Prediction of death in patients with primary intracerebral hemorrhage: a prospective study of a defined population

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Object. Predictors of early (30-day) and long-term (1-year) mortality rates after primary intracerebral hemorrhage (ICH) were studied in a large population in southern Sweden.

Methods. All cases of primary ICH, verified using computerized tomography (CT) scanning or autopsy study, were prospectively registered at the 12 hospitals covering a defined population of 1.14 million during the calendar year 1996. Mortality was analyzed in relation to CT findings (hematoma location and volume and ventricular extension) and clinical parameters (patient age and sex, level of consciousness on admission, and history of preictal risk factors) by using univariate and multivariate statistical methods.

Three hundred forty-one cases of primary ICH were detected. The overall mortality rate was 36% at the 30-day and 47% at the 1-year follow up. Multivariate analysis revealed that initial level of consciousness, hematoma volume, and a history of heart disease were independent predictors of death at 30 days postictus. One year after bleeding, independent predictors of mortality were the initial level of consciousness, patient age, and hematoma location.

Conclusions. Primary ICH remains a stroke subtype associated with a high mortality rate and for which the level of consciousness on admission is the strongest predictor of fatal outcome both at 30 days and during the 1st year after bleeding. A preictal history of heart disease increased the 30-day mortality rate.

Key Words • intracerebral hemorrhage • prognosis • risk factor • outcome

Primary ICH, which affects 13 to 35 individuals per 100,000 every year, is a stroke subtype associated with high morbidity and mortality rates; that is, 35 to 50% can be expected to die within the first month after bleeding.1–3,9,11,17 Although most cases occur among the elderly, a significant proportion of patients are young or middle aged.19 Despite the severity of the disease, little is known about its optimal management, and no conclusive data have been published showing any significant benefit of surgical or medical treatment.

To optimize treatment of the individual patient as well as to evaluate general treatment strategies for primary ICH, it is essential to define reliable predictors of evolution and outcome. Data from previous studies in which multivariate analysis was used have demonstrated a range of variables independently related to an increased risk of death. The factors that have been shown most consistently to predict mortality or poor outcome are a patient’s initial level of consciousness and hematoma volume.4,6,10,12–16,20–22,27 In addition, location of hemorrhage, VE of hematoma, hydrocephalus, pulse pressure, focal neurological deficits, and patient age have, to a varying extent, been of prognostic value.4,6,7,10,22,27 Juvela15 tried to identify preictal factors other than patient sex and age that might influence outcome; he found that the amount of alcohol consumed within one week prior to bleeding was an independent determinant of poor outcome, whereas hypertension, diabetes mellitus, smoking, anticoagulant therapy, or use of nonsteroidal antiinflammatory drugs were not.

Although the earlier mentioned studies provide reliable information on prognostic factors and predictors of mortality with the aid of multivariate analysis, they were usually carried out in selected patients referred to major hospitals or restricted to patients with supratentorial hemorrhages. Population-based studies, however, have offered only limited data on factors that might influence outcome.1–3,9,11,14 We have, therefore, investigated the mortality rates at 30 days and during 1 year after bleeding in a large well-defined population in southern Sweden by prospective registration of all cases of verified primary ICH.17 The prognostic value of hemorrhage characteristics, initial patient status, and history of a range of proposed preictal risk factors were analyzed using uni- and multivariate methods.

Clinical Material and Methods

Twelve hospitals, including forensic or pathology departments, serving a defined population of 1.14 million in southern Sweden participated in the study. All cases of primary ICH were registered prospectively from January 1 to December 31, 1996.
On admission to the hospital, an acute assessment of the patient’s level of consciousness was made according to the RLS, which is the most commonly used scale in Sweden, or the GCS. For statistical analysis, the patients were categorized as alert (RLS 1, GCS 14–15), drowsy (RLS 2–3, GCS 8–13), or comatose (RLS 4–8, GCS 3–7). A history of the following factors were recorded: 1) arterial hypertension (that is, whether the patient was on antihypertension medication at the time of bleeding or previously had repeated measurements of blood pressure > 160/95 mm Hg); 2) diabetes mellitus (insulin-dependent as well as noninsulin-dependent); 3) previous cerebrovascular disease (ischemic or hemorrhagic stroke); 4) heart disease (coronary disease or atrial fibrillation); and 5) ongoing treatment with oral anticoagulant (warfarin or dicumarol) or antiplatelet (acenetylsalicylic acid) drugs.

Diagnosis was confirmed within 1 to 2 days by performing either CT studies, which are routinely used for the evaluation of acute stroke at all participating hospitals, or autopsy studies. Primary ICH was defined as a focal collection of blood in the brain parenchyma appearing as a uniform high-attenuation area on a CT scan and unrelated to infarct, tumor, trauma, aneurysm, or arteriovenous malformation, or, alternatively, a necropsy examination revealing an intracerebral hematoma. Angiography was performed if the hematoma or clinical characteristics indicated an aneurysm or arteriovenous malformation as the cause of bleeding; an angiography finding positive for either of these entities excluded the patient from the study. All CT scans were evaluated by one of the authors (O.G.N.) or a radiologist. The hematomas were classified according to their location as lobar (cortical or subcortical), central (basal ganglia, thalamus, internal capsule, deep periventricular white matter, or purely intraventricular), cerebellar, or brainstem. Hematoma volume was estimated from the CT scans by using the formula $A \times B \times C/2$, where $A$ is the greatest hematoma diameter, $B$ is the diameter 90° to $A$, and $C$ is the vertical depth of the hematoma. Information regarding hematoma volume could not be obtained in 46 cases. Massive VE of the hematoma was defined as such if two or more of the ventricles were filled with blood.

For each patient with primary ICH, a special study form was filled out during the acute phase. Information concerning time of death was obtained from the official Swedish population register, with 1 year after the time of bleeding as the end point. Fatal cases in the community were searched for at the forensic/pathology departments covering the whole population. For more details concerning the study design and case ascertainment, see Nilsson, et al.

Statistical analysis was carried out using SPSS software for personal computers (SPSS Inc., Chicago, IL). An overall survival analysis for men and women was performed using Kaplan–Meier estimates. Univariate analyses of the association between the earlier mentioned clinical and radiological variables, and case fatality at 30 days and 1 year after bleeding were calculated using chi-square statistics. Multivariate analyses of independent predictors of mortality were performed with the aid of multiple logistic regression at 30 days after ictus and Cox regression analysis for the entire 1-year follow-up period. A probability value of less than 0.05 was considered statistically significant.

**Results**

There were 341 patients diagnosed with primary ICH. The median patient age was 74 years and 44% of patients were female. The most deaths occurred during the 1st month after the hemorrhage. Thus, 61 (18%, 95% CI, 14–23%) were dead at 2 days, 124 (36%, 95% CI 30–43%) at 30 days, and 162 (47%, 95% CI 40–55%) at 1 year. Survival curves for 1 year after hemorrhage calculated using Kaplan–Meier analysis for male and female patients are shown in Fig. 1. As indicated by the diagram, female patients had a significantly higher mortality rate (log-rank test statistic 5.9, $p = 0.015$). Twenty-six patients underwent surgical intervention with craniotomy and evacuation of the hematoma. At 30 days, the mortality rate among surgically treated patients was 31% (eight patients). Fifteen patients who underwent surgery had lobar hematomas with volumes ranging from 21 to 60 cm³, ten of whom were alive at 30 days. Four of seven patients harboring central hematomas measuring 10 to 160 cm³ were alive at 30 days, whereas all four patients with cerebellar hematomas measuring 7 to 21 cm³ were alive at 30 days. Due to the small number of cases, however, statistical analysis has not been performed.

**Univariate Analyses**

**Thirty-Day Mortality Rate Related to Hematoma Location and Volume and VE.** The 30-day mortality rate was significantly related to location of the hematoma (chi-square test, $p = 0.001$; Table 1). This was due to an 80% (12 of 15 patients) mortality rate among patients with a hematoma located in the brainstem, compared with a 39% rate (68 of 176 patients) in those with hematomas in the lobar region, 30% (36 of 121 patients) in the central area, and 28% (eight of 29 patients) for those with hematomas in the cerebellar region. There was no statistically significant difference in mortality rates among those with hematomas located in the lobar, central, or cerebellar region ($p = 0.2$). A larger volume hematoma significantly increased the risk of death ($p < 0.001$); that is, 72% of patients with hematoma volumes larger than 60 cm³ were dead at 30 days, whereas only 19% were dead among those with hematomas smaller than 30 cm³. Extension of blood into the cerebral ventricles more than doubled the 30-day mortality rate ($p < 0.001$), with a 64% (50 of 78 patients) mortality rate in patients with...
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VE compared with 28% (74 of 263 patients) among those without.

Thirty-Day Mortality Related to Patient Age and Sex, Level of Consciousness, and Presence of Risk Factors. Increasing age had a significantly negative impact on survival, with 43% dead in the oldest age group (>75 years; 70 of 164 patients) compared with 22% (11 of 49 patients) between the ages of 0 and 54 years and 34% (43 of 128 patients) between 55 and 74 years (p = 0.001; Table 2). Patient sex affected 30-day mortality (p = 0.001), with a higher rate among female patients (42%, 64 of 152 female patients) compared with male patients (32%, 60 of 189 male patients). Reliable information regarding level of consciousness on admission was impossible to obtain in eight cases. Another 21 patients were already dead before arriving to the hospital. Among the remaining 312 patients, almost half (47%, 148 patients) were alert (RLS 2–3, GCS 8–13), and 21% (64 patients) were unconscious (RLS 1, GCS 14–15), and 32% (100 patients) were drowsy (RLS 4–8, GCS 3–7) on admission to the hospital. Thirty-day mortality was highly dependent on the patient’s initial level of consciousness (p < 0.001). Patients who arrived unconscious had a mortality rate of 83%, in contrast to 7% for alert and 34% for drowsy patients. Among the risk factors known to be present before the time of bleeding, heart disease was significantly associated with increased 30-day mortality (p < 0.001). Thus, of the 92 patients with known heart disease 47 (51%) were dead at 30 days, compared with 74 (30%) of 249 patients in whom heart disease was not present. Arterial hypertension, diabetes mellitus, or previous stroke did not affect fatality rate. Patients treated with oral anticoagulation agents exhibited a 52% (21 of 40 patients) 30-day mortality rate compared with 32% (98 of 301 patients) for those without treatment (p = 0.018). Antiplatelet therapy did not affect the mortality rate.

One-Year Mortality Rate Related to Hematoma Location and Volume and VE. Hematoma site and volume as well as VE were still highly significant determinants of mortality at 1 year (Table 1). Thus, brainstem hematomas carried an 80% (12 of 15 patients) fatality rate compared with 28 to 47% for patients with hematomas located elsewhere (p = 0.006). Hematomas larger than 60 cm³ were associated with a 77% (33 of 43 patients) mortality rate compared with 30% (61 of 206 patients) for those with hematomas smaller than 30 cm³ and 41% (19 of 46 patients) for those with a mass between 30 and 60 cm³ (p < 0.001). Ventricular extension of blood doubled the mortality rate to 73% (57 of 78 patients; p < 0.001).

One-Year Fatality Rate Related to Patient Age and Sex, Level of Consciousness, and Presence of Risk Factors. Similar to the 30-day results, patient age and sex, level of consciousness, and heart disease significantly affected mortality at 1 year (Table 2). Thus, 54% (88 of 164 patients) in the oldest age group (>75 years) were dead compared with 24% (12 of 49 patients) of those between the ages of 0 and 54 years and 34% (43 of 128 patients) of those between 55 and 74 years of age (p < 0.001). Again, female patients showed a higher fatality rate (52%, 79 of 152 female patients) compared with male patients (39%, 73 of 189 male patients; p = 0.014). For patients who were unconscious on admission, the mortality rate was 86% (55 of 64 patients), in contrast to 16% (24 of 148 patients) for alert and 46% (46 of 100 patients) for drowsy patients (p < 0.001). Heart disease was significantly associated with an increased 1-year mortality rate (p = 0.001). Of 92 patients with known heart disease 54 (59%) were dead, compared with 95 (39%) of 249 in whom...
heart disease was not present. The remaining factors were not associated with increased mortality rate.

**Multivariate Analyses**

**Thirty-Day Mortality.** Stepwise logistic regression analysis of all factors at Day 30, revealed that the level of consciousness on admission (drowsy: OR 5.2, p < 0.001; unconscious: OR 42, p < 0.001), hematoma volume larger than 60 cm³ (OR 3.6, p = 0.005), and a preictal history of heart disease (OR 2.4, p = 0.01) were independent predictors of the 30-day mortality rate (Table 3).

**One-Year Overall Mortality.** Multivariate Cox regression analysis that included the entire year after bleeding revealed that level of consciousness on admission (drowsy: HR 3.6, p < 0.001; unconscious: HR 15.2, p < 0.001), age older than 75 years (HR 3.3, p = 0.001), and hematoma site (brainstem compared with lobar: HR 5, p < 0.001) were independent predictors of 1-year mortality rates (Table 4).

**Discussion**

Researchers of only a few studies with large population-based designs have used multivariate statistical methods to determine independent predictors of death or poor outcome after primary ICH.4,8,14 and the data has been collected retrospectively. In the present prospective study, all diagnosed cases of primary ICH in a population of 1.14 million were registered during 1 year at 12 hospitals (including departments of pathology and forensic medicine). Because the CT scanning rate in patients with stroke is high in Sweden18 and only a very low proportion (3–5%) are treated in a setting other than a hospital,18 one can assume that very few cases of primary ICH went undetected in our study. It is possible, however, that some patients with stroke in the community were not examined at the hospitals and therefore not correctly diagnosed as having primary ICH. For instance, some elderly patients in the community with minor neurological deficits may not have undergone CT scanning, and there may have been fatal cases in which necropsy was not performed.

The overall case fatality rate was 18% at 2 days, 36% at 30 days, or 47% at 1 year after time of bleeding, which is in general agreement with data from previous population-based reports.19 The 30-day mortality rate has ranged from 35% in Australia,1 44% in the United States,3 and up to 50 to 51% in France,11 England,2 and Finland.4 Surprisingly, a recent population-based study conducted by Inagawa, et al.,20 showed a 30-day mortality rate after primary ICH of only 14%. The reasons for such a low case fatality rate are not clear, although it was suggested that the remarkable results were due to a more aggressive management policy and improvements in medical and surgical procedures.14 The importance of well-organized and specialized management of patients with ICH has been further supported by Rønning, et al.,21 who demonstrated significantly better survival curves for patients treated in dedicated stroke centers compared with conventional hospitals. In the present study, only 26 patients underwent surgical evacuation of the hematoma and their overall 30-day mortality rate was 31%. Interestingly, all patients who had undergone surgery for cerebellar hematomas were alive at 30 days. Statistical analysis was not meaningful, however, due to the low number of surgical cases.

**Predictors of 30-Day Mortality Rate**

The short-term (30-day) mortality rate was, as expected, mainly determined by initial level of consciousness and hematoma volume, which has been repeatedly reported previously.4,6,10,12,14–16,20–22,27 Indeed, previous authors have been able to predict 30-day mortality with high sensitivity and specificity by taking into account only hemorrhage volume and initial GCS score.4,27 A novel finding in the present study was that a preictal history of heart disease was an independent predictor of death at 30 days, with a more than twofold increase in mortality rate compared with those without history of heart disease. Interestingly, this effect was specific for heart disease and there was no trend toward any influence on mortality from, for example, previous stroke. As previously reported by Juvela,23 hypertension, diabetes mellitus, anticoagulant therapy, or antiplatelet therapy did not influence short- or long-term mortality. The results thus suggest that information regarding previous heart disease should always be obtained during the acute situation when deciding on optimal management of an individual patient. To our knowledge, an independent influence of

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**TABLE 3**

Independent predictors of 30-day mortality rate according to stepwise logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>level of consciousness (GCS score)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>alert (14–15)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>drowsy (8–13)</td>
<td>5.2</td>
<td>2.3–11.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>comatose (3–7)</td>
<td>42</td>
<td>15.6–113.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>age group (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–60</td>
<td>1.3</td>
<td>0.6–3.2</td>
<td>0.48</td>
</tr>
<tr>
<td>&gt;60</td>
<td>3.6</td>
<td>1.5–9</td>
<td>0.005</td>
</tr>
<tr>
<td>heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>present</td>
<td>2.4</td>
<td>1.2–5</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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**TABLE 4**

Independent predictors of mortality rate during the 1-year follow up according to Cox regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
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<tr>
<td>level of consciousness (GCS score)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>alert (14–15)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>drowsy (8–13)</td>
<td>3.6</td>
<td>2.1–6.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>comatose (3–7)</td>
<td>15.2</td>
<td>8.8–26.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>age group (yrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–54</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55–74</td>
<td>1.9</td>
<td>0.9–3.9</td>
<td>0.08</td>
</tr>
<tr>
<td>≥75</td>
<td>3.3</td>
<td>1.6–6.9</td>
<td>0.001</td>
</tr>
<tr>
<td>hematoma site</td>
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<td></td>
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</tr>
<tr>
<td>lobar</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>central</td>
<td>1.2</td>
<td>0.8–1.8</td>
<td>0.49</td>
</tr>
<tr>
<td>cerebellar</td>
<td>0.4</td>
<td>0.2–1.2</td>
<td>0.12</td>
</tr>
<tr>
<td>brainstem</td>
<td>5</td>
<td>2.1–11.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Predictors of death in patients with primary ICH

Precrual heart disease on mortality after primary ICH has never been reported and therefore our finding must be confirmed by other study data. Ventricular extension of blood was not an independent prognostic factor in the present study. The literature is inconsistent regarding VE; that is, some authors have demonstrated a clear association between VE and mortality rate by using multivariate analysis, whereas others have not.

We have previously reported on the prevalence of different risk factors for various hematoma locations after primary ICH. There was no statistically significant difference in the prevalence of any of the potential risk factors such as patient sex, hypertension, diabetes mellitus, prior stroke, heart disease, or anticoagulant or antiplatelet therapy. Thus, a precrual history of heart disease was documented in 30% of patients with hematomas in the lobar region, 26% of those with central hematomas, 27% of those with brainstem hematomas, and 22% of those with hematomas in the cerebellum. This further supports the finding that preexisting heart disease is an independent predictor of death after primary ICH.

Predictors of 1-Year Mortality Rate

During the entire 1-year follow up the strongest independent predictor of death was the patient’s initial level of consciousness; again, we stress this factor as the most important to consider in making decisions and prognoses within the clinical setting. Although age did not independently influence case fatality at 30 days, a patient age older than 74 years was an independent predictor of mortality within 1 year. A similar correlation between age and long-term (1 or 2 years), but not short-term mortality rates has been reported previously. It has been suggested that early death is most directly related to hemorrhage severity (for example, volume), whereas long-term morbidity and mortality rates are determined more by a patient’s general condition and immobilization complications with increasing age.

The third independent predictor of mortality during the 1st year after primary ICH was hematoma location and, in fact, patients with brainstem hemorrhages had the worst outcome, with no less than 80% dying. Data from only a few studies have demonstrated hematoma location as an independent prognostic factor with the aid of multivariate analysis. Subcortical hemorrhages have been associated with a better prognosis than combined ganglionic or pontine hemorrhages.

Conclusions

The present prospective study provides insight concerning predictors of death after primary ICH given a population-based perspective. Knowledge of such prognostic factors is imperative in clinical decision making for an individual patient and in designing trials and new treatment strategies for patients with primary ICH. Apart from a patient’s level of consciousness on admission, hematoma volume and location, and patient age, which have been previously reported as independent predictors of death in more selected patient, the present study also identified a history of heart disease as a significant determinant of the 30-day mortality rate.

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