Magnitude of Hematoma Volume Measurement Error in Intracerebral Hemorrhage

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Background and Purpose—Limiting intracerebral hemorrhage (ICH) and intraventricular hemorrhage (IVH) expansion is a common target for acute ICH studies and, therefore, accurate measurement of hematoma volumes is required. We investigated the amount of hematoma volume difference between computed tomography scans that can be considered as measurement error.

Methods—Five raters performed baseline (<6 hours) and 24-hour total hematoma (ICH+IVH) computer-assisted volumetric analysis from 40 selected ICH patients from the Predicting Hematoma Growth and Outcome in Intracerebral Hemorrhage Using Contrast Bolus CT (PREDICT) study cohort twice. Estimates of intrarater and interrater reliability are expressed as intraclass correlation coefficients and minimum detectable difference (MDD).

Results—Total hematoma volumetric analyses had excellent intra- and interrater agreements (intraclass correlation coefficients 0.994 and 0.992, respectively). MDD for intra- and interrater volumes was 6.68 and 7.72 mL, respectively, and were higher the larger total hematoma volume was and in patients with subarachnoid hemorrhage or IVH. MDD for total hematoma volume measurement of 10.4 mL was found in patients with largest hematoma volumes. In patients with subarachnoid hemorrhage or IVH, MDD for total hematoma volume was 10.3 and 10.4 mL, respectively. In patients without IVH, MDD for intra- and interrater pure ICH volumes were 3.82 and 5.83 mL, respectively.

Conclusions—A threshold higher than 10.4 mL seems to be reliable to avoid error of total hematoma volume measurement in a broad range of patients. An absolute ICH volume increase of >6 mL, commonly used as outcome in ICH studies, seems well above MDD and, therefore, could be used to reliably detect ICH expansion. (Stroke. 2016;47:1124-1126. DOI: 10.1161/STROKEAHA.115.012170.)

Key Words: computed tomography ■ intracerebral hemorrhage ■ measurement ■ planimetry ■ subarachnoid hemorrhage

Intracerebral hemorrhage (ICH) and intraventricular hemorrhage (IVH) expansion are independent determinants of poor outcomes and, therefore, are a common target for acute ICH studies. Given that hematoma expansion is commonly used as outcome in ICH studies, accurate measurement of hematoma volumes is of utmost importance for the validity of such studies. The measurement of hematoma volume, however, is examiner-dependent, and some of the hematoma volume difference between baseline and follow-up computed tomography (CT) scans may be because of measurement error. Further, this error may increase with the hematoma volume size.

The knowledge of what amount of the hematoma volume difference between CT scans can be considered as measurement error becomes critical when choosing a dichotomous expansion definition for a given ICH study. In this study, we aimed to investigate the minimum detectable difference (MDD) for total hematoma (ICH+IVH) volume in a cohort of ICH patients from the Predicting Hematoma Growth and Outcome in Intracerebral Hemorrhage Using Contrast Bolus CT (PREDICT) study.

Methods

Study Population
Forty acute (<6 hours) ICH patients from the PREDICT study were included. Cases were selected based on the previously calculated
baseline total hematoma volume performed by a stroke neurologist (A.M. Demchuk) using Quantomo computerized planimetry software.\textsuperscript{4,5} Ten consecutive scans of each of the following categories were selected by a research nurse (T. Stewart): ≤10 mL, >10 to 30 mL, >30 to 50 mL, and >50 mL. Each group included patients from several sites (but no >4 of the same site per category), patients with different slice thickness (but no >2 of ≤3 mm per category), the same slice thickness through the hematoma in each patient, and with available baseline and follow-up CT scans.

**Image Analysis**

Five raters (D. Rodriguez-Luna and S. Subramaniam, stroke neurologists; >3 years of experience; E. Klourfeld, stroke fellow; 3 years of experience; and B.J. Diederichs and P. Jo, radiology residents, 2 years and ≤1 year of experience, respectively) measured baseline and follow-up total hematoma (ICH+IVH) volumes from the 40 selected CT scans twice, presented in a blinded, random fashion over 2 different reading sessions, separated by a minimum of 14 days.\textsuperscript{7} The presence of subarachnoid hemorrhage (SAH) and IVH was recorded.

**Statistical Analysis**

Estimates of interrater and intrarater reliability were calculated using a 2-way random-effects ANOVA and expressed as intraclass correlation coefficients (ICC).\textsuperscript{7} The MDD, defined as the change in volume between successive measurements that can be detected with 95% confidence intervals, was determined for total hematoma volume for all patients and for each volume category. In a second step, subgroup analyses categorized by the presence of SAH or IVH were performed.

### Table. Intraclass Correlation Coefficients and Minimal Detectable Difference for Total Hematoma Volume (ICH+IVH)

| Volume category | All | Intrarater | Intrarater
<table>
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<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>ICC (95% CI)</td>
<td>MDD, mL</td>
</tr>
<tr>
<td>All</td>
<td>40</td>
<td>0.994 (0.991–0.996)</td>
<td>6.68</td>
</tr>
<tr>
<td>≤10 mL</td>
<td>10</td>
<td>0.992 (0.978–0.996)</td>
<td>0.79</td>
</tr>
<tr>
<td>&gt;10–30 mL</td>
<td>10</td>
<td>0.979 (0.929–0.992)</td>
<td>2.52</td>
</tr>
<tr>
<td>&gt;30–50 mL</td>
<td>10</td>
<td>0.939 (0.872–0.969)</td>
<td>4.30</td>
</tr>
<tr>
<td>&gt;50 mL</td>
<td>10</td>
<td>0.976 (0.950–0.988)</td>
<td>8.22</td>
</tr>
<tr>
<td>Presence of SAH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>0.995 (0.990–0.998)</td>
<td>3.12</td>
</tr>
<tr>
<td>Yes</td>
<td>20</td>
<td>0.988 (0.979–0.993)</td>
<td>8.21</td>
</tr>
<tr>
<td>Presence of IVH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29</td>
<td>0.997 (0.994–0.998)</td>
<td>3.82</td>
</tr>
<tr>
<td>Yes</td>
<td>11</td>
<td>0.985 (0.971–0.992)</td>
<td>8.79</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; ICC, intraclass correlation coefficient; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; MDD, minimal detectable difference; and SAH, subarachnoid hemorrhage.

**Discussion**

In the present study, we report ICCs and MDDs for total hematoma (ICH+IVH) volume measurement obtained using computerized planimetry in a population with a broad range of hematoma volumes. Further, we report detailed assessment of the relationship between hematoma size and measurement precision and MDD for total hematoma volume measurement depending on the presence of SAH and IVH.

Computerized planimetry has been shown to be superior in the measurement of hematoma expansion as compared with visual approximations using the ABC/2 method.\textsuperscript{4,8} The software used in this study allowed raters to drive a computer algorithm to rapidly identify hematoma volumes in real-time with visual feedback, minimizing, or in some cases eliminating, the need for feedback, minimizing, or in some cases eliminating, the need for

**Results**

Median total hematoma (ICH+IVH) volume was 34.7 (interquartile interval, 11.5–56.8) mL. Total hematoma volumetric analyses had excellent intra- and interrater agreements (Table). MDD for intra- and interrater volumes was 6.68 and 7.72 mL, respectively, and were higher the larger total hematoma volume was. Patients with SAH (50%) had slightly lower intra- and interrater agreements but higher MDD than patients without SAH.

Total hematoma volumetric analyses had excellent agreements for stroke neurologists (ICC 0.994; 95% confidence interval 0.991–0.996), stroke fellow (ICC 0.997; 95% confidence interval 0.995–0.999), and radiology residents (ICC 0.993; 95% confidence interval 0.990–0.996). MDD for the different reader types were 7.74, 6.03, and 7.94 mL, respectively.

Twenty-nine (72.5%) patients presented ICH without IVH. In this subgroup, ICH volumetric analysis had excellent agreements (Table). MDD for intra- and interrater ICH volumes were 3.82 and 5.83 mL, respectively.
for manual tracing. In general, total hematoma volume measurements can be obtained in 2 to 10 minutes per scan. Scans depicting large, irregular hematomas with the presence of SAH or IVH require the longest time and largest effort to assess accurately. User-assisted computerized planimetry is, therefore, easy to use and entirely feasible for routine use in clinical trials and could soon become standard in some clinical contexts.

The knowledge of the magnitude of hematoma volume measurement error is essential because the dichotomous definition of hematoma expansion chosen in ICH studies must be greater than the MDD. In this study, planimetric volume measurements had excellent ICC for assessing total hematoma volume irrespective of different volume categories or the presence of SAH or IVH. The overall MDD for total hematoma volume measurement was slightly below 8 mL. However, MDD increased with the hematoma volume size. Therefore, baseline ICH volume should be taken into account in ICH expansion definitions. Larger hematomas are more likely to distort anatomic landmarks, which may increase the imprecision of volume measurements and therefore the MDD. Further, there is a mathematical proportional relationship between the MDD and the standard error of the mean volume, meaning that there will always be larger MDD for larger hemorrhage volume categories. Finally, the presence of SAH or IVH may blur boundaries between parenchymal and subarachnoid or intraventricular blood and, consequently, MDD was greater in the presence of SAH or IVH.

A higher MDD should be taken into account when assessing larger hematomas and those with SAH or IVH in ICH studies. Interestingly, an MDD for total hematoma volume measurement of 10.4 mL was found in patients with largest hematoma volumes, as well as in the subgroups of patients with SAH or IVH. Despite any subsequent measurement on hematoma volume is prone to measurement error and that our results can be interpreted within a population with similar attributes to ours, a threshold >10.4 mL seems to be reliable to avoid error of total hematoma volume measurement in a broad range of patients.

In contrast to MDD, that reflects the absolute error of measurement, the minimally important difference reflects the amount of hematoma expansion required to reliably predict a negative clinical outcome. Based primarily on the results of the Recombinant Activated Factor VII Intracerebral Hemorrhage Trial, an absolute ICH volume increase of 6 mL is frequently used as the minimally important difference in ICH studies, including the PREDICT study. In the present study, the MDD for pure ICH measurement compared favorably with the commonly used 6 mL threshold, meaning that overall it could be used to reliably detect ICH expansion according to that definition.

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