Determinants of Outcome in Anticoagulation-Associated Cerebral Hematoma Requiring Emergency Evacuation

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Objective: To analyze the likelihood of recovery and prognostic factors in patients with massive anticoagulation-associated intracerebral hemorrhage treated with surgical evacuation after reversal of anticoagulation.

Design: Retrospective case series.

Setting: Neurological-Neurosurgical Intensive Care Unit at Mayo Clinic.

Patients: Seventeen consecutive patients with large anticoagulation-associated intracerebral hemorrhage.

Intervention: Surgical evacuation of intracerebral hemorrhage.

Main Outcome Measure: Functional outcome was assessed using the modified Rankin scale.

Results: Before surgery, all patients had pronounced (>1-cm) shift of the septum pellucidum and one third had clinical signs of uncal herniation. Still, favorable outcome (modified Rankin scale score ≤3) was achieved by 11 patients (65%). All patients with good recovery awoke within 36 hours of surgery. Older age (P = .05) and serious systemic complications after surgery (P < .01) were significantly associated with lack of neurological recovery and fatal outcome.

Conclusions: Emergency surgery for select deteriorating patients with large anticoagulation-associated intracerebral hemorrhage is compatible with favorable outcome despite the presence of clinical and radiological signs of herniation before the evacuation.

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ANTICOAGULATION ALLOWS blood to dissect unhindered into the brain parenchyma. Frequent hematoma expansion explains the high in-hospital mortality of anticoagulation-associated intracerebral hemorrhage (ICH), especially among older patients with diabetes mellitus.1,2

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In our previous study on the usefulness of emergency surgery for expanding hematoma, we unexpectedly noted a more favorable outcome in patients with anticoagulation-associated ICH.3 We speculated that international normalized ratio (INR) correction with fresh frozen plasma and vitamin K may have limited clot volume and brainstem injury due to shift. All studies on surgery in ICH have considered initially stable patients and evacuated the hematoma at discretionary intervals.4,5 There are no studies on the effect of emergency craniotomy in anticoagulated, neurologically deteriorating patients.

We analyzed our experience with surgical treatment of patients with anticoagulation-associated ICH to assess the chances of recovery and determinants of functional outcome.

METHODS

We reviewed the medical records and radiological information of all patients with anticoagulation-associated ICH admitted to St Mary’s Hospital Neurological-Neurosurgical Intensive Care Unit at Mayo Clinic who underwent surgical evacuation between 1977 and 2004. We operationally defined anticoagulation-associated ICH as any ICH occurring in patients treated with warfarin with an INR of 1.4 or higher or receiving intravenous heparin with documented elevation of partial thromboplastin time. Hemorrhages caused by head trauma or underlying vascular anomalies and cases of hemorrhagic transformation of ischemic infarction were excluded.

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We collected data on patients’ demographic information and comorbid conditions, type of anticoagulation, and indication for anticoagulant therapy. The time at onset of neurological symptoms ascribed to the ICH, INR at the time of ICH diagnosis, time to reversal of INR less than 1.4 or partial thromboplastin time less than 34 seconds (upper level of normal range), and time of neurological decline (defined as a decrease in the Glasgow Coma Scale sum score ≥2 points) were gathered. Intervals from ICH symptoms to surgery and from time of clinical decline to surgery were calculated. We noted the Glasgow Coma Scale sum score at the time of surgery and the presence of clinical signs of herniation. We collected radiological data including location of the hematoma, presence of intraventricular hemorrhage, presurgical hematoma volume (using the ABC/2 method), and presurgical degree of shift of midline structures (septum pellucidum and pineal gland).

We also compiled postoperative clinical information including time to awakening (defined as ability to follow simple commands), severe medical complications (defined as new organ failure, sepsis, myocardial infarction, cardiac arrhythmia with hemodynamic compromise, ischemic stroke, or pulmonary embolism), length of hospital stay, disposition on hospital discharge, and functional outcome using the modified Rankin scale for assessment. Favorable functional outcome was defined as a modified Rankin scale score of 3 or lower at 1 year. In patients with long-term follow-up, we recorded if anticoagulation was ever restarted and how long after the ICH this decision was made.

Statistical analysis was performed using the Fisher exact test to compare the distribution of dichotomous variables and the 2-tailed t test for continuous variables. The methods of this research were approved by our institutional review board.

RESULTS

We identified 17 patients with anticoagulation-associated ICH. Mean age was 69 years (range, 46-86 years) and 65% of the patients were men. History of hypertension was present in 72%. Indication for anticoagulation was atrial fibrillation in 35%, mechanical valve in 29%, and others in 47% (ie, recent venous thromboembolism, recent myocardial infarction, symptomatic basilar stenosis despite antiplatelets, previous stroke caused by presumed cardiac embolism). Intracerebral hemorrhage was associated with warfarin use in 76% and heparin infusion in 24% of cases. Median INR level at the time of ICH diagnosis was 2.5 (mean, 3.5 [range, 1.6-9]). Anticoagulation with heparin was reversed using protamine sulfate while elevated INR was reversed using vitamin K and fresh frozen plasma in doses deemed appropriate for each case. Median time to reversal of anticoagulation was 6.5 hours (range, 2-48 hours). All patients had an INR less than 1.4 and partial thromboplastin time less than 34 seconds prior to surgery.

Surgery was performed after a median time of 18 hours (range, 2-120 hours) from ICH symptom onset and 5 hours (range, 1-12 hours) from acute clinical worsening. Median Glasgow Coma Scale sum score at the time of surgery was 9 (range, 5-14). Before surgery, physical examination findings revealed signs of herniation in 5 patients (29%).

Brain imaging showed ICH affecting the left hemisphere in 8 patients (47%) and the presence of intraventricular hemorrhage in 6 (35%). Mean hematoma volume was 75 mL³ (range, 30-110 mL³). Shift of midline structures was uniformly present; mean displacement of the septum pellucidum was 10.8 mm (range, 6-17 mm) and mean shift of the pineal gland was 4.6 mm (range, 2-7 mm). The Figure illustrates one of our cases.

Functional outcome at 1 year was favorable (modified Rankin scale score ≤3) in 11 (65%) of 17 patients, and 5 of the 6 patients who failed to recover meaningfully died.
within 6 months of the ICH (including 4 patients who died during the acute hospitalization). The Table shows the distribution of clinical and radiological variables according to clinical outcome. Patients with unfavorable outcome were significantly older (P = .05). All patients with heparin-associated ICH (including 2 patients with clinical signs of herniation) achieved favorable recovery after surgery. There was no difference between the groups in the prevalence of history of hypertension, indication of anticoagulation, INR at the time of ICH diagnosis, time to surgery, depth of coma, size of hematoma, or degree of midline shift. All patients with unfavorable outcome developed severe medical complications. In fact, 3 of 5 patients with fatal outcome awoke within the first day after surgery but later had systemic complications. Withdrawal of care was decided only in 1 case (patient with sepsis and persistent coma). Meanwhile, no patient with favorable recovery had severe medical complications during the postoperative course. All patients with good recovery awoke within 36 hours of surgery. Median length of hospital stay was 13 days (range, 4-169 days). Median follow-up of survivors was 3.5 years.

Anticoagulation was reinitiated in 6 (50%) of 12 survivors, and it was used permanently in 4 (all were patients with atrial fibrillation or mechanical valve, mean follow-up of 6 years) and transiently in 2 (indications were venous thromboembolism and acute coronary syndrome). Median interval between ICH and reinitiation of anticoagulation was 25 days (range, 8 days to 4 months). No patient had complications from the recurrent use of anticoagulation.

It may occur at any time after initiation of oral anticoagulation and during heparin infusion. This subset of hemorrhages differs from spontaneous cases because patients may have a higher chance of clinical worsening, often during active reversal of anticoagulation. Even after correction of INR, hematomas may still expand. Data on the functional outcome of deteriorating patients with anticoagulation-associated ICH are limited and the results after surgery in this population, to our knowledge, have not been previously analyzed. Our study, albeit limited in number of patients reviewed, found that almost two thirds of the patients had favorable functional recovery. Fatal outcome was more common in older patients and resulted from major systemic complications, often after improvement in consciousness had occurred following the surgery. Failure to awaken after surgery in 2 patients resulted in a fatal outcome. Location in the dominant hemisphere and ventricular rupture were indicators of poor outcome but did not reach statistical significance in this small sample. In a small number of patients, anticoagulation was resumed without complications.

Clinical deterioration with signs of uncal herniation occurred in a third of the patients. Midline shift was noted on presurgical computed tomographic scans in all cases. Therefore, it is unlikely that our patients would have recovered spontaneously. Only a very small minority of patients with anticoagulation-associated ICH treated at our center undergo surgical evacuation. Careful patient selection probably played a crucial role in determining the favorable outcomes observed in our series. Rapid reversal of anticoagulation, accessibility of the hematoma, and perception of good rehabilitation potential were some of the factors most often cited to favor surgery.

### Table
Clinical and Radiological Variables in 17 Patients Who Underwent Surgery for Evacuation of Anticoagulation-Associated Cerebral Hematomas Distributed According to Functional Outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Favorable Outcome (mRS Score ≥3)</th>
<th>Unfavorable Outcome (mRS Score &gt;3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean (range)</td>
<td>65 (46-78)</td>
<td>76 (59-89)*</td>
</tr>
<tr>
<td>Men, No. (%)</td>
<td>8 (73)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>History of hypertension, No. (%)</td>
<td>7 (64)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Warfarin use, No. (%)</td>
<td>7 (64)</td>
<td>6 (36)</td>
</tr>
<tr>
<td>Heparin infusion, No. (%)</td>
<td>4 (100)</td>
<td>0</td>
</tr>
<tr>
<td>INR, median (mean [range])</td>
<td>4 (4.5 [1.6-9])</td>
<td>2.4 (2.4 [1.8-3])</td>
</tr>
<tr>
<td>Time to reversal of anticoagulation, h, median (range)</td>
<td>7.5 (2-36)</td>
<td>5.5 (3-48)</td>
</tr>
<tr>
<td>Time from ICH onset to surgery, h, median (range)</td>
<td>24 (2-120)</td>
<td>9 (3-48)</td>
</tr>
<tr>
<td>Time from clinical decline to surgery, h, median (range)</td>
<td>5 (1-12)</td>
<td>5 (3-12)</td>
</tr>
<tr>
<td>GCS sum score on surgery, mean (range)</td>
<td>10.5 (5-14)</td>
<td>8.8 (5-14)</td>
</tr>
<tr>
<td>Clinical signs of herniation, No. (%)</td>
<td>4 (36)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Left hemisphere ICH, No. (%)</td>
<td>4 (36)</td>
<td>4 (66)</td>
</tr>
<tr>
<td>Intraventricular hemorrhage, No. (%)</td>
<td>3 (27)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Hematoma volume, mL, mean (range)</td>
<td>74 (30-112)</td>
<td>77 (46-110)</td>
</tr>
<tr>
<td>Midline septum pellucidum shift, mm, mean (range)</td>
<td>11 (6-17)</td>
<td>10.6 (7-15)</td>
</tr>
<tr>
<td>Midline pineal gland shift, mm, mean (range)</td>
<td>4.8 (3-7)</td>
<td>4.3 (2-6)</td>
</tr>
<tr>
<td>Severe postsurgical medical complications, No. (%)</td>
<td>0</td>
<td>6†</td>
</tr>
</tbody>
</table>

Abbreviations: GCS, Glasgow coma scale; ICH, intracerebral hemorrhage; INR, international normalized ratio; mRS, modified Rankin scale.

*P < .05.
†P < .01.
Our study clearly suggests that emergency surgery for select deteriorating patients with large anticoagulation-associated ICH is compatible with favorable outcome. Recovery can be expected in 2 of 3 patients who fully awaken within 36 hours of the evacuation. Failure to do so increases the chance of further medical complications that can become fatal.

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REFERENCES

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