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# **Correlation of age and hematoma volume in patients with spontaneous lobar intracerebral hemorrhage**

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## **Conflict of Interest**

There is no conflict of interest.

## **Contributions**

J.B.K., M.K., and H.B.H designed the study and wrote the manuscript. J.B.K., R.S., C.M., I.C.K., and D.S. obtained clinical data by reviewing institutional databases and the patient's medical charts. H.L. and S.K. analyzed the images and obtained all neuroradiological data. J.B.K., R.S., I.C.K., and D.S. contacted all patients and obtained the pre-admission- and functional outcome-data of the analyzed patients. All authors have read the manuscript, agree with the contents, and approved the final version of the manuscript.

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## **Abstract**

### **Background**

Lobar intracerebral hemorrhage [LH] is gaining importance in the ageing population, however there are only limited data regarding specific clinical characteristics and risk factors of elderly patients with LH.

### **Methods**

This retrospective analysis of patients with spontaneous supratentorial hemorrhage included 174 consecutive patients (78 LH and 96 deep ICH [DH]). Clinical data including the pre-admission status, neuroradiological findings, initial presentation, treatment, and outcome were evaluated through institutional databases, patient's medical charts and by mailed questionnaires. Logistic regression analyses were calculated for initial parameters predisposing LH and for treatment and outcome parameters associated with LH.

### **Results**

Age-stratified volume analysis revealed increasing hematoma volumes for LH ( $\leq 70$ y: 26.2ml, 70-80y: 37ml,  $>80$ y: 61.3ml), whereas DH showed no relation between volume and age ( $\leq 70$ y: 10.1ml, 70-80y: 23.2ml,  $>80$ y: 12.1ml). DH patients had significantly higher HbA1c levels. Post-ICH seizures were more frequent after LH. Logistic regression analyses identified the parameters: age, hematoma volume, and post-ICH seizures to be associated with LH, whereas intraventricular hemorrhage, extraventricular drainages and elevated HbA1c were related to DH.

## Conclusion

Hematoma volumes are **substantially** increasing in LH patients that are older than 70 years. Pathologic HbA1c levels are significantly associated and predisposing for DH. These findings further support the ongoing debate of different disease entities for supratentorial ICH **(i.e. association of cerebral amyloid angiopathy and lobar ICH versus diabetes induced atherosclerosis in deep ICH)**. Future studies should focus on identifying specific pathologic characteristics and risk factors for both bleeding sites to implement specific preventive measures, i.e. amyloid angiopathy modulating therapies for LH, and to avoid risk factors that are specific for each hemorrhage location.

## Introduction

Spontaneous intracerebral hemorrhage [ICH] is one of the most devastating cerebrovascular diseases with a 30-day mortality rate up to 35-52%, and poor clinical outcome leaving only 20% of patients functionally independent (mRS<3) at 6 months (1, 2). Generally, the incidence of ICH among first ever strokes is slightly decreasing and ranges from 10-15%, however the absolute amount of ICH has increased over the last 10 years and its rate is expected to double by the year 2050 (3-5). However, among ethnic populations there are differences in incidence as well as hemorrhage location (6). Deep ICH [DH] is the most common location (36-67%), followed by lobar ICH [LH] (15-52%), cerebellar (7-11%) and brainstem hemorrhage (4-9%) (6-8). Identified risk factors for all ICH are hypertension, male sex, age, alcohol abuse, and other less established risk factors are smoking, diabetes, anemia, higher fibrinogen levels, lower LDL and triglycerides as well as renal and hepatic insufficiency (5, 9-11).

The major consentaneous risk factor for LH is cerebral amyloid angiopathy [CAA] (12). Incidence rates of CAA are strongly age dependent, being only 2.3% for patients younger than 75 years of age, but being 8% for 75-84 year-old-, and 12.1% for over 85 year-old patients, respectively, while post mortem examinations of ICH patients revealed incidences as high as 23%-54% (12, 13). Overall, 30 day mortality after LH ranges from 11-30%, and up to 57% at one year, with the best prognosis for patients with smaller hematoma volume and better levels of consciousness on admission (12, 14). A superficial location and less intraventricular hemorrhage [IVH] has also been reported favorable to outcome, whereas older age of patients is less favourable (15). LH has been shown to be associated with higher rates of recurrent ICH, higher occurrence of post stroke seizures, and an increased incidence of LH in the elderly population has been proposed (4, 5, 16). Given these specific features and

in light of the divergent risk profile, LH has been assumed to reflect a different disease entity (5).

The majority of previous studies reported only on small numbers of elderly patients with supratentorial ICH, thus representing limited data regarding their clinical characteristics and vascular risk factors (11). Considering the growing relevance of LH in ageing populations, we compared a broad spectrum of patient characteristics including pre-admission status, past medical and medication history, clinical, neuroradiological and laboratory parameters as well as treatment and functional outcome among both supratentorial hemorrhage sites. Our aim was to further specify characteristics of a lobar location of ICH in elderly patients.

## Methods

### Patient selection

This retrospective study included consecutive patients with supratentorial ICH who were admitted to the neurocritical care or stroke-unit of the Department of Neurology, University of Erlangen, from January 2007 until February 2009. The analysis was based on our institutional database into which all relevant clinical and neuroradiological data of ICH patients were included. From 236 patients with the diagnosis of ICH we excluded posterior fossa hematomas (n=48), and by definition did not include patients with secondary ICH, i.e. ICH related to oral anticoagulant therapy, trauma, tumor, arteriovenous malformations, **cerebral** venous thrombosis, subarachnoid hemorrhage, or with acute thrombolysis or coagulopathy with platelet counts below 50.000/ $\mu$ l. Moreover, we excluded those patients who were lost to follow-up (n=14). Hence, 174 patients (78 LH and 96 DH) of central European descent remained for analysis.

### Parameter acquisition

*Clinical presentation;* All in-hospital parameters (GCS, NIHSS, ICH-score, body temperature, and mean arterial blood pressure) were obtained by reviewing the patient's medical charts, emergency protocols, and institutional databases.

*Laboratory parameters;* Data were obtained by reviewing the patient's medical charts and institutional databases. Data are presented as continuous variables. Initial on admission data are presented.

*Pre-admission status and past medical history;* Data of patients prior to admission were obtained by a mailed standardized questionnaire. Whenever this questionnaire did not return within 6 weeks, a semi-quantitative phone interview was conducted with patients, or their closest relatives, respectively. Telephone interviews were performed by four physicians

(J.B.K., R.S., I.C.K., D.S.) who were trained and certified for data collection on disability and quality of life. Written or oral consent was obtained from all patients or their relatives. The pre-admission data consisted of: body mass index, history of ischemic or hemorrhagic stroke, history of epileptic seizures, history of cardiac event (myocardial infarction or peripheral arterial embolism), use of nicotine (>2 pack years), alcohol abuse (defined as >80g ethanol/day), intake of aggregation inhibitors, intake of statines, diagnosis of hypercholesterolemia, diagnosis of arterial hypertension according to established criteria (17), and diagnosis of diabetes mellitus (18).

*In-hospital treatment;* Parameters were obtained by reviewing the patient's medical charts. Treatment data was: Need of ventilation (in days), hospital length of stay (in days), requirement of external ventricular drainage [EVD] (for occlusive hydrocephalus (19)), or lumbar drainages (for post-hemorrhagic communicating hydrocephalus (20)), intraventricular fibrinolysis using rt-PA (21), diagnosis of pneumonia, and sepsis according to established criteria (22, 23).

*Outcome findings;* Mortality and functional outcome data were obtained by mailed questionnaires and structured phone interviews, as appropriate, as described above for pre-admission data. The functional outcome was assessed after 3 months and 1 year (73% by filled in questionnaires and 27% by telephone interviews), and was evaluated using the modified Rankin scale [mRS] (24). Favorable outcome was defined as mRS 0–2. Mortality was evaluated at 3 months and 12 months after ICH. Post ICH-seizures were scored if patients developed focal or generalized seizures ( $\geq 2$ ) within one year after stroke (25).

### Imaging

Diagnosis of ICH was made immediately after hospital admission by either CT (SIEMENS Somatom Volume Zoom, Erlangen, Germany) or MRI (SIEMENS Sonata, 1.5 Tesla, Erlangen, Germany). Two neuroradiologists (H.L. and S.K.) who were blinded to all clinical

data reviewed the scans independently in randomized order. For all cases in which there was discrepancy regarding neuroradiological parameters a second consensus analysis was made. Time from symptom onset to initial imaging was between 0-6h, 86.9% of patients had initial CT and 13.1% patients MRI scans. All patients received follow-up imaging within 48h. Location of hemorrhage was defined as lobar *versus* deep (latter including thalamic hematomas). Hematoma volume was calculated according to the formula of ellipsoids ( $ABC/2$ ) (26). IVH or subdural extensions were not taken into account for volume measurement. IVH was documented and scored using the Graeb score summation (27). Hematoma growth was defined as an increase of intraparenchymal hemorrhage volume >33% as measured by image analysis on follow-up CT or MRI (28). Midline shift was measured on initial imaging at the site of maximal deflection in mm.

### Statistical Analysis

Statistical Analysis was performed with the SPSS 17.0 software package ([www.spss.com](http://www.spss.com)) and Statview version 5.0 ([www.jmp.com](http://www.jmp.com)). The significance level was set at  $\alpha = 0.05$ . Statistical tests were two-sided. Data distribution was assessed with the Kolmogorov-Smirnov test. Normally distributed data are presented as mean  $\pm$  SD and was compared using the Student T-test. Other data are presented as median with IQR (25<sup>th</sup>-75<sup>th</sup> percentile), and were compared using the Mann-Whitney-U-test. The Pearson  $\chi^2$ - or Fisher's exact tests were used to analyse frequency distributions of categorized variables between LH *versus* DH. The correlation of age and hematoma volume with hemorrhage location was shown graphically using the Whisker-Box-plot and locally weighted scatterplot smoothing [LOWESS] with a = 0.25-0.5 and a tension = 66. Regarding the parameter age, we a priori decided to trichotomize the patients into those younger than 70 years, between 70 and 80 years, and older than 80 years (29). One univariate logistic regression analysis was calculated to determine parameters that were associated with LH. Two stepwise forward inclusion multivariable logistic regression

models were calculated for parameters that were significant or showed a trend in the univariate analysis ( $p < 0.1$ ) with lobar ICH as the dependent variable. The first multivariate model was calculated with parameters that were predisposing for LH (table 4 a-d). A second multivariate regression model was calculated to identify those parameters arising not until the course of treatment that were independently related to LH (table 4 e).

## Results

The demographic, pre-admission and neuroradiological characteristics of all patients are shown in table 1. **The time to hospital arrival as well as the chosen imaging modality did not differ between patients with lobar and deep ICH.** The clinical and laboratory findings on admission are given in table 2.

Mean age was 70.2 years (range = 35-98y). The comparison of age between lobar and deep hemorrhage revealed significant overall differences (73.8 *versus* 67.6 years), even more when focussing on age stratified patients (i)  $\leq 70$ y, (ii)  $>70$ y, and (iii)  $>80$ y, respectively (table 1). LH was significantly more frequent among the older age group (i.e.  $>70$ y, LH (n=52), DH (n=39);  $p<0.001$ ). Lesion volume was significantly higher in LH than in DH (42.7 *versus* 11.9 ml). The correlation of age, volume and lesion site is shown in figure 1 and displays a **substantial** volume increase for LH patients with a take off at  $>70$  years. In contrast DH patients showed no correlation of volume and age. A history of prior hemorrhagic stroke was significantly more often with LH. IVH as well as the Graeb score was significantly higher and more frequent in DH ( $p<0.001$ ).

Significant laboratory findings in LH patients were higher HDL-values ( $p=0.043$ ) as well as lower HbA1c levels ( $p=0.042$ ). Given the significance of HbA1c, a dichotomized analysis revealed significantly less patients with a pathologically elevated HbA1c (i.e.  $>6.5\%$ ; LH (9/78), *vs.* DH (31/96),  $p<0.01$ ).

Treatment procedures and the outcome findings are given in table 3. LH patients required neurocritical care for a significantly shorter period of time ( $p=0.046$ ) and were less frequently mechanically ventilated ( $p=0.015$ ). As shown in table 1, patients with LH suffered less often

from IVH, hence rarely required placement of an EVD ( $p < 0.001$ ). In this regard DH patients required intraventricular fibrinolysis more often ( $p < 0.001$ ) as well as lumbar drainage placement ( $p < 0.001$ ). Moreover, complications like pneumonia, and sepsis, were more commonly appreciated with DH ( $p = 0.049$ , and  $p = 0.024$ ). Mortality rates and the functional outcome measures revealed no significant differences among both groups. The only outcome difference for LH was the development of post-ICH seizures ( $p = 0.028$ ).

The univariate associations of significant parameters or those showing a trend with LH are listed in table 4. The multivariate logistic regression models are shown in table 5. With respect to pre-admission status and initial presentation the parameters (i) age and (ii) hematoma volume were independently predisposing for LH, whereas (iii) presence of IVH, and (iv) elevated HbA1c levels were inversely correlated (table 5a). Regarding the regression analysis for treatment and outcome the incidence of post-ICH seizures was independently related to LH, whereas requirement of an EVD was inversely associated (table 5b).

## **Discussion**

In the present study we compared clinical, neuroradiological, and laboratory parameters of patients with supratentorial hemorrhage to identify specific parameters that were independently related to LH. Key findings of LH were: (i) increasing age resulted in an increase of hematoma volume, and (ii) pathologically elevated levels of HbA1c were less common. Moreover, (iii) the frequency of IVH with consecutive need of EVD was lower, and (iv) the rate of post-ICH seizures higher in patients with LH. The following aspects emerged from the data.

The present study discovered a previously unnoticed age-volume correlation in LH. Each parameter, older age and greater hematoma volume, has been separately described to be independently associated with LH. However there were only limited data on the exact correlation of these factors with various patient characteristics, radiological features and outcome. With respect to increasing hematoma volumes in the elderly LH patient, one has to refer to CAA, as the strongest age dependent risk factor for LH (4, 12, 15, 16). CAA is defined by the deposition of  $\beta$ -amyloid protein in the media and adventitia of vessels of the cortex and leptomeninges (13). Therefore the finding of larger hematoma volumes in older patients with LH could be based on greater vascular fragility because of a higher prevalence of severe angiopathy with fibrinoid necrosis (13, 16). In addition, a more pronounced parenchymal atrophy of the cerebral lobes with less consecutive tamponade effect of the hematoma itself and hence greater volumes, might also be attributable in elderly patients. We could not find significant differences for other factors influencing volume, such as the use of aggregation inhibition, hepatic dysfunction, coagulation parameters, or prevalence of hypertension amongst DH and LH. With respect to hypertension as the strongest independent risk factor for ICH (4, 30), we were not able to elucidate any relationship with LH, neither a

different prevalence, nor greater hematoma volumes, nor more frequent hematoma growth on control scans. Therefore the findings presented here may support the idea of previous studies that arterial hypertension should be considered as a secondary side finding in the elderly LH patient, and not as primary causative factor for LH. If correct this which is in line with the hypothesis of different disease entities as the primary cause for DH and LH can be prospectively tested in the future (4, 11, 12, 31).

This aspect of different disease entities seems also supported by the finding of significantly elevated HbA1c levels in DH patients. Evaluation of other previously noted cerebrovascular risk factors did not show differences amongst our patient cohort. Special attention should be given to HbA1c as a diagnostic and surveillance marker (18, 32). As glycosylated hemoglobin can be considered a widely accepted parameter for the assessment of an atherosclerotic risk profile (5, 18, 32), its elevation may also be relevant as driving co-factor for DH. Given the difficulty of assessing prior history of long standing diabetes and compliant drug taking behaviour (33), and in light of diabetes as a already proposed weak risk factor for ICH in general (5), patients with elevated HbA1c levels should be screened for further atherosclerotic progression and risk factors that are predisposing for DH to optimize primary prevention of ICH.

IVH in supratentorial hemorrhage occurs more frequently with larger hematoma volumes and is influenced by hemorrhage location as the basal ganglia and thalamus are located more closely to the ventricular system (5, 11) In line with these studies, IVH was also less frequently associated with LH in our series (34), therefore resulting in fewer placements of EVD, LD and use of intraventricular fibrinolysis (20, 35). IVH has previously been shown to be related to a higher mortality and poorer functional outcome (35), however, given the finding in LH with fewer IVH, we could not show significant outcome differences between

patients with DH and LH. This may be based on the average older age of LH patients and potentially more co-morbidities and larger hematoma volumes in LH. Hence, it appears plausible that those two predictors (IVH & volume) were counterbalancing functional outcome of LH *versus* DH. Additionally, patients with IVH received an aggressive treatment regimen including EVD, intraventricular fibrinolysis, and lumbar drainages, which also could have contributed to an equivalent mortality and functional outcome after supratentorial hemorrhage (20, 35, 36).

Regarding the development of seizures after spontaneous ICH, the reported incidences range between 2.8-18.7%, and predictors for their development are cortical involvement, subdural hematoma and hematoma volume (37). In line with these studies, LH was strongly associated with the occurrence of seizures. However, hematoma volume was not associated with an increased frequency of seizures in our series (data not shown). Interestingly, patients who received EVD placement did not reveal an increased rate of seizures as compared to patients without EVD, irrespective of hematoma site. Although based on a small number of patients who received an EVD (n=45), this finding could indicate that cortical trauma caused by an EVD may not lead to a decreased seizure threshold. Furthermore, we did not detect outcome differences among patients with and without post-ICH seizures (4, 30, 37).

Our study has certain limitations: (i) due to the nature of this retrospective, single-center investigation, the patient number of n=174 appears rather small to draw definite conclusions on patient characteristics. (ii) No “gold standard” test for CAA such as autopsy was applied to all subjects. (iii) Confirmation of the duration of diabetes, arterial hypertension, and the extent of subsequent atherosclerosis in brain and whole body was not evaluated. (iv) The impact of exclusion of both posterior fossa bleedings and ICH related to oral anticoagulants on the findings is unknown. (v) The mailed questionnaire was filled-out by patients, their relatives or

legal attorneys and may have been answered wrongly with respect to the time-point of follow-up and the validity of mRS estimation (38). (vi) As we did not focus on first ever ICH only, but included patients with recurrent ICH, this selection bias might have impacted hematoma volume at presentation as well as functional outcome. (vii) Finally results may have been biased by 14 patients who were lost to follow-up.

Concluding the findings of our study, we identified a highly significant age-volume correlation in elderly patient with LH only, whereas pathologically elevated HbA1c levels were attributable to basal ganglia and thalamus bleedings. In light of a still the tremendous disease burden of ICH and its growing relevance in the aging population, future studies should focus on (i) establishing novel CAA-modulating treatment strategies and (ii) further attempts to definitively classify LH (as amyloid-angiopathic disease) and (iii) DH (as atherosclerotic disease). If this classification proves correct, then treating these two supratentorial hemorrhage locations more specifically with respect to different risk factors and patient characteristics could be very important.

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## Table and Figure legends

- Table 1. Demographic, past medical history, and neuroradiologic characteristics.  
Significant parameters are expressed in bold.
- Table 2. Initial clinical presentation and baseline laboratory findings.
- Figure 1. Correlation of age and hematoma volume, categorized according to lesion site.  
(A) Box plot (median, IQR, 75<sup>th</sup> – 25<sup>th</sup> percentile) and (B, C) LOWESS  
(tension =66).
- Table 3. In-hospital therapy and outcome findings.
- Table 4. Univariate regression analysis for identification of parameters associated with LH. (a) Demographic characteristics and past medical history, (b) neuroradiologic data, (c) initial clinical presentation, (d) baseline laboratory data, (e) in-hospital treatment and outcome findings. Data are calculated as continuous or categorizes variables (see tables 1-3). All parameters given in table 1-3. were analyzed univariately. For reasons of simplification only significant parameters or those showing a trend ( $p < 0.1$ ) are displayed.
- Table 5. Multivariate logistic regression models. (A) Predictors for LH (table 4 a-d). (B) Analysis of treatment and outcome parameters that were univariately related to LH (table 4 e). Variables that remained independently related to LH ( $p < 0.05$ ) are expressed in bold.

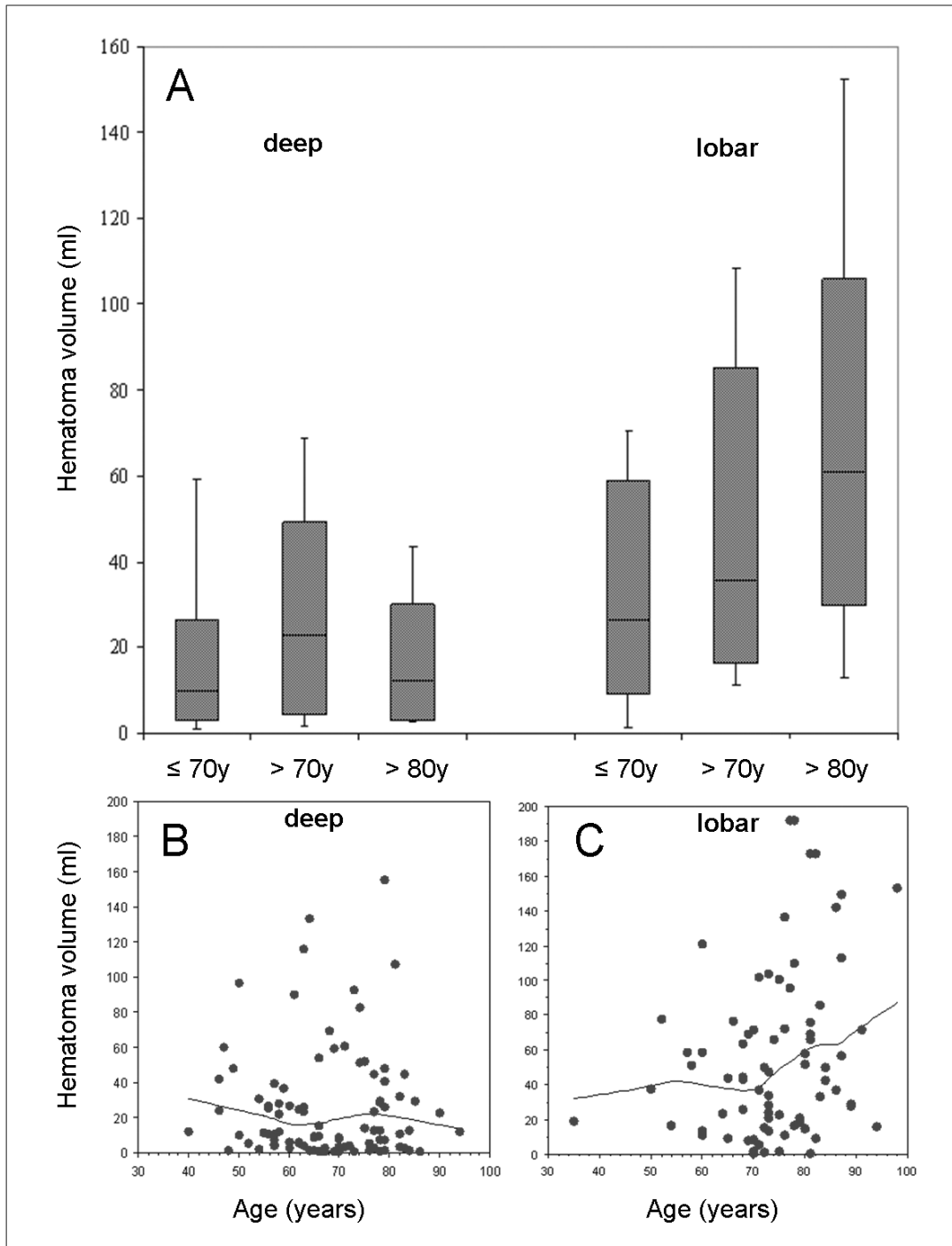
**Table 1.**

<b>Total ICH (n= 174)</b>	<b>Lobar ICH (n=78)</b>	<b>Deep ICH (n=96)</b>	<b><i>p-value</i></b>
Age (mean ± SD)	<b>73.8 ± 10.7</b>	<b>67.6 ± 11.3</b>	<b>&lt;0.001</b>
age≤70y	<b>26 (33.3%)</b>	<b>57 (59.4%)</b>	<b>0.001</b>
age>70y	<b>52 (66.7%)</b>	<b>39 (40.6%)</b>	<b>&lt;0.001</b>
age>80y	<b>22 (28.2%)</b>	<b>12 (12.5%)</b>	<b>0.012</b>
Female	37 (47.4%)	48 (50.0%)	0.762
<b><u>Prior admission status &amp; past medical history</u></b>			
BMI (mean, ± SD)	26.1 ± 5.1	27.4 ± 5.7	0.132
HTN	54 (65.4%)	72 (75.0%)	0.396
Hypercholesterolemia	29 (37.1%)	26 (27.1%)	0.190
Diabetes	14 (17.9%)	16 (16.6%)	0.574
Ischemic stroke	18 (23.1%)	13 (13.5%)	0.076
<b>Hemorrhagic stroke</b>	<b>17 (22.1%)</b>	<b>2 (2.1%)</b>	<b>&lt;0.001</b>
Cardiac event	8 (10.3%)	7 (7.3%)	0.335
Aspirin use	31 (39.7%)	32 (33.3%)	0.380
Statine use	21 (26.9%)	19 (19.8%)	0.265
Alcohol abuse	26 (33.3%)	36 (37.5%)	0.566
Smoking	30 (38.5%)	38 (39.6%)	0.887
Epilepsy	4 (5.1%)	1 (1.0%)	0.207
<b><u>Neuroradiologic data</u></b>			
<b>Lesion volume [cm<sup>3</sup>] (median, IQR)</b>	<b>42.7 (16.1-72.1)</b>	<b>11.9 (3.1-37.3)</b>	<b>&lt;0.001</b>
<b>Vol. for age≤70y [cm<sup>3</sup>] (median, IQR)</b>	<b>26.2 (9.1-58.6)</b>	<b>10.1 (3.1-26.9)</b>	<b>0.028</b>
<b>Vol. for age&gt;70y [cm<sup>3</sup>] (median, IQR)</b>	<b>37.0 (17.6-86.7)</b>	<b>23.2 (4.7-49.6)</b>	<b>0.001</b>
<b>Vol. for age&gt;80y [cm<sup>3</sup>] (median, IQR)</b>	<b>61.3 (30.1-106.3)</b>	<b>12.1 (2.9-30.1)</b>	<b>0.008</b>
Left hemisphere	46 (59.0%)	49 (51.1%)	0.296
<b>IVH</b>	<b>26 (30.9%)</b>	<b>58 (69.0%)</b>	<b>0.001</b>
<b>Graeb score (median, IQR)</b>	<b>0 (0-2)</b>	<b>3 (0-10)</b>	<b>&lt;0.001</b>
Hematoma growth	8 (10.3%)	10 (10.4%)	0.999
Midline shift [mm] (median, IQR)	0 (0-6.8)	2 (0-7.3)	0.288

**Table 2.**

<b>Total (n=174)</b>	<b>Lobar ICH (n=78)</b>	<b>Deep ICH (n=96)</b>	<b><i>p-value</i></b>
	<b>Median, (IQR)</b>	<b>Median, (IQR)</b>	
GCS	14 (5-15)	12 (5-15)	0.297
NIHSS	7.5 (5-21)	13 (8-29)	0.114
ICH score	2 (0-3)	2 (0-3)	0.547
MAP [mmHg]	115 (98-128)	117 (103-140)	0.120
Temperature [°C]	37.0 (36.4-37.4)	36.8 (36.1-37.3)	0.200
Hemoglobin [mmol/l]	8.26 (7.45-9.00)	8.38 (7.70-9.38)	0.351
Hematocrit	0.383 (0.342-0.420)	0.396 (0.370-0.428)	0.288
Fibrinogen [mmol/l]	10.58 (8.91-11.94)	9.85 (8.29-11.03)	0.103
<b>HDL [mmol/l]</b>	<b>1.43 (1.17-1.82)</b>	<b>1.27 (1.04-1.59)</b>	<b>0.043</b>
LDL [mmol/l]	3.07 (2.73-3.82)	3.15 (2.50-4.16)	0.855
Cholesterol [mmol/l]	4.89 (4.47-5.62)	5.04 (4.21-6.16)	0.687
TAG [mmol/l]	0.97 (0.77-1.57)	1.21 (0.94-1.79)	0.080
Cholinesterase [kU/l]	6.7 (6.0-7.5)	6.6 (5.3-8.0)	0.965
Gamma GT [U/l]	27 (19-43)	29 (18-68)	0.279
	<b>Mean, (± SD)</b>	<b>Mean, (± SD)</b>	
Leukocytes [10 <sup>9</sup> /l]	10.3 (± 4.3)	11.3 (± 10.5)	0.444
CRP [mg/l]	12.7 (± 20.5)	15.8 (± 33.2)	0.486
Thrombocytes [10 <sup>9</sup> /l]	256 (± 105)	246 (± 82)	0.482
Glucose [mmol/l]	7.44 (± 2.78)	7.66 (± 2.89)	0.623
<b>HbA1c [%]</b>	<b>5.8 (± 0.7)</b>	<b>6.4 (± 1.2)</b>	<b>0.042</b>
Creatinine [µmol/l]	85.0 (± 24.8)	105.3 (± 123.9)	0.165
Urea nitrogen [mmol/l]	12.78 (± 6.68)	13.82 (± 6.89)	0.328

**Figure 1.**



**Table 3.**

<b>Total</b> <b>(n=174)</b>	<b>Lobar ICH</b> <b>(n=78)</b>	<b>Deep ICH</b> <b>(n=96)</b>	<b><i>p-value</i></b>
<u>In-hospital treatment &amp; complications</u>			
DNT / DNR orders	16 (21.1%)	14 (14.6%)	0.303
<b>Ventilation</b>	<b>26 (33.3%)</b>	<b>49 (51.0%)</b>	<b>0.015</b>
<b>Days of ventilation (median, IQR)</b>	<b>0 (0-2)</b>	<b>2 (0-14)</b>	<b>0.006</b>
<b>EVD</b>	<b>10 (12.8%)</b>	<b>35 (36.5%)</b>	<b>&lt;0.001</b>
<b>Lumbar drainage</b>	<b>3 (3.8%)</b>	<b>23 (24.0%)</b>	<b>&lt;0.001</b>
<b>Intraventricular lysis</b>	<b>1 (1.3%)</b>	<b>22 (22.9%)</b>	<b>&lt;0.001</b>
PEG tube placement	9 (11.5%)	16 (16.7%)	0.330
<b>Pneumonia</b>	<b>30 (38.5%)</b>	<b>51 (53.1%)</b>	<b>0.049</b>
<b>Sepsis</b>	<b>6 (7.7%)</b>	<b>19 (19.8%)</b>	<b>0.024</b>
<b>Length of stay [days] (mean, ± SD)</b>	<b>11.9 (± 7.8)</b>	<b>14.6 (± 9.4)</b>	<b>0.046</b>
<u>Outcome</u>			
In hospital mortality	16 (20.5%)	18 (18.8%)	0.848
90 day mortality	21 (26.9%)	30 (31.3%)	0.617
1 year mortality	27 (34.6%)	38 (39.6%)	0.532
NIHSS at discharge (median, IQR)	6.0 (3-13)	8.5 (4-16)	0.226
mRS 90day (median, IQR)	4 (3-6)	5 (3-6)	0.587
mRS 90d (0-2)	19 (24.4%)	21 (21.9%)	0.921
mRS 1 year (median, IQR)	4 (3-6)	5 (3-6)	0.733
mRS 1y (0-2)	25 (32.1%)	36 (37.5%)	0.700
<b>Post stroke seizure</b>	<b>22 (28.2%)</b>	<b>14 (14.6%)</b>	<b>0.028</b>
History of EVD & post stroke seizure	5 (22.7%)	5 (35.7%)	0.462

**Table 4.**

<b>Univariate variables</b>	<b>Lobar ICH (n=78) Odds ratio (95% CI)</b>	<b>p-value (p&lt;0.1)</b>
<u>a.) Demographics &amp; Prior admission status &amp; past medical history</u>		
Age	1.053 (1.022-1.085)	0.0006
Prior hemorrhagic stroke	13.098 (2.922-58.721)	0.0008
<u>b.) Radiologic data</u>		
Lesion volume [cm <sup>3</sup> ]	1.019 (1.010-1.028)	<0.0001
IVH	0.362 (0.195-0.673)	0.0013
Graeb score	0.796 (0.722-0.878)	<0.0001
<u>c.) Initial clinical presentation</u>		
MAP [mmHg]	0.989 (0.977-1.002)	0.0979
<u>d.) Laboratory parameters</u>		
HbA1c [%]	0.593 (0.347-1.013)	0.0558
HDL [mmol/l]	1.029 (1.004-1.055)	0.0256
Gamma GT [U/l]	0.534 (0.281-1.012)	0.0545
<u>e.) Outcome &amp; Treatment</u>		
Length of stay [days]	0.965 (0.931-1.000)	0.0489
Ventilation [days]	0.499 (0.268-0.927)	0.0279
EVD	0.256 (0.117-0.561)	0.0007
Lumbar drainage	0.129 (0.037-0.447)	0.0013
Intraventricular fibrinolysis	0.044 (0.006-0.337)	0.0026
Pneumonia	0.556 (0.300-1.030)	0.0621
Sepsis	0.348 (0.131-0.921)	0.0336
Post stroke seizures	2.268 (0.989-5.203)	0.0532

**Table 5.**

<b>Multivariate</b>	<b>Lobar ICH (n=78)</b>	<b><i>p-value</i></b>
	<b>Odds ratio (95% CI)</b>	<b>(<i>p</i>&lt;0.05)</b>
a.) <u>predictors</u>		
<b>Age [years]</b>	<b>1.065 (1.001-1.132)</b>	<b>0.0457</b>
Prior ICH	18.863 (0.455-782.461)	0.1222
<b>Volume [cm<sup>3</sup>]</b>	<b>1.107 (1.048-1.170)</b>	<b>0.0003</b>
<b>IVH</b>	<b>0.089 (0.017-0.460)</b>	<b>0.0039</b>
Initial MAP [mmHg]	1.002 (0.972-1.033)	0.8926
<b>HbA1c [%]</b>	<b>0.402 (0.189-0.855)</b>	<b>0.0180</b>
HDL [mmol/l]	1.015 (0.980-1.051)	0.4088
b.) <u>outcome &amp; treatment</u>		
Ventilation [days]	1.815 (0.543-6.069)	0.3331
<b>EVD</b>	<b>0.200 (0.040-0.992)</b>	<b>0.0489</b>
Pneumonia	1.251 (0.448-3.492)	0.6686
Sepsis	0.469 (0.109-2.012)	0.3079
Hospital stay [days]	0.979 (0.923-1.037)	0.4665
<b>Post stroke seizures</b>	<b>2.844 (1.059-7.640)</b>	<b>0.0381</b>

