.88)	0.071	
External ventricular drainage	2.21 (1.12–4.41)	0.021	
Hypodensity during admission	3.78 (2.08–6.93)	<0.001	0.81
Cerebral hypodensities			
Clipping			
BMI ≥30.0 kg/m ²	2.68 (1.21–6.20)	0.015	
Modified Fisher Grades 3–4	3.32 (1.52–7.53)	0.002	
Intracerebral hemorrhage	4.65 (1.81–13.76)	0.001	0.75
Coiling			
BMI ≥30.0 kg/m ²	0.72 (0.40–1.25)	0.245	
Modified Fisher Grades 3–4	2.23 (1.17–4.47)	0.141	
DCI	4.99 (2.96–8.52)	<0.001	0.74

* Unit odds ratio, indicating the increase in odds ratio for every 1-unit increase in age.

our study groups, potentially limiting the generalizability of our results. Finally, functional outcomes were not determined at the same time point for each patient, although they were determined at least 90 days after the ictus in most patients. Prospective studies are needed to further assess the effect of BMI on outcomes after aSAH.

Conclusions

In the present study, we observed a differential effect of elevated BMI on the incidence of poor functional outcome and cerebral hypodensities after aSAH, depending on whether the ruptured aneurysm was treated with clipping or coiling. Although these findings need to be confirmed, they may aid in the selection of treatment modality for patients with ruptured aneurysms.

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Disclosures

Dr. Lanzino is a consultant for Medtronic.

Author Contributions

Conception and design: all authors. Acquisition of data: Rinaldo. Analysis and interpretation of data: all authors. Drafting the article: Rinaldo. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Lanzino. Statistical analysis: Rinaldo. Study supervision: Lanzino, Rabinstein.

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