Racial differences in intracerebral haemorrhage outcomes in patients with obesity

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Summary

Objective

This study was conducted to determine the role of obesity and race in intracerebral haemorrhage (ICH) outcomes.

Methods

The Get with the guideline-Stroke database was queried for all admitted patients with spontaneous ICH. Secondary causes of ICH were excluded. Body mass index (BMI) was classified using the Center for Disease Control guidelines. Race was classified as White or non-White. Demographics, clinical, imaging data were retrieved. Outcome measures were hematoma expansion at 24 h and discharge disposition.

Results

A total of 428 patients were included in our analysis. Female gender, past history of congestive heart failure, diabetes mellitus, HbA1c, blood pressure, ICH volume, ICH location, intraventricular haemorrhage and hospital length of stay deferred across BMI categories. On multivariate analysis, along with obese categories, age, ICH location and ICH volume were independent predictors of poor outcomes (hematoma expansion and poor discharge disposition). After adjusting for these variables, obesity remained a predictor of poor disposition outcome compared with normal and overweight subjects; Normal vs. Obese OR 0.26 CI 0.115–0.593 p = 0.0014; Obese vs. Overweight OR 3.79 CI 1.68–8.52 p = 0.0013. Nonetheless, obesity did not influence hematoma expansion. Overall, BMI-race classification did not influence outcomes. However, among non-Whites, the obese category had higher odds of a poor disposition outcome than normal (OR 6.84 CI 2.12–22.22 p = 0.0013) or overweight (OR 8.45 CI 2.6–27.49 p = 0.0004) categories.

Conclusion

An obesity paradox in ICH was not observed in our cohort. In the non-White population, patients with obesity were likely to be associated with poor disposition outcome. Similar findings were not observed in White population.

Keywords: intracerebral haemorrhage, obesity, outcomes, racial diversity.

Introduction

Obesity is an established risk factor for cardiovascular disease including acute cerebrovascular disease – acute ischemic and haemorrhagic strokes (1). Links between obesity and stroke are well-established (1). Stroke is the fifth leading cause of death in the United States and constitutes a leading cause of chronic disability. Conversely, several reports show that obesity is associated with better outcomes following several acute conditions – heart failure, carotid endarterectomy, sepsis, bypass surgery and vascular surgery (2–5). Similar reports of better outcomes in patients with obesity following ischemic and haemorrhagic strokes in the literature remain
controversial (6–10). The debates surrounding the concept of obesity paradox in ‘stroke’ include factors such as definition, classification and duration of obesity and the influence of race and racial diversity in obesity (11,12). Of these, race is the most poorly understood.

Compared with White populations, the African–American populations of the United States have a higher incidence of obesity and are more likely to have worse outcomes (13). Obesity along with several other factors likely play a role in outcome differences between races following acute stroke (14,15). However, it remains unclear if outcomes will differ in patients with obesity of different races following an acute intracerebral haemorrhage (ICH).

Several studies have explored outcomes of patients with obesity following ischemic stroke in the literature (7,11,12). Nonetheless, studies on the outcomes of patients with obesity following ICH are limited (10). Second, most reports on obesity paradox in ‘stroke’ do not account for racial diversity in their study. One study from South Korea on outcome of obese patients following spontaneous ICH primarily represents patients of Asian descent (10). Thus, a study within the stroke belt of the United States with a racially diverse population was conducted to determine and compare the outcomes of patients with obesity following ICH among White and non-White populations. This study explores the hypothesis that outcomes will differ between White and non-White patients with obesity following acute ICH.

Methods

The Get with the guideline-Stroke database was queried for all patients admitted to Ochsner Medical Center, New Orleans, LA; during the period 1 November 2012 to 31 March 2016. The Get with the guideline-Stroke database is a mandated database of all acute stroke patients by the Joint Commission on Accreditation of Healthcare Organizations presenting to primary and comprehensive certified stroke centres in the United States. All patients admitted with a diagnosis of ICH were identified for inclusion in the study. Inclusion criteria were age ≥18 years, symptom onset within 24 h and ICH confirmed on computed tomography (CT) or magnetic resonance imaging. Exclusion criteria included patients with prior admissions for ICH, haemorrhagic conversion of ischemic strokes, traumatic brain injury, primary or secondary brain malignancy, post-operative intracranial haemorrhages, vascular malformations and venous sinus thrombosis.

Data on demographics, medical history, clinical, laboratory, imaging characteristics and discharge disposition were collected.

• Imaging – All neuroimaging studies of all patients for initial and follow up CT studies were reviewed. Routinely, a follow-up head CT is obtained at 6-h intervals until hematoma size is stable and/or at 18–24 h. Data on hematoma volume, location and the presence of intraventricular haemorrhage with Graeb scores were collected. ICH volume was calculated using the ABC/2 formula, a previously validated formula for estimating hematoma volume (16). The Graeb score is a 12-point scale based on gross haemorrhage size and dilatation of the ventricles, higher scores representing worse intraventricular haemorrhage (17). Hematoma location was classified as Deep (thalamic and basal ganglia) nuclei, cerebellum, brainstem and lobar. Hematoma expansion is defined as an increase in hematoma volume by ≥30% on follow up 24 h neuroimaging.

• Discharge disposition – All records of discharge locations were reviewed and documented as (1) home with self-care or outpatient therapy; (2) inpatient acute rehabilitation; (3) skilled nursing facility; (4) long-term acute care facility; or (5) deceased. A discharge disposition to home and inpatient acute rehabilitation was classified as a good outcome, while discharge to a skilled nursing, long-term acute care facilities and death were classified as poor outcome. Previous studies have demonstrated and validated the discharge disposition as an outcome measure for ICH (18–20).

• Body mass index (BMI) and obesity classification – Patients with ICH were admitted to the neuroscience intensive care unit at Ochsner Medical Center, New Orleans, LA. On admission, the patients were weighed and their height measured using a flexible tape by the nursing staff. The BMI was then calculated using the formula weight(kg)/height(m)². BMI was classified using the Center for Disease Control guidelines.

• Statistical analysis – Initial analysis was conducted to determine if the means or proportions of various covariates differed between BMI categories. Pearson’s chi-squared statistic was used to test for differences between the categorical variables while t tests were used to analyse the continuous variables. Further analysis used generalized linear logistic models to investigate the odds ratios for combinations of race and BMI category. For these models, the discharge disposition code was expressed as a dichotomous outcome of good (discharge home and inpatient acute rehabilitation disposition) and poor (skilled nursing, long-term acute care facilities and death) outcomes. Similarly, change in hematoma volume was measured as a
Table 1 Baseline and clinical characteristics

| BMI (kg/m²) | <18.5 | 18.5–24.9 | 25–29.9 | 30–34.9 | ≥35 | P-value |
|------------|-------|-----------|---------|---------|-----|---------|
| n          | 15    | 131       | 138     | 68      | 76  |         |
| Race, White (%) | 6(40.00) | 69(52.67) | 76(55.07) | 30(44.12) | 37(48.68) | 0.5185 |
| Gender, female (%) | 11(73.33) | 7(5.34) | 9(6.57) | 4(5.88) | 17(22.37) | 0.0002 |
| Age, median (SD), mean, years | 67.91(19.67) | 64.02(16.44) | 65.50(14.79) | 62.92(14.79) | 59.91(14.05) | 0.108 |
| Hypertension, (%) | 13(92.86) | 119(86.86) | 19(27.94) | 55(80.88) | 69(80.79) | 0.0543 |
| DM, (%) | 2(14.29) | 44(32.12) | 19(27.94) | 29(38.16) | 0.0444 |
| CHF, (%) | 1(7.14) | 9(6.57) | 3(4.41) | 17(22.37) | 0.0002 |
| Hyperlipidemia, (%) | 3(21.43) | 50(36.50) | 19(27.94) | 33(43.42) | 0.0756 |
| CKD, (%) | 0(0) | 17(12.41) | 6(8.82) | 7(9.21) | 0.6375 |
| Prior Stroke, (%) | 2(14.29) | 12(17.65) | 18(23.68) | 0.6433 |
| Smoking, (%) | 7(46.67) | 40(28.99) | 18(23.68) | 0.1687 |
| Prior use of antiplatelets, (%) | 3(20.00) | 26(18.84) | 14(18.42) | 0.1614 |
| Prior use of anticoagulant, (%) | 2(13.33) | 18(13.04) | 17(22.37) | 0.0872 |
| Admission SBP, median (SD), mmHg | 185.5(50.50) | 171.7(35.69) | 188.7(40.56) | 190.2(40.33) | 0.0054 |
| Admission glucose, mean mg/dl | 126.7(45.58) | 155.7(80.13) | 157.6(77.10) | 164.183.12 | 0.4135 |
| HbA1c, mean, (SD) | 5.74(0.72) | 6.17(1.48) | 6.27(1.37) | 6.61(1.72) | 0.0315 |
| Mechanical ventilation, (%) | 5(33.33) | 70(50.72) | 26(38.24) | 30(43.97) | 0.1161 |
| ICH Location | Deep nuclei, (%) | 1(6.67) | 72(62.17) | 27(39.71) | 0.2112 |
| Cerebellum, (% | 1(6.67) | 17(12.32) | 8(11.76) | 10(13.16) | 0.3857 |
| Brainstem, (%) | 1(6.67) | 11(7.97) | 5(7.35) | 5(6.88) | 0.8512 |
| Lobar, (%) | 5(33.33) | 53(42.41) | 32(47.06) | 25(32.89) | 0.3174 |
| Intraventricular haemorrhage, (%) | 9(60.00) | 74(53.62) | 37(51.14) | 30(39.47) | 0.1085 |
| ICH volume, mean, (SD) mL | 38.03(42.53) | 38.51(47.07) | 27(39.71) | 26.29(35.69) | 0.2489 |
| 24 h ICH volume, mean, (SD), mL | 38.61(44.86) | 37.94(51.08) | 45.27(69.51) | 24.99(28.53) | 0.0823 |
| Greab score, mean, (SD) | 2.80(3.59) | 3.24(3.95) | 3.01(3.89) | 2.20(3.32) | 0.4161 |
| >30% Hematoma expansion, n (%) (poor outcome) | 1(7.14) | 27(23.99) | 59(84.39) | 16(24.62) | 0.1259 |
| Hospital LOS, mean, (SD), days | 10.47(7.99) | 14.34(18.44) | 10.75(10.11) | 12.93(14.09) | 0.1102 |
| Disposition | Home/rehab, (%) (good outcome) | 8(53.33) | 61(44.20) | 45(66.18) | 46(60.53) | 0.0113 |
| SNF/LTAC/hospice or death, (%) (poor outcome) | 7(46.67) | 7(54.20) | 23(33.82) | 30(43.97) | 0.0113 |

BMI, body mass index; DM, diabetes mellitus; ICH, intracerebral haemorrhage; CKD, chronic kidney disease; CHF, congestive heart failure; HBA1c, haemoglobin A1c; LOS, length of stay; LTAC, long-term acute care; SBP, systolic blood pressure; SNF, skilled nursing facility.
dichotomous outcome: a change less than 30% vs. change greater than or equal to 30%. In both models, odds ratios were adjusted for age, hypertension, diabetes mellitus, HbA1c, congestive heart failure (CHF), primary hematoma location, admission blood pressure and ICH volume.

Results

A total of 563 patients diagnosed with ICH were identified in our Get with the guideline-Stroke database. Of these, 135 were excluded (34 incomplete data, 21 haemorrhagic transformation of acute ischemic stroke, 20 isolated intraventricular haemorrhages, 14 traumatic ICH, 10 postoperative haemorrhage following brain tumour resection, 7 subacute/chronic ICH, 7 vascular malformations, 6 haemorrhagic brain tumours, 3 subarachnoid haemorrhage, 3 subdural hematoma, 2 parenchymal calcifications and 8 with no “in-house” imaging). Four hundred and twenty eight patients were included in the disposition outcome analysis (good vs. poor). Seventy-three patients did not have a follow up 24 h neuroimaging and were not included in the hematoma expansion outcome analysis (>30% increase in hematoma volume) but were included in the disposition outcome analysis. However, results based on disposition outcome were similar with or without the inclusion of the 73 patients without a follow up CT imaging at 24 h.

Of the 428 patients, 50% were female gender, 49.1% were non-White (43.7% African American, 0.9% Asian, 1.9% non-White Hispanic and 2.6% others), and the White population constituted of non-Hispanic Whites. Except for the underweight category, the frequency of White patients decreased with increasing BMI category; however, this was not statistically significant (Table 1).

The initial results show that several of the variables were different between the BMI categories. Gender, histories of CHF and diabetes mellitus (DM) were different between BMI categories. The other variables that were different related to blood pressure measurements and HbA1c. ICH volume, ICH location, intraventricular haemorrhage and hospital length of stay did not differ between BMI categories. Good outcome discharge disposition differed significantly across BMI categories; however, there was no difference in hematoma expansion across BMI categories (Table 1). Overall comparison of the White and non-White populations showed age, admission systolic blood pressure, anticoagulant use and

| Variable                                      | Non-White | White    | P-value |
|-----------------------------------------------|-----------|----------|---------|
| n                                             | 208       | 215      |         |
| Gender, female, n (%)                         | 107(51.44)| 104(48.37)| 0.5278  |
| Age, years, mean, (SD)                        | 60.48(14.67) | 66.79(15.56) | 0.0000 |
| Admission systolic blood pressure, mmHg, mean, (SD) | 186.1(37.82) | 174.7(40.84) | 0.0034 |
| Admission glucose in mg/dl                    | 152.7(74.66) | 157.0(73.84) | 0.5516 |
| Haemoglobin A1c, % mean (SD)                  | 6.25(1.60) | 6.13(1.42) | 0.4276 |
| Hypertension, n (%)                            | 184(89.32) | 168(78.14) | 0.0019 |
| Diabetes mellitus, n (%)                      | 63(30.58) | 58(26.98) | 0.4138 |
| Congestive heart failure, n (%)               | 18(8.74) | 18(8.37) | 0.8933 |
| Hyperlipidaemia, n (%)                        | 58(28.16) | 78(36.28) | 0.0748 |
| Chronic kidney disease, n (%)                 | 23(11.17) | 20(9.30) | 0.5281 |
| Prior stroke, n (%)                            | 50(24.27) | 39(18.14) | 0.1234 |
| Smoking history, n (%)                        | 59(28.37) | 68(31.63) | 0.4643 |
| Antiplatelet agents, n (%)                    | 31(14.90) | 48(22.33) | 0.0502 |
| Anticoagulant usage, n (%)                    | 19(9.13) | 37(17.21) | 0.0143 |
| Mechanical ventilation within 72 h, n (%)     | 94(45.19) | 101(46.98) | 0.7128 |
| Positive blood cultures, n (%)                | 10(12.66) | 10(13.89) | 0.8237 |
| Deep nuclei, n (%)                             | 113(54.33) | 100(46.51) | 0.1080 |
| Cerebellum, n (%)                              | 24(11.54) | 19(8.84) | 0.3580 |
| Brainstem, n (%)                               | 7(3.37) | 19(8.84) | 0.0192 |
| Lobar, n (%)                                   | 74(35.58) | 98(45.58) | 0.0362 |
| Intraventricular haemorrhage, n (%)           | 98(47.12) | 106(49.53) | 0.6193 |
| Graeb score, mean, (SD)                       | 2.89(3.87) | 2.87(3.75) | 0.9489 |
| Hematoma volume, mL, mean (SD)                | 32.84(43.65) | 41.08(51.03) | 0.0755 |
| >30% Intracerebral hematoma expansion, n (%)  | 37(21.1) | 32(18.1) | 0.4856 |
| Hospital length of stay, (days)               | 12.79(13.56) | 11.50(14.03) | 0.3367 |
| Poor disposition, n (%)                       | 95 (45.67) | 108 (50.23) | 0.3481 |
ICH location were significantly different between the groups (Table 2).

As expected, logistic analysis demonstrated age (Estimate 0.027 SE 0.009 p = 0.0027), ICH location (Estimate 1.456 SE 0.488 p = 0.0031), and ICH volume (Estimate 0.035 SE 0.005 p < 0.0001) as independent predictors of poor disposition outcomes. In addition, there was a significant effect of normal BMI category on poor disposition outcomes (Estimate –0.574 SE 0.919 p = 0.0112).

Only age (Estimate 0.024 SE 0.011 p = 0.029) and hypertension (Estimate 1.048 SE 0.406 p = 0.01) were independent predictors of hematoma expansion outcome (Table 3). Subsequently, data analyses were adjusted for age, hypertension, DM, CHF, blood pressure and ICH volume, and differences in odds ratios for poor outcomes in BMI category were determined. Results demonstrated that patients with obesity were significantly more likely to have a poor disposition outcome as compared with both normal and overweight subjects – Normal vs. Obese OR 0.26 CI 0.115–0.593 p = 0.0014; Obese vs. Overweight OR 3.79 CI 1.68–8.52 p = 0.0013 (Table 4).

Overall, race did not influence disposition or hematoma expansion (>30% increase in ICH volume) outcomes. However, within the non-White population, the obese category (BMI 30 – <34.9 kg/m²) had higher odds of a poor disposition outcome than normal weight (OR 6.84 CI 2.12–22.22 p = 0.0013) and overweight categories (OR 8.45 CI 2.6–27.49 p = 0.0004). Similar odds were not observed in other BMI category comparisons in the non-White population or in any BMI category in the White population (Table 5).

### Discussion

The obesity paradox was not detected in this ICH cohort. On the contrary, obesity was associated with poor disposition outcomes. However, no relationship between obesity and 24-h hematoma expansion was observed.

**Table 3** Logistic model of outcomes

|                      | Estimate | Standard error | P-value |
|----------------------|----------|----------------|---------|
| Race (Non-White)     | 0.1156   | 1.3256         | 0.7461  |
| BMI (normal)         | –0.5739  | 0.919          | 0.0112  |
| BMI (obese)          | 0.1854   | 0.9854         | 0.8509  |
| BMI (overweight)     | 0.3442   | 0.9083         | 0.705   |
| BMI (severe obese)   | 0.01668  | 0.9484         | 0.986   |
| Age                  | 0.02725  | 0.009011       | 0.0027  |
| Hypertension         | 0.2848   | 0.3521         | 0.491   |
| Diabetes mellitus    | 0.4082   | 0.2726         | 0.1352  |
| Congestive heart failure | 0.9076   | 0.4432         | 0.412   |
| ICH primary location*| 1.456    | 0.4887         | 0.0031  |
| Admission SBP        | 0.000838 | 0.00764        | 0.4981  |
| ICH volume           | 0.03535  | 0.004711       | <0.0001 |

BMI, body mass index; ICH, intracerebral haemorrhage; SBP, systolic blood pressure.

*Reference ICH primary location – brainstem.

**Table 4** Odds ratios comparing BMI categories and disposition outcome

| BMI category      | Odds ratio | Lower confidence limit for odds ratio | Upper confidence limit for odds ratio | P-value |
|-------------------|------------|--------------------------------------|--------------------------------------|---------|
| Normal vs. Obese  | 0.261      | 0.115                                | 0.593                                | 0.0014  |
| Normal vs. Overweight | 0.99      | 0.554                                | 1.770                                | 0.9739  |
| Normal vs. Severely Obese | 0.582   | 0.285                                | 1.189                                | 0.137   |
| Normal vs. Underweight | 0.517   | 0.133                                | 2.013                                | 0.3409  |
| Obese vs. Overweight | 3.787     | 1.683                                | 8.521                                | 0.0013  |
| Obese vs. Severe Obese  | 2.224     | 0.910                                | 5.437                                | 0.0794  |
| Obese vs. Underweight  | 1.979     | 0.457                                | 8.576                                | 0.3607  |
| Overweight vs. Severely Obese | 0.587  | 0.294                                | 1.174                                | 0.1317  |
| Overweight vs. Underweight  | 0.522   | 0.135                                | 2.029                                | 0.3475  |
| Severely Obese vs. Underweight | 0.89    | 0.216                                | 3.666                                | 0.8711  |

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Several studies demonstrated higher markers of inflammation which have been widely studied. In some, in combination with hemorrhagic strokes, outcomes have focused primarily on ischemic stroke, and outcomes following ICH was observed at the time of hospital discharge. However, this study included patients with both ischemic and hemorrhagic strokes and was conducted in a predominantly White Scandinavian population. In this study, the primary outcomes measured are directly related to acute ICH (disposition at hospital discharge and hematoma expansion >30%). Similar to previous reports on outcomes close to the ictus, no obesity paradox on outcomes following ICH was observed at the time of hospital discharge.

Studies on obesity and acute illness are frequently fraught with methodological limitations in measuring obesity. It is well described that waist circumference and waist–hip ratio are more reflective and sensitive in predicting outcomes than BMI (25). ICH is an acute illness and in most cases, patients are critically ill which likely precludes detailed anthropometric measurements. In this study, we classified patients with Classes II and III obesity separately as ‘severe obesity’ (BMI >35.0 kg/m²). Previous studies have shown that BMI >35.0 kg/m² correlates with higher waist circumference above cut off predictive values (1,26). However, after adjusting for confounding variables such as age, DM and hypertension, there was no difference in outcomes. The possibility that the relative younger age in this group likely impacted on the aggressiveness of clinical management in the study cohort cannot be excluded.

This study has several strengths. This is the first report on the role of obesity on ICH outcomes with a relatively high number of African Americans. Second, this study separated the severe obese category (>35.0 kg/m²) who historically are known to carry a higher risk for cardiovascular disease. Third, selected outcomes (hematoma expansion >30% and hospital disposition) reflect the primary disease process, ICH. However, there are limitations to the results of this study. Despite the relative large sample size, the retrospective nature of our study renders our conclusions observational. Poor records limited detailed analysis of some variables – images from patients referred to our institution to compare ICH volume changes, time of symptom onset and last known normal. Second, prior studies have demonstrated the superiority of other anthropometric measurements over BMI, such as waist circumference, waist–hip ratio and body fat by dual-energy X-ray absorptiometry. In this study cohort,
these measurements were not routinely obtained and are limited by the acuity of the patients particularly due to critically raised intracranial pressure, cerebral edema with or without brain herniation at presentation. Third, despite adjusting for premorbid conditions such as hypertension, CHF and DM, the severity of these premorbid conditions using tools such as the Charlson comorbidity index was not available in the study and not measured. Hence, the ability to independently ascribe ICH outcomes to the presence of obesity alone is limited. Due to the retrospective nature of the study, the methods of obtaining height measurements by the nursing staff may be limited by factors such as patient acuity on presentation and ongoing resuscitative efforts. Lastly, the non-inclusion of the 73 (17%) patients without a follow up CT head for the outcome analysis of hematoma expansion may have created a selection bias. However, to further minimize the effect of selection bias on outcomes, they were included in the disposition outcome analysis report while the analysis excluding these patients (not reported) obtained similar results. Regardless of these limitations, the findings are unique and illustrate the need to further examine the role of excess adiposity and race on ICH acute outcomes.

In conclusion, this study did not detect an obesity paradox following ICH. Conversely, obesity was associated with poor disposition outcomes following ICH particularly in the non-White, but not White population. Finally, neither obesity nor race influenced hematoma expansion. Prospective research is needed to examine the role of excess adiposity and race on both acute and long-term health outcomes following ICH.

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Conflict of Interest Statement

The authors declare no conflict of interest.

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