Outcomes after intracerebral hemorrhage from arteriovenous malformations

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ABSTRACT

Objective: To compare outcomes after intracerebral hemorrhage (ICH) from cerebral arteriovenous malformation (AVM) rupture and other causes of ICH.

Methods: We performed a retrospective population-based study using data from the Nationwide Inpatient Sample. We used standard diagnosis codes to identify ICH cases from 2002 to 2011. Our predictor variable was cerebral AVM. Our primary outcomes were inpatient mortality and home discharge. We used logistic regression to compare outcomes between patients with ICH with and without AVM while adjusting for demographics, comorbidities, and hospital characteristics. In a confirmatory analysis using a prospective cohort of patients hospitalized with ICH at our institution, we additionally adjusted for hematoma characteristics and the Glasgow Coma Scale score.

Results: Among 619,167 ICH hospitalizations, the 4,485 patients (0.7%, 95% confidence interval [CI] 0.6–0.8) with an AVM were younger and had fewer medical comorbidities than patients without AVM. After adjustment for confounders, patients with AVM had lower odds of death (odds ratio [OR] 0.5, 95% CI 0.4–0.7) and higher odds of home discharge (OR 2.0, 95% CI 1.4–3.0) than patients without AVM. In a confirmatory analysis of 342 patients with ICH at our institution, the 34 patients (9.9%, 95% CI 7.2–13.6) with a ruptured AVM had higher odds of ambulatory independence at discharge (OR 4.4, 95% CI 1.4–13.1) compared to patients without AVM.

Conclusions: Patients with ICH due to ruptured AVM have more favorable outcomes than patients with ICH from other causes. *Neurology*® 2017;88:1882–1888

GLOSSARY

ARUBA = A Randomized Trial of Unruptured Brain Arteriovenous Malformations; **AVM** = arteriovenous malformation; **CAESAR** = Cornell Acute Stroke Academic Registry; **CI** = confidence interval; **ICD-9-CM** = *International Classification of Diseases, Ninth Revision, Clinical Modification*; **ICH** = intracerebral hemorrhage; **NIS** = Nationwide Inpatient Sample; **OR** = odds ratio.

Intracerebral hemorrhage (ICH) constitutes 10% to 20% of all strokes and is associated with significant morbidity and mortality.^{1,2} Numerous types of pathology can result in ICH. One such etiology is rupture of an underlying cerebral arteriovenous malformation (AVM).^{1,2} The annual bleeding risk with an AVM ranges from 0.9% to 4%.^{3–5} Although AVMs are relatively less common, they are an important ICH mechanism because they often affect young patients and can thus result in a large burden of life-years lost.⁶

While AVM rupture can result in death or severe neurologic disability,^{4,7} very few studies have assessed the relationship between AVM rupture and ICH outcomes. These studies suggested that outcomes after AVM rupture may be more favorable than outcomes after ICH from other causes.^{8,9} However, most of the data are derived from small cohorts of patients studied retrospectively in single-center settings and subject to selection biases.¹⁰ In fact, the only population-based study to date had a modest sample size and compared 90 patients with ruptured AVMs from the Scottish Intracranial Vascular Malformation Study with 50 patients

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From the Department of Neurology (S.B.M., A.E.M., S.S.O., A.G., H.S.M., C.I., B.B.N., H.K.), Clinical and Translational Neuroscience Unit (S.B.M., A.E.M., G.G., C.I., B.B.N., H.K.), Feil Family Brain and Mind Research Institute, and Department of Neurological Surgery (B.H., H.S.M.), Weill Cornell Medicine; and Department of Neurology (D.R.), Columbia College of Physicians and Surgeons, New York, NY.

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with spontaneous ICH from the Oxford Vascular Study.⁹ These shortcomings limit the generalizability of the results. We therefore aimed to study the relationship between AVM rupture and outcomes after ICH using a large, nationally representative sample of patients. Our hypothesis was that patients with ICH as a result of a ruptured AVM have better outcomes than patients with ICH due to other causes.

METHODS Design. We performed a retrospective cohort study using the Nationwide Inpatient Sample (NIS).¹¹ The NIS includes data on ≈ 8 million inpatient hospitalizations each year that together represent a 20% stratified sample of all non-federal American hospitals.¹¹ Because the NIS does not contain data on traditional measures of ICH severity such as hematoma volume, hematoma location, and the Glasgow Coma Scale score, we performed a confirmatory analysis using data from patients hospitalized with ICH at New York–Presbyterian Hospital/Weill Cornell Medical Center from 2011 to 2015.

Standard protocol approvals, registrations, and patient consents. The Weill Cornell Medical Center institutional review board approved this study and waived the requirement for informed consent because of minimal risk to patients.

Patients. We identified patients hospitalized with ICH in the NIS between January 1, 2002, and December 31, 2011, using the validated ICD-9-CM code 431, which has a high sensitivity and specificity.^{12,13} We excluded patients who were <18 years of age or diagnosed with traumatic brain injury. We also excluded visits that ended in transfer to a higher-acuity hospital to prevent double counting of the same patient, as is customarily done in NIS studies.^{14,15} The majority of these transfers occurred within the first 24 hours, as a result of which the outcomes of these patients may not reflect the entire hospital course for ICH admission. In a sensitivity analysis, we included all patients regardless of their transfer-out status.

Measurements. Our primary predictor was AVM. As in prior studies, patients with AVMs were identified using the ICD-9-CM code 747.81.¹⁶ The modified Charlson Comorbidity Index was used to adjust for underlying medical comorbidities.¹⁷ This index, which incorporates 17 different comorbidities, has been previously validated as an effective outcome adjustment method for analyses using administrative data.¹⁷ For descriptive reporting, we delineated patients who underwent endovascular embolization of AVM with ICD-9-CM code 39.72 and those who underwent surgical resection using diagnosis code 01.59¹⁶; in exploratory post hoc analyses, we assessed whether these treatments were associated with discharge outcomes. We identified palliative care services using the ICD-9-CM code V66.7.¹⁸ Our primary outcomes were inpatient mortality and home discharge disposition, a validated surrogate for functional outcome.¹⁹

Confirmatory cohort. All patients with stroke (both ischemic and hemorrhagic) at New York–Presbyterian Hospital/Weill Cornell Medical Center are prospectively enrolled into the American Heart Association's Get With The Guidelines–Stroke registry. This registry provides the foundation for the Cornell Acute Stroke Academic Registry (CAESAR), which is then supplemented through retrospective collection of additional clinical, laboratory, and radiographic data. For this analysis, we included

all available cases of ICH in CAESAR (spanning from 2011 to 2015). A single board-certified neurointensivist (S.B.M.) reviewed all medical records to determine the presence of a ruptured AVM as the cause of ICH; determined the Spetzler-Martin score and presence of an intranidal aneurysm if an AVM was present; measured the size of the ICH using the ABC/2 method²⁰; noted the location of the ICH (lobar vs supratentorial subcortical vs infratentorial) and presence of intraventricular extension; and ascertained the Glasgow Coma Scale score as documented per our hospital protocol on the admission note. The outcome variables of inpatient mortality and independent ambulation at discharge were prospectively collected in the CAESAR registry. Ambulatory status at discharge has been used in prior studies as a valid measure of functional outcome.^{21,22} In a small subset of patients with missing variables, ambulatory status at discharge was independently adjudicated by 2 neurologists (S.B.M. and G.G.), one of whom (G.G.) was blinded to AVM status; any disagreements were independently resolved by a third neurologist (H.K.) who was also blinded to AVM status.

Statistical analysis. The Pearson χ^2 test was used to compare categorical variables between patients with and without AVM. The Mann-Whitney U test was used for continuous variables because the data were not normally distributed. Bivariate and multivariate logistic regression was used to evaluate the association between AVM and ICH outcomes. The covariates in the multivariate model included demographic factors (age, sex, race, and insurance status), hospital-level characteristics (rural vs urban location, teaching status, bed size, and annual ICH volume), and clinical variables known to affect outcomes in ICH: Charlson Comorbidity Index inserted as quartiles, ICH risk factors (hypertension, hyperlipidemia, diabetes mellitus, anticoagulant use), mechanical ventilation, infections (pneumonia, sepsis, meningitis, urinary tract infection), and documented palliative care services. All covariates associated with outcomes at the bivariate level with a value of $p < 0.05$ were inserted into the multivariate model. To account for the lack of data on ICH severity, we performed secondary analyses in which we stratified patients by receipt of mechanical ventilation and receipt of ventriculostomy because these factors are surrogates of severe ICH. In addition, we studied the relationship between AVM rupture and ICH outcomes in 2 different age subgroups: 20 to 40 and 41 to 60 years. This analysis was performed to mitigate any residual confounding by age, given that patients with AVM were younger. We additionally performed stratified analyses by receipt of palliative care and survival past 72 hours. All analyses were 2-tailed and performed with Stata (version 14.0, College Station, TX); statistical significance was defined as a value of $p < 0.05$. Standard weights provided by the Healthcare Cost and Utilization Project were used to obtain national estimates of inpatient hospitalizations for ICH.

RESULTS Patient characteristics. On the basis of national sampling weights provided by the NIS, there were 630,969 hospitalizations for ICH from 2002 to 2011 across the United States. Of these, we excluded 11,803 visits because of age <18 years ($n = 2,455$), traumatic brain injury ($n = 5,163$), or transfer to another hospital ($n = 4,165$). Among the 619,167 hospitalizations included in this analysis, 4,485 (0.7%, 95% confidence interval [CI] 0.6–0.8) involved patients with a documented AVM. Patients with AVM were younger (52 vs 72 years, $p < 0.001$)

and were more often male (52.5% vs 49.3%, $p < 0.001$) compared to patients without AVM. Moreover, patients with ICH with AVM were more likely to be treated at large, urban hospitals with a high ICH case volume (table 1). Stroke risk factors such as hypertension, diabetes mellitus, and hyperlipidemia were less prevalent among patients with AVM (table 2). Conversely, seizures were more common among

patients with AVM (19.0% vs 9.9%, $p < 0.001$). Similarly, hydrocephalus treated with CSF shunting was almost twice as common among patients with ICH with AVM compared to those without (13.6% vs 6.5%, $p < 0.001$). Among patients with AVM, 909 (20.2%) underwent surgical or endovascular treatment for the AVM during the initial hospitalization for ICH; the 3 main treatment modalities included surgical resection ($n = 610$, 13.6%), endovascular treatment ($n = 235$, 5.2%), and combined endovascular and surgical resection ($n = 64$, 1.4%).

Primary analysis. The inpatient mortality rate among patients with ICH with AVM was 12.9% (95% CI 10.8–15.2) compared to 29.5% (95% CI 28.8–30.3) in patients with ICH without AVM. Conversely, rates of home discharge were 46.9% (95% CI 43.9–50.5) among patients with AVM compared to 19.7% (95% CI 19.0–20.5) among patients without AVM. After adjustment for demographics, medical comorbidities, and surrogates of ICH severity, patients with AVM had lower odds of death (odds ratio [OR] 0.5, 95% CI 0.4–0.7) and higher odds of favorable discharge (OR 2.0, 95% CI 1.4–3.0) than patients without AVM (table 3). Our results were unchanged in a sensitivity analysis that included patients who were transferred to a higher-acuity hospital.

Stratified analyses. Patients with ruptured AVM had favorable ICH outcomes in the analyses stratified by age, mechanical ventilation, presence of ventriculostomy, survival beyond the first 72 hours, and receipt of palliative care (table 4). Among patients with ruptured AVM, those who underwent endovascular embolization and/or surgical resection of the AVM during the index hospitalization had lower odds of inpatient mortality (OR 0.31, 95% CI 0.24–0.39) and higher odds of home discharge (OR 1.2, 95% CI 1.01–1.42) compared to those who were managed conservatively.

Confirmatory analyses. We identified 342 consecutive patients with ICH admitted to our institution, of whom 34 (9.9%, 95% CI 7.2–13.6) had a ruptured AVM. The mean $\pm$ SD Spetzler-Martin grade was 2.4 ± 1.3 , and intranidal aneurysms were present in 7 (20.6%). Patients with ruptured AVM were younger (42.7 vs 62.7 years, $p < 0.001$) and had fewer stroke risk factors such as hypertension (25.0% vs 62.9%, $p = 0.002$) and hyperlipidemia (12.5% vs 33.2%, $p = 0.02$) (table 5). AVM-related ICH was more likely to be lobar compared to ICH from other causes (70.6% vs 50.0%, $p = 0.031$). Our standard practice is to perform staged endovascular embolization followed by surgical resection of the AVM during the index hospitalization for ICH. Hence, all patients with AVM-related ICH who survived

Table 1 Demographic and hospital characteristics of patients with ICH in the NIS

Characteristic	ICH with AVM (n = 4,485)	ICH without AVM (n = 614,682)	p Value ^a
Age, median (IQR), y	52 (40–65)	72 (58–82)	<0.001
Sex, n (%)			<0.001
Male	2,353 (52.5)	302,821 (49.3)	
Female	2,128 (47.5)	311,584 (50.7)	
Race, n (%)			<0.001
White	3,342 (50.0)	320,436 (52.1)	
Black	521 (11.6)	79,911 (13.0)	
Hispanic	404 (9.0)	44,947 (7.3)	
Asian	155 (3.5)	21,948 (3.6)	
Other	145 (3.2)	17,209 (2.8)	
Missing	1,018 (22.7)	130,231 (21.2)	
Hospital geographic region, n (%)			<0.001
Northeast	875 (19.5)	114,851 (18.7)	
Midwest	959 (21.4)	129,917 (21.1)	
South	1,441 (32.1)	240,964 (39.2)	
West	1,209 (27.0)	128,949 (21.0)	
Hospital location, n (%)			<0.001
Rural	111 (2.5)	45,970 (7.5)	
Urban	4,235 (97.5)	564,194 (92.5)	
Hospital bed size, n (%)			<0.001
Small	255 (5.7)	45,230 (7.4)	
Medium	740 (16.7)	129,982 (21.3)	
Large	3,442 (77.6)	434,953 (71.3)	
Hospital ICH volume, n (%) ^b			<0.001
1–23 cases/y	512 (11.4)	147,960 (24.1)	
24–27 cases/y	794 (17.7)	154,388 (25.1)	
48–85 cases/y	1,433 (32.0)	157,016 (25.5)	
>85 cases/y	1,746 (38.9)	155,317 (25.3)	
Health insurance, n (%)			<0.001
Medicare	1,272 (28.4)	383,406 (62.5)	
Medicaid	580 (12.9)	50,370 (8.2)	
Private	2,099 (46.9)	1,251,119 (20.4)	
Other	529 (11.8)	54,721 (8.9)	

Abbreviations: AVM = arteriovenous malformation; ICH = intracerebral hemorrhage; IQR = interquartile range; NIS = Nationwide Inpatient Sample.

^aA value of $p < 0.05$ was considered significant.

^bHospital ICH volume was categorized into quartiles.

Table 2 Comorbidities, complications, and procedures performed on patients with ICH in the NIS

Comorbidities	ICH with AVM (n = 4,485), n (%)	ICH without AVM (n = 614,682), n (%)	p Value ^a
Modified Charlson Comorbidity Index			
0	3,110 (70.0)	264,145 (43.4)	
1	789 (17.8)	164,004 (27.0)	
2	346 (7.8)	90,835 (14.9)	
≥3	198 (4.5)	89,036 (14.6)	
Diabetes mellitus	425 (9.6)	1,281,712 (21.1)	<0.001
Hypertension	1,930 (43.3)	463,832 (76.3)	<0.001
Hyperlipidemia	679 (15.1)	143,522 (23.3)	<0.001
Anticoagulant use	85 (1.9)	42,529 (6.9)	<0.001
Inpatient complications			
Seizures	852 (19.0)	60,767 (9.9)	<0.001
Pneumonia	368 (8.2)	43,312 (7.0)	0.003
Urinary tract infection	458 (10.2)	82,813 (13.5)	<0.001
Sepsis	129 (2.9)	19,734 (3.2)	0.221
Venous thromboembolism	79 (1.7)	10,457 (1.7)	0.897
Hydrocephalus	612 (13.6)	39,723 (6.5)	<0.001
Palliative care	161 (3.6)	41,241 (6.7)	<0.001
Procedures performed			
Mechanical ventilation	1,164 (26.0)	174,712 (28.4)	<0.001
Angiogram	1,850 (41.2)	43,763 (7.1)	<0.001
Craniectomy	39 (0.9)	1,597 (0.3)	<0.001
Craniotomy	109 (2.4)	5,182 (0.8)	<0.001
Intracranial embolization	235 (5.2)	1,426 (0.2)	<0.001
Ventriculostomy	587 (13.1)	38,877 (6.3)	<0.001
Permanent CSF shunt	117 (2.6)	4,847 (0.8)	<0.001
Inpatient mortality	580 (12.9)	181,086 (29.5)	<0.001
Home discharge	2,105 (46.9)	121,196 (19.7)	<0.001

Abbreviations: AVM = arteriovenous malformation; ICH = intracerebral hemorrhage; NIS = Nationwide Inpatient Sample.

^a A value of $p < 0.05$ was considered significant.

underwent definitive surgical treatment for the AVM. In multiple logistic regression models adjusted for age, hypertension, baseline hematoma volume, hematoma location, intraventricular hemorrhage, and admission Glasgow Coma Scale score, an AVM-related etiology was associated with a higher odds of independent ambulation at discharge (OR 4.4, 95% CI 1.5–13.1) compared to other etiologies (table 3). There was a nonsignificant lower likelihood of inpatient mortality in AVM-associated cases of ICH (OR 0.9, 95% CI 0.2–7.8).

DISCUSSION In a nationally representative cohort, patients with ICH with AVM had lower inpatient mortality and were more likely to have a favorable discharge disposition compared to patients with ICH

without AVM. These results remained largely unchanged across several sensitivity analyses. Furthermore, in a confirmatory cohort from our institution, AVM-related ICH was associated with a more favorable ambulatory status at discharge even after adjustment for traditional markers of ICH severity such as the Glasgow Coma Scale score and hematoma size and location.

Data from a randomized trial of unruptured brain AVMs (A Randomized Trial of Unruptured Brain Arteriovenous Malformations [ARUBA]) showed that medical management alone was superior to surgical or endovascular treatment.²³ Our results build on the findings of ARUBA in 2 ways. First, our findings inform the understanding of the natural history of AVM-related bleeds should they occur during conservative management, indicating that such bleeds have a more favorable prognosis than typical cases of ICH. Furthermore, there is a paucity of evidence on the management of AVMs if they do rupture. Our data suggest that definitive treatment of ruptured AVMs is associated with better outcomes, although this finding may be subject to selection bias and hence requires further study. Among patients with ruptured AVMs, the fact that only 40% underwent an angiogram and only half of these patients subsequently had definitive treatment of the AVM suggests that the national practice in the United States may be to defer AVM treatment until after the acute phase of ICH. Lack of follow-up data prevented further exploration of these results.

Our findings align with prior single-center studies documenting a lower case fatality rate after AVM rupture compared to other cases of spontaneous ICH.^{8,9,24} This may be attributed to the fact that patients with AVM-associated ICH are younger and as a result have fewer medical comorbidities,^{6,25,26} but we found more favorable functional outcomes even after adjusting for age and comorbidities. Furthermore, it is unlikely that the better outcomes were due to smaller ICH volumes because our confirmatory analysis adjusted for hematoma size. It is believed that hematomas resulting from AVM rupture mostly within the AVM nidus itself or in the venous side of the malformation, thus sparing the healthy brain parenchyma and potentially explaining the better outcomes associated with AVM.^{6,25,26} In addition, one may speculate that the secondary injury after ICH may be relatively milder in these patients compared to ICH from other causes. It is also intriguing that hydrocephalus was more common among patients with AVM. In the context of ICH, hydrocephalus is often associated with intraventricular hemorrhage.²⁷ In a retrospective study of 87 patients with AVM-related ICH, factors associated with hydrocephalus were Glasgow Coma Scale, intraventricular

Table 3 Logistic regression models evaluating the relationship between AVM rupture and ICH outcomes

Outcome	Inpatient mortality		Home discharge	
	OR (95% CI)	p Value	OR (95% CI)	p Value
NIS cohort				
Unadjusted	0.35 (0.28–0.43)	<0.001	3.60 (3.22–4.02)	<0.001
Adjusted (demographics, comorbidities, hospital characteristics, infections, and palliative care)	0.53 (0.40–0.71)	<0.001	2.03 (1.38–2.98)	<0.001
CAESAR cohort	Inpatient mortality		Independent ambulation at discharge	
Unadjusted	0.46 (0.15–1.37)	0.162	5.57 (2.53–12.26)	<0.001
Adjusted (age, hypertension, GCS score, hematoma volume, hematoma location, IVH)	0.85 (0.19–7.82)	0.625	4.39 (1.47–13.06)	0.008

Abbreviations: AVM = arteriovenous malformation; CAESAR = Cornell Acute Stroke Academic Registry; CI = confidence interval; GCS = Glasgow Coma Scale; ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; NIS = Nationwide Inpatient Sample; OR = odds ratio.

Covariates included in the regression model are listed in parentheses.

A value of $p < 0.05$ was considered significant.

hemorrhage, and the presence of an AVM-associated aneurysm.²⁸ Intraventricular hemorrhage is an independent predictor of morbidity after ICH,²⁹ yet we found that patients with AVM, despite a higher frequency of hydrocephalus, had better outcomes compared to patients with other causes of ICH. Further research on the relationship among hydrocephalus, intraventricular hemorrhage, and AVM outcomes may be illuminating.

This study has some noteworthy limitations. First, the NIS lacked information on well-validated ICH severity measures such as the Glasgow Coma Scale score and ICH volume and location. There were no data on AVM characteristics such as size, location, venous drainage, presence of an associated aneurysm,

and prior rupture history. However, this information was available in our confirmatory cohort and was controlled for in the multivariable analyses. Although our confirmatory analysis is subject to selection bias resulting from a single-center patient cohort with a relatively high AVM incidence, it nonetheless aids in confirming the results of the primary analysis. Second, errors in misclassification resulting from our use of ICD-9-CM codes are also possible, but the ICD-9-CM code for ICH has been previously validated to have high specificity and positive predictive value.^{12,13} While the code for AVM has been used in prior studies,^{16,30} data on the sensitivity and specificity of the code are lacking. ICD-9-CM codes for major diagnoses in these types of administrative datasets have generally been shown to be reliable.³¹ Furthermore, although diagnosis coding may be imperfect, random coding errors would bias the results toward the null and are hence unlikely to account for the measured differences in outcome found in this study. Moreover, the incidence of AVM-related ICH in our study was 0.7%, which corroborates the prevalence of AVM among incident ICH cases by 2 other population-based studies, the Northern Manhattan Stroke Study (1.4%)³² and the New York Islands AVM study (incidence of 0.51 per 100,000 per years).³³ It is important to note that ICD-9-CM codes do not allow differentiation between an AVM implicated in the ICH and an AVM discovered as an incidental finding. However, this would be expected to be a conservative limitation because this type of misclassification, to the small degree that it may have occurred, would tend to confound the 2 groups under consideration.

Third, it is possible that our findings may have been due to immortal time bias, in which only those

Table 4 Logistic regression models evaluating the relationship between AVM rupture and ICH outcomes in different subgroups in the NIS

Subgroups	Inpatient mortality		Home discharge	
	Adjusted OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
Age 20–40 y	0.22 (0.13–0.38)	<0.001	1.47 (1.08–2.01)	<0.001
Age 41–60 y	0.49 (0.36–0.66)	<0.001	2.0 (1.64–2.45)	<0.001
Mechanical ventilation ≤96 h	0.38 (0.24–0.58)	<0.001	1.72 (1.44–2.02)	<0.001
Mechanical ventilation >96 h	0.48 (0.42–0.55)	<0.001	1.57 (1.28–1.93)	<0.001
No ventriculostomy	0.34 (0.26–0.43)	<0.001	2.06 (1.76–2.40)	<0.001
Ventriculostomy only	0.78 (0.63–0.96)	0.019	1.43 (1.12–1.84)	0.004
Survived >72 h	0.54 (0.42–0.69)	<0.001	1.75 (1.51–2.01)	<0.001
No palliative care	0.33 (0.29–0.42)	<0.001	2.31 (1.89–4.45)	<0.001

Abbreviations: AVM = arteriovenous malformation; CI = confidence interval; ICH = intracerebral hemorrhage; OR = odds ratio.

Each regression model was adjusted for demographics, comorbidities, hospital characteristics, infections, and palliative care.

A value of $p < 0.05$ was considered significant.

Table 5 Baseline characteristics of patients with ICH in CAESAR

	ICH with AVM (n = 34)	ICH without AVM (n = 308)	p Value ^a
Mean age (SD), y	42.7 (15.8)	62.7 (18.1)	<0.001
Women, n (%)	11 (34.4)	134 (43.7)	0.313
Race, n (%)			0.470
White	25 (78.1)	259 (84.4)	
Black	5 (15.6)	24 (7.8)	
Other	2 (6.3)	24 (7.8)	
Diabetes mellitus, n (%)	2 (6.3)	49 (15.9)	0.144
Hypertension, n (%)	8 (25.0)	193 (62.9)	<0.001
Hyperlipidemia, n (%)	4 (12.5)	102 (33.2)	0.016
Admission GCS score <9, n (%)	6 (17.6)	102 (33.1)	0.066
ICH volume >30 cm ³ , n (%)	8 (25.3)	111 (36.1)	0.146
Location, n (%)			0.031
Lobar	24 (70.6)	154 (50.0)	
Deep	5 (14.7)	114 (37.0)	
Infratentorial	5 (14.7)	40 (13.0)	
Intraventricular hemorrhage, n (%)	14 (47.2)	130 (42.2)	0.908
Withdrawal of care, n (%)	2 (5.9)	68 (22.1)	0.026
Inpatient mortality, n (%)	4 (13.3)	75 (25.0)	0.032
Independent ambulation at discharge, n (%)	21 (61.8)	89 (28.9)	<0.001

Abbreviations: AVM = arteriovenous malformation; CAESAR = Cornell Acute Stroke Academic Registry; GCS = Glasgow Coma Scale; ICH = intracerebral hemorrhage.

^aA value of $p < 0.05$ was considered significant.

patients with ICH who survived the initial course of their illness were investigated for an underlying AVM, thus creating a spurious association between AVMs and better outcomes. However, our findings were unchanged in a sensitivity analysis limited to patients who survived the first 72 hours after admission. Furthermore, our confirmatory analysis of patients at our medical center represents an aggressive protocol in which all ICH cases are screened for an underlying vascular malformation with at least a CT angiogram, so it is unlikely that immortal time bias substantively explains our results. Fourth, although it would have been informative to compare AVM-related ICH cases to hypertensive ICH cases only, this was not possible because of the lack of relevant details in our data. Finally, we were unable to differentiate between primary and recurrent ICH in the NIS; however, given the low annual rate of ICH recurrence ($\approx 2\%$),^{34,35} this is less likely to have significantly affected our results. This limitation also prevented assessment of rebleeding risk among patients with ICH in our cohort.

Using both data from a nationally representative cohort and more detailed clinical data from our own institution, we found that patients with ICH due to a ruptured AVM had lower inpatient mortality

and more favorable functional outcomes compared to patients with other etiologies of ICH. Further research is needed to identify optimum strategies for educating providers and patients about the natural history of unruptured AVMs and the risks and benefits of available management strategies so as to enable fully informed, shared decision making for this complex condition. In addition, we found that patients with ruptured AVMs who received surgical treatment during the index hospitalization had better outcomes than patients managed conservatively, suggesting that further studies are warranted to define optimum treatment strategies and the timing of these interventions in the event that an AVM does rupture.

AUTHOR CONTRIBUTIONS

Dr. Murthy had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Murthy, Kamel. Acquisition, analysis, or interpretation of data: Murthy, Gialdini, Kamel. Drafting of the manuscript: Murthy, Omran, Kamel. Critical revision of the manuscript for important intellectual content: Murthy, Merkler, Omran, Hartley, Gialdini, Gusdon, Mangat, Roh, Iadecola, Navi, Kamel. Statistical analysis: Murthy, Kamel. Obtained funding: Murthy, Iadecola, Navi, Kamel. Administrative, technical, or material support: Murthy, Kamel. Study supervision: Kamel.

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