Simultaneous Multiple Intracerebral Hemorrhages (SMICH)

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Background and Purpose—Simultaneous multiple intracerebral hemorrhages (SMICHs) are uncommon. Few single-center studies have analyzed characteristics and outcome of SMICH. We analyzed clinical characteristics and outcome of SMICH patients from 2 comprehensive stroke centers.

Methods—Baseline imaging from consecutive intracerebral hemorrhage (ICH) patients (n=1552) from Helsinki ICH study and Royal Melbourne Hospital ICH study was screened for SMICH. ICH pathogenesis was classified according to the structural lesion, medication, amyloid angiopathy, systemic/other disease, hypertension, undetermined classification system (SMASH-U). ICH caused by trauma, tumor, and aneurysmal rupture was excluded. Baseline clinical and radiological characteristics and 90-day mortality were compared between SMICH and single ICH patients. Association of SMICH with 90-day mortality was assessed in multivariable logistic regression models adjusted for predictors of ICH outcome.

Results—Of 1452 patients, 85 (5.9%) were classified as SMICH. SMICH were more often female (58% versus 42%; P=0.004), had lower baseline Glasgow Coma Scale (12 versus 14; P=0.008), and more frequent lobar location (59% versus 34%; P<0.001) compared with single ICH. The SMASH-U pathogenesis of SMICH patients was less often hypertensive (20% versus 37%; P=0.001), more often systemic coagulopathy (12% versus 3%; P<0.001), and trended toward more cerebral amyloid angiopathy (32% versus 23%; P=0.071). SMICH was not associated with 90-day mortality univariate (37% versus 35%; P=0.610), multivariable (odds ratio, 0.783; 95% confidence interval, 0.401–1.529; P=0.0473), or propensity score–matched analyses (odds ratio, 0.760; 95% confidence interval, 0.352–1.638; P=0.473).

Conclusions—SMICH occurs in ≈1 in 20 ICH, more commonly with lobar located hematomas and systemic coagulopathy with less hypertensive angiopathy. The associated mortality is similar to single ICH. Given varied etiologies, SMICH management should target the underlying pathology. (Stroke. 2017;48:0000–0000. DOI: 10.1161/STROKEAHA.116.015186.)

Key Words: cerebral hemorrhage ■ mortality ■ multiple ■ pathogenesis

Outcome after intracerebral hemorrhage (ICH) is often poor and relates to the pathogenesis and volume of the hematoma.1,2 Treatment strategies are limited to blood pressure control and stroke unit care.3 Simultaneous multiple ICHs (SMICHs) have been noted on baseline imaging in several small case series (total n=323; Table 1) with a prevalence of ≈0.8% to 5.7% of patients4–12 and seem to be associated with worse outcome compared with patients with single ICH.13,14 However, previous series reported mortality unadjusted for baseline imbalances in clinical and radiological characteristics. Reported pathogenesis of SMICH are also controversial and biased by exclusion of patients with cerebral amyloid angiopathy1 and nonprimary ICH secondary to anticoagulation,4 cerebral venous sinus thrombosis,5,6 and structural vascular causes.7,10

In this study, we describe the clinical and radiological characteristics, pathogenesis, and 90-day mortality of patients with SMICH treated across 2 comprehensive stroke centers.

Methods

Consecutive patients from the Helsinki ICH study2 and the Royal Melbourne Hospital (RMH) ICH study13 were screened for the presence of SMICH. The Helsinki ICH study is a retrospective analysis

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of consecutive ICH patients admitted to Helsinki University Hospital between January 2005 and March 2010. The RMH ICH study included consecutive ICH patients admitted between October 2007 and January 2012, with one report published on impact of warfarin on hematoma location and volume. The diagnosis of ICH in both studies was based on the World Health Organization definition of stroke requiring rapidly developing clinical signs of focal or global disturbance of cerebral function leading to death or lasting >24 hours with no apparent cause other than a vascular one, always combining with the imaging finding of ICH. In both studies, cerebral hemorrhage caused by trauma, tumor, hemorrhagic transformation of cerebral infarction with or without thrombolysis, or primary subarachnoid hemorrhage were excluded. Traumatic ICH was diagnosed as per routine clinical practice based on all available history, clinical findings, and imaging findings. Coexisting acute subdural or epidural hematomas or coup-countercoup contusions would result in a diagnosis of traumatic ICH.

We defined SMICH as 2 or more discrete, noncontiguous acute intraparenchymal hematomas on initial diagnostic computed tomography. For the present analysis, we additionally excluded patients without available baseline planimetric data because of unavailable baseline computed tomographic images or films unsuitable for computerized imaging analysis performed at another institution, pure ventricular hemorrhage, and where patients presented on >1 occasion only the first episode was included. T.Y.W. screened all patients for SMICH. N.Y. then reviewed the images of potential patients. Ineligible patients were excluded by mutual agreement. In the case of disagreement, A.M. was consulted for a final decision regarding inclusion.

Images at both centers were acquired using multislice computed tomographic scanners (Helsinki, Siemens Somatom Plus 4, Siemens Medical, Germany, and GE Medical Systems LightSpeed Ultra/LightSpeed VCT, GE Healthcare, United States; RMH, Siemens Somatom Sensation, Siemens Medical, Germany). Hematoma volume was calculated using semiautomated planimetry, using Analyze 12.0 (Biomedical Imaging Resource; Mayo Clinic). Hemorrhage was classified lobar if the ICH involved cortical surface or the juxtacortical region of the frontal, parietal, temporal, or occipital lobes; deep when located within the deep structures (caudate, lentiform, thalamus, internal, or external capsule). In SMICH, the hematoma with the largest volume was used for location and etiologic determination. The total volume of all the hematomas in SMICH was used for other analyses. Etiologic classification for the cause of ICH was graded according to the SMASH-U classification. The total volume of all the hematomas was considered when ICH could not be classified into other categories. Other systemic causes include hepatic cirrhosis, systemic myeloproliferative disease, infection, drug-induced coagulopathy. Cerebral venous sinus thrombosis was considered a cause if the thrombosis caused a primary bleed, not if there was first an ischemic stroke and then a hemorrhagic transformation of the same. Cerebral venography was performed in younger patients, cases with predisposing factors, and those with suspicious imaging, such as ragged cortical ICH. Medication-related ICH was classified in a patient on warfarin with international normalized ratio ≥2.0, novel oral anticoagulants within 3 days, full-dose heparin, or systemic thrombolysis for nonstroke indication. Sole antiplatelet use was not considered medication-related pathogenesis. Cerebral amyloid angiopathy was confirmed in patients ≥55 years of age with a lobar, cortical, or subcortical hematoma. Hypertensive angiopathy was considered in patients with pre-ICH hypertension with deep or infratentorial hematoma. Finally, undetermined pathogenesis was considered when ICH could not be classified into other categories.

Table 1: Summary of Reported Studies in Patients With Simultaneous Intracerebral Hemorrhages (SMICHS)

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>SMICH/Single ICH (n/total, %)</th>
<th>Country</th>
<th>SMICH Pathogenesis</th>
<th>Age</th>
<th>Total ICH Volume, mL</th>
<th>SMICH Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weisberg, 1981</td>
<td>12/600 (2%)</td>
<td>United States</td>
<td>Undetermined: 12 (100%)</td>
<td>NR</td>
<td>NR</td>
<td>3/12 (33%), follow-up time not defined</td>
</tr>
<tr>
<td>Mauricio et al, 2001</td>
<td>4/142 (2.8%)</td>
<td>Argentina</td>
<td>Hypertension: 4 (100%)</td>
<td>55</td>
<td>NR</td>
<td>0/4 (0%) at 3 mo</td>
</tr>
<tr>
<td>Yen et al, 2005</td>
<td>10/1304 (0.8%)</td>
<td>Taiwan</td>
<td>Hypertension: 10 (100%)</td>
<td>61</td>
<td>NR</td>
<td>6/10 (60%) at 6 mo</td>
</tr>
<tr>
<td>Sorimachi et al, 2007</td>
<td>9/190 (4.7%)</td>
<td>Japan</td>
<td>Hypertension: 9 (100%)</td>
<td>69</td>
<td>11</td>
<td>NR</td>
</tr>
<tr>
<td>Stermer et al, 2010</td>
<td>29/522 (5.6%)</td>
<td>United States</td>
<td>CAA: 3 (10.3%); hypertension: 11 (37.9%); secondary ICH: 15 (51.7%)</td>
<td>59</td>
<td>7</td>
<td>11/79 (24%)</td>
</tr>
<tr>
<td>Takeuchi et al, 2011</td>
<td>20/2198 (0.9%)</td>
<td>Japan</td>
<td>Hypertension (100%)</td>
<td>61</td>
<td>28</td>
<td>9/20 (45%) at discharge</td>
</tr>
<tr>
<td>Laiwattana et al, 2014</td>
<td>105/352 (3.6%)</td>
<td>Mixed</td>
<td>NR</td>
<td>61</td>
<td>NR</td>
<td>46/105 (44%), follow-up time not defined</td>
</tr>
<tr>
<td>Yeh et al, 2014</td>
<td>136/3785 (3.6%)</td>
<td>Taiwan</td>
<td>CAA: 14 (10.3%); hypertension: 14 (10.3%); structural vascular: 3 (2.2%); medication: 16 (11.8%); systemic: 70 (51.5%); undefined: 19 (13.9%)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Chen et al, 2016</td>
<td>32/562 (5.7%)</td>
<td>France</td>
<td>CAA: 8 (25.0%); deep vessel vasculopathy: 5 (15.6%); undefined: 19 (59.4%)</td>
<td>69</td>
<td>31</td>
<td>25/32 (78%) at 6 mo</td>
</tr>
<tr>
<td>Current study</td>
<td>85/1452 (5.9%)</td>
<td>Australia, Finland</td>
<td>CAA: 27 (31.7%); hypertension: 17 (20.0%); structural vascular: 5 (5.9%); medication: 14 (16.5%); systemic: 10 (11.8%); undefined: 12 (14.1%)</td>
<td>74</td>
<td>22</td>
<td>31/83 (37%) at 3 mo</td>
</tr>
</tbody>
</table>

CAA indicates cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; and NR, not reported.

†This systematic review consists of publications in both English and non-English journals and contains both case reports and case series including 34 patients from series by Mauricio et al, 2001 Yen et al, 2005 and Takeuchi et al, 2011.
or investigations >90 days from ICH. If not, we contacted the unit they were transferred to. If no data on vital status were available, the patients were considered lost to follow-up. In Helsinki, we additionally had comprehensive vital status data from the national death registry kept by Statistics Finland.

Institutional approval for the observational registry study was granted from relevant authorities in Helsinki and Melbourne with no requirement for patient consent, allowing for all consecutive patients to be included.

### Statistical Analysis

Data are reported as median with interquartile range or n (%) and analyzed with Mann-Whitney U test, Pearson χ², or Fisher exact tests as appropriate. Association with 90-day mortality was assessed in a multivariable logistic regression model adjusted for baseline Glasgow Coma Scale (GCS), baseline ICH volume, age, male sex, previous warfarin use, ventricular extension, and infratentorial location. There were no missing data for the covariates included in the logistic regression model; therefore, only patients with missing outcome data were excluded from this analysis. Testing for collinearity demonstrated no multicollinearity between the variables with all variance inflation factors <1.5. To validate the findings from the logistic regression model, the primary analysis was repeated using matched controls. We used propensity score matching with the nearest neighbor method to match SMICH patients and single ICH patients 1:2 on baseline demographic variables (age and male sex), medication use (warfarin, antiplatelet agent, antihypertensive medications, statins), medical history (atrial fibrillation, ischemic heart disease, dyslipidemia, diabetes mellitus, previous ICH, or ischemic stroke), radiological characteristics (ICH volume and ICH location), and pathogenesis. Patients with missing baseline and outcome information were included in the univariate comparison between SMICH and single ICH patients but excluded from the propensity score matching analysis. We used R 3.1.0 and the MatchIt package¹⁶ for propensity score matching and SPSS 23 (IBM, Armonk, NY) for other statistical analyses. A 2-sided P value <0.05 was considered statistically significant.

### Results

From the pool of 1552 patients (Helsinki n=1013, RMH n=539), 100 (6.4%) were excluded because of lack of appropriate baseline planimetric data (70), recurrent admission (19), and pure intraventricular hemorrhage (11; Figure). Of the remaining 1452 patients, 85 (overall 5.9%; Helsinki 47/978 [4.8%], RMH 38/474 [8.0%]) patients were classified with SMICH according to the predefined criteria.

### SMICH Location and Laterality

There were 197 discrete hematomas in the SMICH patients, and 36 (42%) patients had hematomas located bilaterally. Most patients had 2 hematomas with 14 (16%) patients having 3 or more hematomas on baseline imaging (Table 2). Most of the hematomas were lobar (124, 63%) in location, whereas 54 (27%) hematomas were deep, with 6 (3%) hematomas in the brain stem and 13 (7%) in the cerebellum. None of the 6 patients with simultaneous brain stem and supratentorial deep or lobar hemorrhage had duret brain stem hemorrhage caused by uncal herniation. Fourteen (16%; 6/47 [13%] Helsinki, 8/38 [21%] RMH) SMICH patients had a secondary hemorrhage <5 mm in diameter. Representative images of SMICH are presented in the Figure in the online-only Data Supplement.

### Baseline Clinical Characteristics and Pathogenesis

Patients with SMICH were more often female (58% versus 42%; P=0.004) and had lower baseline GCS (12 versus 14; P=0.008) when compared with patients with single ICH. Other baseline clinical risk factors did not differ (Table 3). In terms of pathogenesis, SMICH patients had more cerebral amyloid angiopathy (32% versus 23%; P=0.071), medication-related ICH (16% versus 14%; P=0.433), systemic defined pathogenesis (12% versus 3%; P<0.001), and structural vascular lesions (6% versus 4%; P=0.418), with less hypertensive angiopathy (20% versus 37%; P=0.001) and undefined causes (14% versus 18%; P=0.324; Table 3). Of the 10 (12%) patients with systemic defined pathogenesis, 4 were attributed to liver cirrhosis, 3 from thrombocytopenia, and 3 had cerebral venous sinus thrombosis. Cerebral venous sinus thrombosis was diagnosed in 2 (0.1%) single ICH patients. Of the medication-related ICH group, warfarin was the cause in 9 of 14 (64%) SMICH and 169 of 184 (92%) single ICH patients, and one of the other medications in 5 of 14 (36%) SMICH and 15 of 184 (8%) single ICH patients. All patients (n=5; 6%) with structural vascular abnormality had multiple cavernous venous malformations. Table in the online-only Data Supplement presents the univariate comparison between SMICH and single ICH patients according to pathogenesis. SMICH patients with cerebral amyloid angiopathy were older (79 versus 74; P=0.034) with lower admission GCS (11 versus 14; P=0.003), medication-related SMICH patients were more often female (63% versus 29%; P=0.021), with less warfarin use (64% versus 92%; P=0.007), and more exposure to antiplatelet agents (50% versus 17%; P=0.007). No other differences were found within these subgroups (Table in the online-only Data Supplement).

### Figure

Study flow chart. ICH indicates intracerebral hemorrhage; IVH, intraventricular hemorrhage; RMH, Royal Melbourne Hospital; and SMICH, simultaneous intracerebral hemorrhage.
Table 2. Location of the Larger Hematomas* in Patients With Simultaneous Multiple Intracerebral Hemorrhages

<table>
<thead>
<tr>
<th>Location of Larger Hematomas</th>
<th>Lobar</th>
<th>Deep</th>
<th>Brain Stem</th>
<th>Cerebellum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobar</td>
<td>38</td>
<td>18</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Deep</td>
<td>…</td>
<td>12</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Brain stem</td>
<td>…</td>
<td>…</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>…</td>
<td>…</td>
<td>…</td>
<td>1</td>
</tr>
</tbody>
</table>

*In 14 (16%) patients with >2 hematomas, the largest 2 hematomas were used to determine location.

Radiological Variables

The dominant hematoma location (Table 3) differed between SMICH and single ICH patients with higher proportion of lobar hematomas (59% versus 34%; P<0.001) and less deeply located (34% versus 52%; P=0.001) or infratentorial ICH (7% versus 14%; P=0.073). The groups did not differ in baseline ICH volume (22 versus 15 mL; P=0.225) or ventricular extension (35% versus 42%; P=0.205). When analyzed by pathogenesis, medication-related SMICH had more lobar (79% versus 28%; P<0.001) and less deep (14% versus 56%; P=0.004) hematomas when compared with single ICH patients, but the groups did not otherwise differ (Table in the online-only Data Supplement).

Mortality

Mortality data were available in 1421 (98%) patients. Of the 31 (2/85 [2%] SMICH and 29/1367 [2%] single ICH) patients with missing mortality data, 9 were from Helsinki and 22 from RMH. There was no difference in mortality at 90 days between patients with SMICH and single ICH (37% versus 35%; P=0.610; Table 3). In medication-related ICH, SMICH had more lobar (79% versus 28%; P<0.001) and less deep (14% versus 56%; P=0.004) hematomas when compared with single ICH patients, but there were no other differences in mortality by etiologic subgroups (Table in the online-only Data Supplement).

Factors associated with 90-day mortality in SMICH patients on univariate analysis were lower baseline GCS (7 versus 14; P<0.001), larger baseline ICH volume (59 versus 12 mL; P<0.001), and presence of ventricular extension (55% versus 25%; P<0.001).

After excluding 31 patients (2 with SMICH) with missing mortality data, 1421 patients were included in the multivariable model with unmatched controls (Table 4). The presence of SMICH was associated with less 90-day mortality (odds ratio, 0.783; 95% confidence interval, 0.401–1.529; P=0.473) although this was not statistically significant. After excluding 52 (3.6%; 4 with SMICH) patients with missing baseline and outcome variables, propensity score matching resulted in 243 patients with balanced baseline characteristics. In the postmatching logistic regression analysis, SMICH was also not associated with 90-day mortality (odds ratio, 0.760; 95% confidence interval, 0.352–1.638; P=0.484; Table 4). In the post hoc analysis, the presence of SMICH was also not associated with 90-day mortality after excluding 14 SMICH patients with small secondary hemorrhage (<5 mm in diameter) in both the unmatched (n=1407; odds ratio, 0.733; 95% confidence interval, 0.351–1.531; P=0.408) and the propensity matched (n=201; odds ratio, 1.330; 95% confidence interval, 0.572–3.090; P=0.507) logistic regression analyses.

Discussion

In this dual-center study of SMICH patients, we derived several points of interest. First, in our large series of consecutive patients, we found a relatively high proportion of SMICH patients (5.9%) compared with previous literature.
Second, mortality did not differ between SMICH patients and those with single ICH, which contrasts with previous reports that did not adjust for baseline variables.1,4,10 Finally, we have detailed the etiologic associations of patients with SMICH.

SMICH has been considered uncommon in ICH (Table 1), but 4 of 6 hospital-based studies in the past decade have reported SMICH presenting in between 4.7% and 5.9% or ≈1 in every 20 of all ICH patients. In 14 (16%) SMICH patients in this study, the secondary hematoma was <5 mm in diameter; therefore, thicker computed tomographic image slices such as 13 mm slices in the study by Weisberg8 may potentially have missed patients with smaller simultaneous hemorrhages.

Mortality in SMICH has been reported to range from 0% to 78% (Table 1) and is likely to be influenced by the pathogenesis and location of the SMICH. Laiwattana et al11 systematically reviewed 105 patients with primary SMICH by combining published case reports and case series and examined the association of location of SMICH and outcome. The authors found that deep SMICH had the highest mortality rate (27/54; 50%) compared with SMICH located in bilateral lobar or cerebellar regions (0/2; 0%) or nonbilateral SMICH (19/49; 37%).11

The SMICH mortality rate of 37% in our study is similar to reports by Weisberg4 (33%) and Stemer et al4 (24%) but lower than that reported by Chen et al10 (78%), Yen et al8 (60%), and Takeuchi et al3 (45%). The higher mortality rate in other studies4,5,10 is likely accounted for by hematoma location and hematoma volume, which are both important mediators of ICH outcome.1,3,13 Yen et al4 and Takeuchi et al3 included only hypertensive SMICH with almost all hematomas located in the deep brain region, whereas 44% of the subjects in the study by Chen et al10 had deep hematomas compared with 27% in our study. The total hematoma volume in studies by Takeuchi et al (28 mL) and Chen et al (31 mL) was higher than our study (22 mL), whereas hematoma volume was not reported in the study by Yen et al (Table 1).

Etiologic consideration after ICH is important because it mediates outcome in ICH patients in both European and Asian patients.2,12 We demonstrated using the SMASH-U classification system2 that the pathogenesis in SMICH is also widely distributed similar to that in patients with single ICH (Table 3), with hypertensive angiopathy and cerebral amyloid angiopathy accounting for 52% of all SMICH. This finding is consistent with a recent report by Chen et al,10 where cerebral amyloid angiopathy and deep vessel vasculopathy accounted for 41% of their SMICH patients. This is in contrast to the study by Yeh et al12, who also classified Taiwanese SMICH patients using the SMASH-U system. The authors reported 51% of SMICH were because of systemic causes, whereas hypertension accounted only for 10% of their cohort likely reflecting ethnic differences for ICH pathogenesis. Future SMICH studies need to standardize ICH classification and include all nontraumatic, nontumor-related ICH patients.

The strengths of our study are the relatively large sample with well-characterized baseline data and 90-day mortality, allowing us to assess the effect of SMICH on mortality after adjustment for known predictors of ICH outcome.

This study has several limitations. First, it is retrospective in nature and is subject to selection bias. We minimized bias by prespecifying objective criteria to define SMICH, and potential cases were screened by neurologists experienced in stroke imaging. Furthermore, only 6.4% of consecutive ICH patients were excluded. Second, as we included centers with patients of predominantly European descent, our results may not be generalizable to patients from other ethnic backgrounds. Third, magnetic resonance imaging was not routinely performed at the study centers during the study period, and only 14 (16%) SMICH patients had follow-up magnetic resonance imaging performed. Consequently, the presence and location of microhemorrhages could not be assessed to assist in etiologic determination. Finally, we did not have functional outcome assessment for our study patients and therefore could not assess the effect of SMICH on functional recovery. However, mortality is a robust outcome measure in ICH.

**Conclusions**

SMICH occurs in ≈1 in 20 ICH patients with higher proportion of lobar hematomas and systemic coagulopathy and less

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**Table 4. Multivariable Logistic Regression Model for Factors Associated With 90-Day Mortality**

<table>
<thead>
<tr>
<th></th>
<th>Total Cohort (n=1421)*</th>
<th>Propensity Score Matching (n=243)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>SMICH</td>
<td>0.783 (0.401–1.529)</td>
<td>0.473</td>
</tr>
<tr>
<td>Age</td>
<td>1.054 (1.039–1.068)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.282 (0.935–1.759)</td>
<td>0.123</td>
</tr>
<tr>
<td>Baseline GCS</td>
<td>0.757 (0.725–0.792)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline ICH volume</td>
<td>1.025 (1.020–1.031)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous warfarin</td>
<td>1.703 (1.118–2.594)</td>
<td>0.013</td>
</tr>
<tr>
<td>Ventricular extension</td>
<td>3.130 (2.301–4.257)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Infratentorial location</td>
<td>1.734 (1.108–2.713)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; GCS, Glasgow Coma Scale; ICH, intracerebral hemorrhage; OR, odds ratio; and SMICH, simultaneous multiple intracerebral hemorrhages.

*Thirty-one patients with missing mortality data were excluded from the unmatched analysis.
often related to hypertensive angiopathy. The presence of SMICH was not associated with excess mortality. Given the varied etiologies, the management of SMICH should therefore target the underlying pathology.

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**Disclosures**

None.

**References**

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Simultaneous multiple intracerebral hemorrhages (SMICH)

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Supplementary figure. Representative images of simultaneous intracerebral hemorrhages (SMICH).
**Supplementary table.** Baseline differences between SMICH and single ICH patients grouped according to etiology.

<table>
<thead>
<tr>
<th></th>
<th>Cerebral amyloid angiopathy</th>
<th>Hypertensive angiopathy</th>
<th>Medication related</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SMICH n=27</td>
<td>Single ICH n=317</td>
<td>p</td>
</tr>
<tr>
<td>Age, years</td>
<td>79 (73-84)</td>
<td>74 (74-81)</td>
<td>0.034</td>
</tr>
<tr>
<td>Male sex</td>
<td>9 (33%)</td>
<td>158 (50%)</td>
<td>0.112*</td>
</tr>
<tr>
<td>GCS</td>
<td>11 (10-14)</td>
<td>14 (11-15)</td>
<td>0.003</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0</td>
<td>8 (2.5%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>11 (41%)</td>
<td>114 (36%)</td>
<td>0.620</td>
</tr>
<tr>
<td>Statin</td>
<td>7 (26%)</td>
<td>78 (25%)</td>
<td>0.820*</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4 (15%)</td>
<td>21 (7%)</td>
<td>0.121*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18 (67%)</td>
<td>188 (60%)</td>
<td>0.454</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (11%)</td>
<td>45 (14%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>0</td>
<td>37 (12%)</td>
<td>0.096*</td>
</tr>
<tr>
<td>Previous ischemic stroke</td>
<td>1 (4%)</td>
<td>25 (8%)</td>
<td>0.707*</td>
</tr>
<tr>
<td>Previous ICH</td>
<td>3 (11%)</td>
<td>24 (8%)</td>
<td>0.457*</td>
</tr>
<tr>
<td>90-day mortality</td>
<td>9 (36%)</td>
<td>92 (30%)</td>
<td>0.652</td>
</tr>
<tr>
<td>Baseline ICH volume, mL</td>
<td>41 (22-81)</td>
<td>31 (10-62)</td>
<td>0.131</td>
</tr>
<tr>
<td>Ventricular extension</td>
<td>9 (33%)</td>
<td>81 (26%)</td>
<td>0.369</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobar</td>
<td>27 (100%)</td>
<td>316 (100%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Deep</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infratentorial</td>
<td>0</td>
<td>1 (0%)</td>
<td>1.000*</td>
</tr>
</tbody>
</table>

*p* Fisher exact test.

GCS indicates Glasgow Coma Scale; ICH, intracerebral hemorrhage; SMICH, simultaneous multiple intracerebral hemorrhages
### Supplementary table (continued). Baseline differences between SMICH and single ICH patients grouped according to etiology

<table>
<thead>
<tr>
<th></th>
<th>Systemic defined etiologies</th>
<th>Structural vascular abnormality</th>
<th>Undefined</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SMICH</td>
<td>Single ICH</td>
<td>SMICH</td>
</tr>
<tr>
<td></td>
<td>n=10</td>
<td>n=45</td>
<td>n=5</td>
</tr>
<tr>
<td>Age, years</td>
<td>62 (42-74)</td>
<td>57 (46-64)</td>
<td>0.432</td>
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<tr>
<td>Male sex</td>
<td>6 (60%)</td>
<td>31 (69%)</td>
<td>0.713*</td>
</tr>
<tr>
<td>GCS</td>
<td>14 (3-15)</td>
<td>15 (10-15)</td>
<td>0.239</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0</td>
<td>1 (2%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>1 (10%)</td>
<td>7 (16%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Statin</td>
<td>1 (10%)</td>
<td>2 (4%)</td>
<td>0.459*</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1 (10%)</td>
<td>3 (7%)</td>
<td>0.563</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (40%)</td>
<td>20 (44%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1 (10%)</td>
<td>2 (4%)</td>
<td>0.459*</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (10%)</td>
<td>7 (16%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>0</td>
<td>1 (2%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Previous ischemic stroke</td>
<td>1 (10%)</td>
<td>3 (7%)</td>
<td>0.563</td>
</tr>
<tr>
<td>Previous ICH</td>
<td>0</td>
<td>2 (4%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>90-day mortality</td>
<td>5 (50%)</td>
<td>16 (36%)</td>
<td>0.486</td>
</tr>
<tr>
<td>Baseline ICH volume, mL</td>
<td>9 (3-55)</td>
<td>19 (4-44)</td>
<td>0.570</td>
</tr>
<tr>
<td>Ventricular extension</td>
<td>3 (30%)</td>
<td>16 (36%)</td>
<td>1.000*</td>
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<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobar</td>
<td>7 (70%)</td>
<td>21 (47%)</td>
<td>0.295*</td>
</tr>
<tr>
<td>Deep</td>
<td>2 (20%)</td>
<td>16 (36%)</td>
<td>0.470*</td>
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<tr>
<td>Infratentorial location</td>
<td>1 (10%)</td>
<td>8 (18%)</td>
<td>1.000*</td>
</tr>
</tbody>
</table>

*Fisher exact test.
GCS indicates Glasgow Coma Scale; ICH, intracerebral hemorrhage; SMICH, simultaneous multiple intracerebral hemorrhages
Supplementary figure. Representative images of simultaneous intracerebral hemorrhages (SMICH).

Representative samples of SMICH with arrows indicating very small hematomas, demonstrating A) lobar, B-C) lobar and deep, D) lobar and brainstem, E-F) lobar and cerebellar, G) lobar, deep and brainstem, H) deep and cerebellar, I-J) lobar, K) cerebellar, L) deep, M-N) deep and cerebellar patterns of SMICH.
Supplementary figure (continued)