Impact of COVID-19 pandemic on treatment and outcomes of cerebral arteriovenous malformations

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Original research

ABSTRACT

Background: There has been a recent decrease in interventional management of cerebral arteriovenous malformations (AVMs). The objective of our study was to evaluate the changing patterns in management of AVMs in the first year of the COVID-19 pandemic.

Methods: The National Inpatient Sample (NIS) database was used. From 2016 to 2020, patients with an International Classification of Diseases, 10th revision (ICD-10) diagnosis code for a cerebral AVM were included. An intervention was defined as ICD-10 code for surgical, endovascular, or stereotactic radiosurgery treatment. Odds ratios (ORs) were calculated using a logistic regression model with covariates deemed to be clinically relevant.

Results: 63,610 patients with AVMs were identified between 2016 and 2020, 14,340 of which were ruptured. In 2020, patients had an OR of 0.69 for intervention of an unruptured AVM (P<0.0001) compared with 2016–19. The rate of intervention for unruptured AVMs decreased to 13.5% in 2020 from 17.6% in 2016–19 (P<0.0001). The rate of AVM rupture in 2020 increased to 23.9% from 22.2% in 2016–19 (P<0.0001). In 2020, patients with ruptured AVMs had an OR for inpatient mortality of 1.72 compared with 2016–19.

Conclusion: In 2020, the rate of intervention for unruptured cerebral AVMs decreased compared with past years, with an associated increase in the rate of rupture. Patients with ruptured AVMs also had a higher odds of mortality.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Recently, there has been a reduction in interventional management of cerebral arteriovenous malformations (AVMs), with a greater emphasis on medical management.

⇒ One study found that this decreased intervention rate was associated with a higher rupture rate at a national level in the US.

WHAT THIS STUDY ADDS

⇒ Our study showed how during the first year of the COVID-19 pandemic, there was a large decrease in interventions for cerebral AVMs, with a corresponding increase in rupture rate.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ Given the significant morbidity associated with ruptured cerebral AVMs, further investigation should be conducted to further assess if there is a causal role between nationwide decreased intervention rates and increased rupture rates.

METHODS

Data source

We used the National Inpatient Sample (NIS) database for our analysis. The NIS is the largest all-payer inpatient database providing data for approximately 35 million annual hospitalizations and is designed to produce regional and national estimates with respect to inpatient utilization, access, cost, quality, and outcomes. More information on this database is available on the NIS webpage.

Definition of cases and covariates

All of the International Classification of Diseases, 10th revision (ICD-10) codes and their associated diagnoses and procedures are listed in the online supplemental table S1, classified consistent with previous works. All patients with a brain AVM identified between 2016 and 2020 were included. AVMs with intracranial or subarachnoid hemorrhage were labeled as ruptured AVMs. Treatment modalities were stratified into surgical excision, endovascular treatment (EVT), and stereotactic radiosurgery (SRS). COVID-19 infection was identified with ICD-10 code U07.1.

Statistical analyses and NIS indices

All analyses were completed using the weighted variable in the NIS, designed to make the data...
nationally representative. The time periods 2016–19 and 2020 were compared. Continuous variables were compared using the Wilcoxon rank sum test and categorical data were compared using \( \chi^2 \) analyses or Fisher’s exact test, when relevant. Differences were considered statistically significant with \( P < 0.05 \). To adjust for patient comorbidities and overall patient health, the Elixhauser comorbidity score was used similarly to previous works.\(^6\) Additionally, the NIS-subarachnoid hemorrhage outcome measure (NIS-SOM) was calculated, which is a surrogate for the modified Rankin Scale. A poor neurological outcome on this scale corresponds to a modified Rankin Scale score of \( \geq 2-3 \).\(^6\) This methodology was developed and validated on ICD-9 codes, using the equivalent translated ICD-10 codes. To determine the odds of intervention in the 2020 period, a logistic regression model was used with age, sex, presence of concurrent cerebral aneurysms, insurance type, hospital teaching status, hospital bed size, race, and weighted Elixhauser comorbidity score as covariates. All analyses were conducted using R statistical software, V4.0.2 (Boston, Massachusetts, USA).

RESULTS

Patient demographics and outcomes

A total of 14340 ruptured and 49270 unruptured cerebral AVMs were identified between 2016 and 2020 for an overall rupture rate of 22.5%. A higher rupture rate was observed in 2020 compared with 2016–19 (23.9 vs 22.2%, \( P < 0.0001 \)). Patients with ruptured AVMs in 2020 were more likely to present to hospitals with a large bed size and teaching status than in 2016–19. They were also more likely to have a poor NIS-SOM score and a higher chance of mortality. In 2020, patients with ruptured AVMs had a poor NIS-SOM score 52.1% of the time versus 50.1% in 2016–19 (\( P = 0.005 \)). Mortality was 10.6% versus 7.2% in 2016–19 (\( P < 0.001 \)). In 2020, the ORs (95% CI) for a poor NIS-SOM score and mortality were 1.12 (1.02 to 1.24, \( P = 0.016 \)) and 1.72 (1.49 to 1.99, \( P < 0.001 \)) compared with 2016–19, respectively. In 2020, 1.0% and 2.1% of patients with ruptured and unruptured AVMs, respectively, had concurrent COVID-19 infection. Full patient characteristics are listed in table 1.

Comparison of treatment for unruptured AVMs

In 2020, AVM patients had lower intervention rates than the 4 years previously, regardless of rupture status. Unruptured AVMs had a larger decrease in treatment (13.3 vs 17.6%, \( P < 0.0001 \)) compared with ruptured AVMs (21.1 vs 23.7%, \( P = 0.003 \)). Both unruptured and ruptured AVMs had lower odds of intervention compared with 2016–19 with multivariate ORs of 0.69 and 0.81, respectively (online supplemental table S3).

The most common type of intervention for unruptured AVMs was EVT, followed by surgery only, and then a combination of EVT and surgery (figure 1, online supplemental table S2). Compared with 2016–19, the number of total interventions that were EVT only decreased from 64.3% to 59.2% in 2020 (\( P < 0.001 \)). The proportion of cases that were combination EVT and surgery increased from 3.8% to 6.5% in 2020 (\( P < 0.001 \)). The proportion of SRS only treatments increased from 0.4% to 1.5% in 2020 (\( P < 0.001 \)).

When unruptured AVM treatment was stratified by age, there was no difference in the intervention rate for age <15 years. Age groups 15–30, 30–45, 45–60, and 60–75 years all saw a decrease in intervention rate of approximately 5% in 2020. The intervention rate increased for patients aged >75 years from 3.7% to 5.3% (\( P = 0.02 \)) (figure 2).

Comparison of treatment for ruptured AVMs

The most common interventions for ruptured AVMs were EVT, surgery, and a combination of surgery and EVT, similar to the treatment of unruptured AVMs (figure 1, online supplemental table S2). Unlike unruptured AVMs, the use of EVT increased from 52.0% in 2016–19 to 56.9% in 2020 (\( P = 0.026 \)). The combination of EVT and surgery decreased from 9.4% to 4.6% (\( P < 0.001 \)). There was no difference in the proportion of interventions that were surgery only. In 2020, there was a decrease in SRS only and increase in the combination of SRS and surgery, but these made up a very small fraction of interventions (figure 1, online supplemental table S2).

In the treatment of ruptured AVMs, there was no difference in the 2020 intervention rate for ages <15, 15–30, and 30–45 years, but a decrease in the intervention rate for ages 45–60 and 60–75 years was observed. Meanwhile, there was an increase in the intervention rate for ruptured AVMs in the >75 years age category (11.6% to 18.3%, \( P = 0.003 \)) (figure 2).

Relationship between intervention and rupture rate

On a year-to-year basis, the intervention rate decreased from 19.3% in 2016 to 16.9% in 2019, and to 13.3% in 2020. From 2016 to 2019, the year to year changes in intervention rate were −1.6%, −1.1%, and 0.3%, for an average yearly rate of change of −0.8%. In 2020, the change was −3.6%. The rupture rate also monotonically increased from 20.8% in 2016 to 23.1% in 2019 and to 23.9% in 2020 (figure 3). Linear regression analysis between the intervention rate and rupture rate demonstrated a slope of −0.50 (−0.84 to −0.15), \( P = 0.019 \), with \( R^2 = 0.88 \).

DISCUSSION

We found that during the first year of the COVID-19 pandemic, the intervention rates for both ruptured and unruptured cerebral AVMs decreased, with lower odds of treatment comparing 2020 with the previous 4 years. In addition, the rupture rate was higher than previous years. Patients with ruptured AVMs in 2020 had worse outcomes, including a higher rate of inpatient mortality and worse NIS-SOM score, corroborated by higher odds of both a poor NIS-SOM score and mortality.

The decreased odds of intervention may be due to current trends in treatment and a higher threshold for intervention due to the pandemic. In recent years, after A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA), more AVMs have been treated with medical management.\(^2\) One study showed, for example, that the OR for intervention of unruptured AVMs was 0.86 comparing the time frame after ARUBA with before publication of this trial.\(^2\) Thus it is possible in 2020, compared with 2016–19, there was continued further adoption of medical management in the post-ARUBA era. Given this overall decreasing rate of intervention before 2020, it cannot definitively be concluded that the COVID-19 pandemic is responsible for all of the changes in decreased intervention. However, given a rate of intervention change of −3.6% from 2019 to 2020, compared with an average rate of change of −0.8% across 2016–19, it is a strong possibility that the pandemic had a significant role. Several studies have shown reductions in clinical volume during the pandemic, with one study showing a 40% reduction in neurosurgical volume during a portion of 2020 relative to the year before.\(^12\) In 2020, there was also a decrease in neurointerventional procedures, such as mechanical thrombectomy for stroke and coil embolization of ruptured intracranial aneurysms.\(^25\) Management of AVMs may also be following these trends.
Concurrent with reduced intervention was a higher rupture rate compared with previous years. This association has been demonstrated previously, where an inverse relation between intervention and rupture rate was identified. On our year by year linear regression analysis from 2016 to 2020 comparing intervention and rupture rate, we found a high R² of 0.88, suggesting a strong relationship between these two variables. While not causal, this suggests the need for further investigation, especially given consistency with previous results. If causal, however, the full effect of the significant reduction in interventions may not be realized as previous studies have found a several year lag period between changes in AVM intervention rate and rupture rate.

For patients with ruptured AVMs, increased inpatient mortality and a higher probability of a poor outcome via the NIS-SOM measure may also be due to delays in care, similar to the increased mortality rate for strokes during 2020 compared with previous years. Increased mortality has also been observed in other emergency presentations, such as acute coronary syndrome, where patients with this condition during periods of 2020 also had increased mortality. We also found decreased odds of intervention in 2020 for ruptured AVMs, contrary to past results. Unlike unruptured AVM management, this is likely not due to changes in the treatment paradigm, but rather solely due to less treatments being performed during the pandemic.

Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Ruptured (n=14340)</th>
<th>Unruptured (n=49270)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2016–19 (n=11260)</td>
<td>2020 (n=3080)</td>
</tr>
<tr>
<td>Age (years) (mean±SD)</td>
<td>49.5±21.6</td>
<td>49.3±21.2</td>
</tr>
<tr>
<td>&gt;80 years (%)</td>
<td>5.8</td>
<td>5.5</td>
</tr>
<tr>
<td>Men (%)</td>
<td>53.7</td>
<td>54.4</td>
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<tr>
<td>Race (%)</td>
<td>0.40</td>
<td></td>
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<tr>
<td>White</td>
<td>52.7</td>
<td>53.2</td>
</tr>
<tr>
<td>Black</td>
<td>15.9</td>
<td>14.6</td>
</tr>
<tr>
<td>Hispanic</td>
<td>16.6</td>
<td>16.2</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>4.8</td>
<td>4.7</td>
</tr>
<tr>
<td>Native American</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Other</td>
<td>4.9</td>
<td>5.5</td>
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<tr>
<td>Insurance type (%)</td>
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<tr>
<td>Medicare</td>
<td>31</td>
<td>27.9</td>
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<tr>
<td>Medicaid</td>
<td>19.3</td>
<td>21.4</td>
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<tr>
<td>Private</td>
<td>38.7</td>
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<tr>
<td>Self-pay</td>
<td>6.4</td>
<td>7.6</td>
</tr>
<tr>
<td>Teaching hospital (%)</td>
<td>76.3</td>
<td>93.5</td>
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<tr>
<td>Hospital bed size (%)</td>
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<td>&lt;0.0001</td>
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<tr>
<td>Small</td>
<td>15.9</td>
<td>7.8</td>
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<tr>
<td>Medium</td>
<td>21.4</td>
<td>21.6</td>
</tr>
<tr>
<td>Large</td>
<td>60.9</td>
<td>70.6</td>
</tr>
<tr>
<td>Length of stay (days) (median (IQR))</td>
<td>6 (3–14)</td>
<td>7 (3–15)</td>
</tr>
<tr>
<td>Weighted Elixhauser comorbidity score (median (IQR))</td>
<td>5 (0–15)</td>
<td>7 (0–16)</td>
</tr>
<tr>
<td>CSF diversion (%)</td>
<td>18.9</td>
<td>20</td>
</tr>
<tr>
<td>Unruptured aneurysm (%)</td>
<td>3.5</td>
<td>2.9</td>
</tr>
<tr>
<td>COVID-19 (%)</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Percutaneous Endoscopic Gastrostomy (%)</td>
<td>9.1</td>
<td>8.4</td>
</tr>
<tr>
<td>Tracheostomy (%)</td>
<td>5.2</td>
<td>5.5</td>
</tr>
<tr>
<td>NIS-SOM outcome (%)</td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>Poor</td>
<td>50.1</td>
<td>52.1</td>
</tr>
<tr>
<td>Good</td>
<td>49.7</td>
<td>47.4</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Inhospital mortality (%)</td>
<td>7.2</td>
<td>10.6</td>
</tr>
<tr>
<td>Routine discharge (%)</td>
<td>43.2</td>
<td>43.5</td>
</tr>
</tbody>
</table>

NIS-SOM, National Inpatient Sample-subarachnoid hemorrhage outcome measure.
pandemic, given only 1.0% of patients with ruptured AVMs had COVID-19.

In terms of interventions performed, in 2020 unruptured AVMs had a significant decrease in EVT and microsurgery with a modest increase in SRS and combined EVT plus microsurgery. Conversely, in 2020, ruptured AVMs saw an increase in EVT while all other treatment types decreased. In the midst of a pandemic, SRS may be more favorable than EVT and surgery due its less invasive nature and it requires less hospital resources with shorter hospital stays. On the other hand, the increase in the combination of EVT with surgery may not reflect changes in treatment modalities, but rather when treatment occurs. Often, patients may undergo preoperative embolization, followed by surgery on another admission. However, during a pandemic, the number of trips to the hospital is ideally minimized, thus this may be a reflection of the increased number of patients receiving dual therapy in one hospitalization.

Conversely, there was an increase in relative utilization of EVT only for ruptured AVMs which may reflect reduced hospital capacity. Given the frequent use of EVT before more curative surgery, it is possible some patients were only receiving EVT with the goal of surgery in the future. However, with more limited resources in 2020, more complete treatment of the AVM may not have been possible on the initial hospital admission, and thus the relative proportion of EVT increased.

Age was another factor considered when looking at interventions. For unruptured AVMs, the pattern generally followed in accord with the lower overall intervention rate, with almost all age categories decreasing in 2020, likely due to a reduced rate of neurosurgical procedures overall during the COVID-19 pandemic. The increased intervention rate for those aged >75 years, however, may not be due to the higher intervention rate in this population, but rather a lower total number of hospitalizations. Given the much higher risk of severe COVID-19 in this population, it is possible that the threshold for admission of these patients was higher than in previous years, with only those with more severe disease requiring intervention being admitted, giving rise to a higher intervention rate.

While overall the rate of intervention was lower for ruptured AVMs, the differences were most prominent in the older cohorts (ages 45–60 and 60–75 years). This likely reflects the greater comorbidity of older populations, and in the context of a pandemic, less aggressive measures may be undertaken in more morbid patients. In common with unruptured AVMs, however, the increased rate in the >75 year age cohort remains unclear but may also be due to the most severe presentations reaching the hospital, and as such requiring a higher rate of intervention.

Limitations
The NIS database has the strength of a large sample size and being nationally representative, but many limitations exist. The first is that the data are observational in nature. As a result, causality is not as strongly supported as a randomized and prospective trial and is also potentially prone to confounders that are not available in the data and not corrected for. Important, there is no granular detail on the characteristics of each patient’s AVM, such as Spetzler–Martin grade, morphology, and location, all important aspects and that impact outcomes and treatment decisions.
In addition, the database does not link patients, and thus patients with several admissions may be represented more than once in our analysis. For example, if a patient had multiple hospitalizations, but only an intervention on one hospitalization, this may artificially decrease the true intervention rate. The NIS also does not capture outpatient management, which may underestimate the actual utilization of radiotherapy. Lastly, the coding practices at each institution may vary and as such may introduce some degree of inaccuracy.

CONCLUSIONS

In 2020, the first year of the COVID-19 pandemic, interventions for unruptured and ruptured AVMs decreased. This corresponded to an increased rupture rate, and for those with ruptured AVMs, worse outcomes. These findings seem to corroborate previous studies suggesting that as unruptured AVM treatments continue to decline, rupture incidence will increase. Furthermore, the COVID-19 pandemic may have accelerated this process because AVM treatments declined even more precipitously during 2020. Given the lack of a significant number of AVM patients with concurrent COVID-19 infection, this suggests that the discrepancy in outcomes during 2020 is likely related to changes in treatment patterns and strain in the healthcare system rather than complications from COVID-19 itself.

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Contributors All authors significantly contributed to this manuscript. Concept and design: RMS, AA, EL, IR, and MS. Data acquisition: EL, VG, and IR. Data analysis and interpretation: RMS, EL, IR, and VG. Literature search: IR, TE, and VG. Drafting the first manuscript: IR, EL, and VG. Revision of the manuscript for important intellectual content: IR, TE, EL, RMS, MS, and AA. Guarantor of study: IAR. Approval of final manuscript version for submission: all authors.

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REFERENCES

The pandemic and neurointervention


