Original Contributions

Prognostic Parameters in Spontaneous Intracerebral Hematomas With Special Reference to Anticoagulant Treatment

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We examined a series of 200 consecutive patients with spontaneous intracerebral hematoma clinically and by computed tomography, excluding patients with trauma, aneurysm, or tumor. Hematoma volume varied from 1 to 230 (average 35) ml, and overall mortality was 30% (60 patients). Of the 200 patients, 14% (28) were receiving anticoagulants; among these 28 patients hematoma volume averaged 72 ml and mortality 57% (16 patients). The 140 survivors were followed for 2–24 months. Our findings indicate that anticoagulation therapy after previous cerebral infarction or embolism of cardiogenic origin did not predispose to intracerebral hemorrhage. Prognosis was poor when the initial level of consciousness was low and the hematoma volume exceeded 50 ml in combination with dilatation of the contralateral ventricle. An intracerebral hematoma of >80 ml volume was always fatal, regardless of therapy. With volumes of 40–80 ml, early surgical evacuation of the lobar hematoma may improve outcome. (Stroke 1991;22:571–576)

Intracerebral hematomas (ICHs) account for about 10% of all strokes. Before the introduction of computed tomography (CT), ICH was diagnosed by ventriculography, angiography, and spectrophotometric analysis of the cerebrospinal fluid (CSF). These methods are of little value for differentiating hemorrhagic and ischemic strokes, and ICHs identifiable by such means have as a rule been large, with an associated high mortality (approximately 50%). Diagnostic accuracy and sensitivity have improved with the use of CT; smaller ICHs may now be detected, producing a decline in the mortality rate. Effective treatment of hypertension in recent years has also contributed to the current lower mortality rate of 30%. Subjects and Methods

We evaluated the hospital case records and CT scans of all patients with ICH admitted to the neurological emergency service of the University Hospital, Linköping, between January 1982 and November 1986. We excluded patients with hemorrhages due to trauma, aneurysms, or tumors but included patients on anticoagulant therapy. The series consisted of 200 patients aged 35–81 (mean 65.4) years, 121 men and 79 women. All underwent CT on admission, in no case earlier than 4–5 hours and usually within 48 hours after the onset. The ICH was classified according to the localization of the largest blood clot as lobar (frontal, parietal, temporal, or occipital), putaminal, thalamic, pontine, or cerebellar. Hematoma rupture into and deformation/dislocation of the ventricles and cisterns were documented. The hematoma volume was estimated by measuring the volume of the blood clot in each CT slice and adding these values. We decided treatment during the first 24 hours, with indications for surgery based on clinical and radiologic findings. All except a few comatose, geriatric patients were considered for surgery.

The patients were divided into six groups according to level of consciousness at the time of admission, using a modified Glasgow coma scale, and outcome was graded at the end of the follow-up period using a modified Rankin scale as totally disabled, partially disabled, or "recovered." The follow-up period was 2–24 (average 8.4) months.

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Table 1. Initial Clinical Findings in Surviving and Dying Patients With Intracerebral Hematoma

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (N=200)</th>
<th>Surviving (n=140)</th>
<th>Dying (n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Onset during daytime</td>
<td>181</td>
<td>91</td>
<td>128</td>
</tr>
<tr>
<td>Consciousness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alert</td>
<td>119</td>
<td>59</td>
<td>119</td>
</tr>
<tr>
<td>Stupor</td>
<td>34</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Coma</td>
<td>47</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td>Nausea</td>
<td>46</td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td>Epileptic fits</td>
<td>16</td>
<td>8</td>
<td>11</td>
</tr>
</tbody>
</table>

Results

Overall mortality was 30% (60 patients, mean age 66.8 years). A history of hypertension, which in most cases was treated, was present in 42% (84) of the patients. The ICH was lobar in 40%, putaminal in 35%, thalamic in 16%, pontine in 2%, and cerebellar in 7% of the patients. There was no definite correlation between hypertension and hematoma location; hypertension was present in 37 of 80 patients with lobar, 28 of 70 with putaminal, 14 of 32 with thalamic, none of four with pontine, and five of 14 with cerebellar ICH. Diabetes was present in 7% (14 patients). The initial symptoms are given in Table 1. In 181 patients (91%) the onset occurred during the daytime, and epileptic fits occurred in 8% (16 patients) during the acute phase.

Altogether 171 patients were treated conservatively, and 52 (30%) of these died. Surgery was performed in the remaining 29 patients. In 21 of these patients (mean age 62 years), the hematoma was evacuated via a craniotomy, and the other eight patients were treated by shunt drainage because of progressive ventricular dilatation. Eight patients treated surgically died. Among the total 200 patients, 28% (56) recovered, 24% (48) were partially disabled, 18% (36) were totally disabled, and 30% (60) died.

Hematoma volume ranged from 1 to 230 (mean 35) ml. Among the fatal cases, mean volume was approximately 70 ml, whereas in the survivors it was only about 20 ml. When the hematoma volume exceeded 60 ml (43 patients), the mortality was 84% (36 cases). The prognostic value of the effect of the hematoma on the ventricles and cisterns is shown in Figure 1. The most common finding, seen in 81% (162 of the patients), was compression of the ipsilateral ventricle; mortality in this group was 36% (58 patients). Obliteration of the cisterns was a slightly graver sign (relative mortality 46% [55 of 120 patients]). Rupture into the ventricular system occurred in 50% (100 patients) (relative mortality 48% [48 patients]). Dilatation of the contralateral ventricle, seen in 35% (70) of the patients, was a very bad prognostic sign (relative mortality 67% [47 patients]) and was ascribed to a disturbance of the CSF circulation. In 11% (22) of the patients no such CT signs were present, outcome was good (mortality 0%), and hematoma volume never exceeded 10 ml.

Concerning lobar ICH, the greater the hematoma volume, the lower the level of consciousness (Figure 2, upper panel). The vertical view of Figure 2 shows the level of consciousness and final outcome for each hematoma volume. All patients with a lobar hematoma volume exceeding 80 ml or a level of consciousness of grade 5 or 6 died regardless of therapy. With hematoma volumes of <30 ml, there was no mortality, and surgically treated patients had no better outcome than those treated conservatively. Patients with a hematoma volume of 40–80 ml and a consciousness level of grades 2–5 are plotted inside the frame in Figure 2. Only the surgically treated patients survived, and they each had a hematoma volume slightly greater than that of the conservatively treated patients, who all died. In this group, the final outcome was good; only one patient was totally disabled. Details of the patients within the frame are given in Figure 3; there was no obvious difference between surgically and conservatively treated patients regarding age, effect of the hematoma on the CSF spaces, lobar localization, or hemispheric lateralization.

Putaminal ICHs are presented in the same way in Figure 4. Mortality was higher and level of consciousness lower with hematoma volumes of 30–70 ml. Only a few patients were operated on. In spite of a very small (<10 ml) hematoma, two patients had a lowered level of consciousness (grade 5).
Level of consciousness

FIGURE 2. Lobar hematomas (80 patients): Scatterplot of level of consciousness (upper panel) and outcome (lower panel) correlated with hematoma volume. Patients within frame are illustrated in more detail in Figure 3. \(\bullet\), conservatively treated and survived; \(\bigcirc\), conservatively treated and died; \(\bigtriangledown\), surgically treated and survived; \(\bigtriangleup\), surgically treated and died.

Figure 3. Lobar hematomas: Scatterplot of detailed data for patients within frame in Figure 2. Location of hematoma: \(f\), frontal; \(p\), parietal; \(t\), temporal; \(o\), occipital; \(dx\), right; \(sin\), left; \(\pm\), rupture to ventricular system.

Owing to obstruction of the CSF circulation. These were treated with a ventricular shunt, and both improved.

Thalamic ICH was seen in 32 patients; one was operated on with a ventricular shunt and three died. Pontine ICH was seen in four patients, and only one survived. Cerebellar ICH occurred in 14 patients; three were operated on with a ventricular shunt. Ten patients with cerebellar ICH survived, of whom two were operated on.

Anticoagulant therapy with warfarin was given in 16 men and 12 women (14%, mean age 71 [range 48–78] years). Of these 28 patients, 11 (39%) were being treated for hypertension. None was receiving aspirin or other antiplatelet drugs, except one who was being treated with warfarin combined with dipyridamole. Cardiovascular symptoms (atrial fibrillation, valve prosthesis, cardiomyopathy) were present in 15 patients, and three had diabetes mellitus.

Among the patients taking warfarin, the mean hematoma volume was 72 (1–230) ml and mortality was high; 16 (57%) of the 28 died. The ICH was lobar in 12, putaminal in nine, cerebellar in four, and thalamic in three. CT showed no signs of multiple ICH. Table 2 shows the reasons for initiating anticoagulant therapy. Prophylactic anticoagulant therapy was given to 13 patients with a previous, CT-confirmed cerebral infarct with a temporal profile of transient ischemic attack/reversible ischemic neurological deficit. In only five of the 13 patients (38%) was the ICH in the same vascular territory as the infarct visible on the previous CT. In six of the 13 patients, the infarct was probably a cardiac embolus due to atrial fibrillation. Two of these six patients had their ICH in the same vascular territory, compared with three of seven patients with a previous atherothrombotic infarction. Of the four patients with cerebellar hematoma, none had a history of stroke within the vertebrobasilar territories, and in three a previously normal CT was available.

The duration of warfarin treatment ranged from 2 to 108 (mean 29.6, median 9) months (Figure 5). The prothrombin time was monitored by the “thrombotest” method (therapeutic range 2.1–3.6 international normalized ratio [INR]). The INR values at the time of the ICH are shown in Figure 6. The eight patients with an INR value of >3.6 had a mean hematoma volume of 91 (range 9–205) ml and a mortality rate of 62% (five of eight). Within the therapeutic range, the mean hematoma volume was 65 (range 1–230) ml and the mortality rate was 56% (10 of 18). The two patients below the therapeutic range had hematoma volumes of 18 ml and 99 ml. No other local or systemic hemorrhagic complications were present at the time of the ICH.

Discussion

The outcome of ICH has been evaluated in several studies,7,11–16 and mortality has ranged between 14% and 58%. In our investigation overall mortality was 30%, which is in accordance with other recent studies.8,14,15 The decline in the incidence of ICH during the past 10 years is probably explained by the current more widespread treatment of hypertension.17

The incidence of ICH is approximately 10% in studies in which all stroke patients were examined by CT during the acute stage of the illness. Small ICHs can be detected only by CT or magnetic resonance imaging, which explains the low incidence of ICH in the Framingham Study, which started before the introduction of CT.18 Most small ICHs resolve with-
out residual impairment and, when included in statistical evaluation, improve the prognosis and reduce the relative mortality among all patients with ICH.

Rupture of the hematoma into the ventricular system is regarded as an unfavorable prognostic sign, with increased acute mortality.\(^{19,20}\) In such patients, we found a mortality of 48%. An even graver prognostic CT finding is dilatation of the contralateral ventricle\(^ {15}\); survival in such patients was only 33% in our series.

The value of surgery in ICH has been a matter of controversy.\(^ {2,8,15,16,21,22}\) Selection criteria are poorly defined. Many authors consider that an indication for surgical treatment of lobar ICH is a progressive neurological deficit alone or in combination with an impaired level of consciousness.\(^ {23-26}\) Better predictors of outcome are the level of consciousness and the hematoma volume. Kase et al\(^ {23}\) regarded 50 ml as the "critical size," and Helweg-Larsen et al\(^ {7}\) found a mortality of 90% when the volume exceeded 50 ml. Bolander et al\(^ {15}\) had only one survivor when the hematoma volume was >80 ml. This tallies with our finding of 84% mortality (36 cases) among 43 patients with a hematoma volume exceeding 60 ml. We found no mortality when the lobar hematoma volume was <30 ml with preserved level of consciousness, and such patients did not benefit from surgery. Only patients with a lobar hematoma volume of 40-80 ml and a reduced level of consciousness may benefit from surgery according to 10 of our series of 200 patients. Both the present study and others\(^ {8,27}\) indicate that infratentorial and small central hematomas should be treated conservatively or by ventricular shunting when there is disturbance of the CSF circulation.

It is well known that anticoagulant therapy increases the risk of ICH.\(^ {10,28,29}\) In fact, 14% of our patients had an anticoagulant-related ICH; such patients also had a worse prognosis, and there were no symptoms of other localized or systemic hemorrhage. Most anticoagulant-related ICHs occurred ≤1 year after starting anticoagulant treatment; 54% (15) occurred within the first 10 months of treatment (Figure 5). Kase et al\(^ {30}\) reported 70% in the first year. The higher mortality and hematoma volume found in our study among patients receiving warfarin is also in accordance with the recently published report by Franke et al,\(^ {31}\) who found an eightfold increased risk of ICH during anticoagulant treatment.

In the Dutch Sixty-Plus Reinfarction Study,\(^ {32}\) >80% of severe hemorrhagic complications occurred in patients with thrombotest values of <10%, corresponding to an INR value of >2.8. In the present study, most patients receiving warfarin (18 of 28) had an INR value within the therapeutic range, and the patient with the largest hematoma volume (230 ml) had an INR value of 2.5! For the 28 patients receiving warfarin mean hematoma volume was larger than for the entire series of 200 (72 versus 36 ml), and in the eight patients receiving the most aggressive anticoagulation treatment (i.e., INR value of >3.6) mean hematoma volume was

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### Table 2. Indications for Anticoagulant Treatment in Patients With Intracerebral Hematoma

<table>
<thead>
<tr>
<th>Disorder</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebrovascular</td>
<td>8</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>7</td>
</tr>
<tr>
<td>Transient ischemic attacks</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac</td>
<td>15</td>
</tr>
<tr>
<td>Valve prosthesis</td>
<td>4</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3</td>
</tr>
<tr>
<td>Atrial fibrillation + minor stroke</td>
<td>6</td>
</tr>
<tr>
<td>Atrial fibrillation + arterial embolism</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>2</td>
</tr>
<tr>
<td>Arteriovascular disease</td>
<td>1</td>
</tr>
</tbody>
</table>

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**FIGURE 4. Putaminal hematomas (70 patients): Scatterplot of level of consciousness (upper panel) and outcome (lower panel) correlated with hematoma volume. •, conservatively treated and survived; ○, conservatively treated and died; ——•—, surgically treated and survived; —O—, surgically treated and died.**

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**FIGURE 5. Scatterplot of duration of anticoagulant treatment before onset of intracerebral hematoma in 28 patients.**
larger than for those patients with an INR value within the therapeutic range (91 versus 65 ml). Only two patients (one of whom had an INR value of 1.08, which is normal for untreated patients) had an INR value below the therapeutic range, indicating that monitoring of the prothrombin time to the lower limit of the therapeutic range may reduce the incidence of anticoagulant-related ICH.

The two main indications for long-term anticoagulant treatment are prophylaxis against cerebral infarction in patients with transient ischemic attack or cardiac sources of emboli. It has been questioned whether patients given anticoagulant treatment for cerebrovascular disease are at greater risk of serious hemorrhagic complications than patients given anticoagulant drugs for other reasons. Like Kase et al., we found no support for the assumption that previous cerebral infarction was of pathogenetic importance for anticoagulant-related ICH. Among the 13 patients with previous cerebral infarction given anticoagulant treatment, only five ICHs occurred in the same vascular territory. Due to the small number of patients in the embolic (six) and atherothrombotic (seven) infarction groups, sure conclusions cannot be drawn concerning the risk for bleeding in the respective groups. Further, 14% (four of 28) of the ICHs in anticoagulant-treated patients were cerebellar compared with 6% (10 of 172) in -untreated patients.

FIGURE 6. Scatterplot of international normalized ratio (INR) values at time intracerebral hematoma occurred in 28 patients.

References

Rådberg et al ICH, CT, and Prognosis 575

**KEY WORDS** • x-ray computed anticoagulants • hematoma • tomography, x-ray computed
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