



Clinical Article

Contributing factors of spontaneous intracerebral hemorrhage development in young adults

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Objective: The incidence of spontaneous intracerebral hemorrhage (ICH) in young people is relatively low; however, it leads to devastating lifelong neurologic deficits. We focused on spontaneous ICH occurring in young adults between 30 and 50 years of age.

Methods: We retrospectively reviewed the records of 139 patients, aged 30–50 years, diagnosed with spontaneous ICH between 2011 and 2021. Cases of ICH attributable to discernible causative lesions were excluded. Demographic data, laboratory results, image findings, and clinical outcome were analyzed.

Results: After exclusions, 73 patients were included in this study. Common characteristics among the study patients included male sex (83.6%), high body mass index ($>25 \text{ kg/m}^2$, 45.8%), smoking history (47.2%), heavy alcohol consumption (30.6%), previously diagnosed hypertension (41.1%), high serum triglyceride level ($>150 \text{ mg/dL}$, 33.3%), and microbleeds or white matter changes observed on magnetic resonance images (51.3%). In the multivariate analysis, previously diagnosed hypertension was the sole significant risk factor for cerebral small vessel (OR 7.769, $P=0.031$). Age, brain stem location, Glasgow Coma Scale score at admission, and hematoma volume were associated with poor outcomes.

Conclusions: Hypertension, obesity, smoking, and cerebral small vessel disease were important factors associated with non-lesional spontaneous intracerebral hemorrhage in young patients. Radiologic changes corresponding to cerebral small vessel disease appeared in young patients (in their 30s) and they were associated with hypertension.

Keywords Cerebral hemorrhage, Cerebral small vessel disease, Hypertension, Young adult

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INTRODUCTION

Spontaneous intracerebral hemorrhage (ICH) is diagnosed in 24.6 patients per 100,000 every year, accounting for 10–20% of all strokes.¹⁾¹⁶⁾ The incidence of spontaneous ICH in young people is relatively low. Among people younger than 45 years of

age, the incidence of spontaneous ICH is 1.9 per 100,000 person-years, compared with 19 per 100,000 person-years among people aged 45–55 years.²⁰⁾ There have been few studies investigating spontaneous ICH among young people because of the low incidence.

About 30–55% of ICH cases in patients younger than 50 years old are caused by lesions such as arteriovenous malformations (AVMs), cavernous malformations (CMs), and tumors.⁶⁾⁸⁾¹⁷⁾ Previous studies have largely included spontaneous ICH associated with structural lesions. However, in the study reported herein, we focused on non-lesional spontaneous ICHs occurring in young adults. We compared demographics between age groups and estimated early neuroradiologic changes.

MATERIALS AND METHODS

We retrospectively reviewed the records of 139 patients, aged 30–50 years, diagnosed with spontaneous ICH between 2011 and 2021. We excluded patients with bleeding caused by structural vasculopathy such as AVMs, CMs, dural arteriovenous fistulas, aneurysms, moyamoya vessels, and other overt vascular abnormalities. We also excluded patients with bleeding from brain tumors, hemorrhagic transformation of cerebral venous thrombosis (CVT), and ischemic stroke. Patients without available vascular imaging data, (from computed tomography, transfemoral cerebral angiography, or magnetic resonance [MR] angiography) were excluded because we could not rule out vascular anomalies in these patients. The remaining 73 patients were included in the analysis.

The following data were collected from patient records: age, sex, body mass index (BMI); history of hypertension, diabetes mellitus (DM), smoking, alcohol use, and drug use; serum level of total cholesterol, triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and hemoglobin A1c (HbA1c); Glasgow Coma Scale (GCS) score at admission and Glasgow Outcome Scale (GOS) score at discharge. GOS 1 means death, GOS 2 means neurovegetative condition, GOS 3

means dependency on daily assistance, GOS 4 means independence from daily support, and GOS 5 means good recovery.¹¹⁾¹³⁾ The study was approved by the relevant local ethics committee (No. 2207-010-19427).

Radiographic analysis

We performed radiologic measurements of hematoma volumes using our hospital's picture archiving and communication system. Two neurosurgeons (J.S.J and Y.S.P) made independent assessments about hematoma volume and location. The volume of each hematoma was calculated using the ABC/2 method,¹²⁾ and the mean value was used in the analyses. Hematoma locations were classified into following four categories: deep brain (thalamus, basal ganglia, internal capsule, and caudate nucleus), cerebellum, brain stem, and lobar regions. In instances where the two neurosurgeons have differing opinions on the location of the hematoma, a consensus was reached through deliberative discussions to determine the most probable origin of the hematoma.

Among the 73 patients, 39 had MR images (MRIs) available for analysis, and we evaluated images for the presence of cerebral microbleeds (CMBs) and white matter hyperintensity (WMH). We checked for WMH in fluid-attenuated inversion recovery (FLAIR) sequences using the Fazekas scale.⁹⁾ Each patient was given two Fazekas grades: one each representing deep and periventricular WMH. Between the two categories, the higher grade was selected as the WMH grade. CMBs were evaluated using susceptibility-weighted imaging (SWI). We defined cerebral small vessel disease (cSVD) as the presence of CMBs or WMH (grade ≥ 1).

Group comparisons

Group comparisons were applied between patients 30–40 versus those 41–50 years of age, between the cSVD versus non-cSVD groups, and between patients with favorable versus poor outcomes. The poor-outcome group comprised patients with GOS scores ≤ 3 at discharge, and the favorable-outcome group comprised those with GOS scores of 4 or 5. Intergroup comparisons were made in terms of all demographic, laboratory, and

radiologic variables.

Statistical analysis

Age, BMI; levels of total cholesterol, TG, LDL, HDL, and HbA1c; and hematoma volume were analyzed using Student's t-test for comparisons between the two groups. Sex ratio, GCS, GOS, hematoma location, and presence of risk factors were analyzed using the chi-square test or Fisher's exact test, as appropriate. We analyzed some risk factors separately, as follows; BMI >25 kg/m², current smoking, heavy alcohol consumption (>15 days per month), previously diagnosed hypertension or DM, low total cholesterol (<160 mg/dL), high TG (>150 mg/dL). *P* values <0.05 were considered statistically significant. Multivariate logistic regression analysis was performed to ensure that variables with *P* value < 0.1 in the univariate analysis were independent risk factors for cSVD in young ICH patients.

RESULTS

Among 139 patients initially screened, the following exclusions were applied: three patients were excluded because of a lack of vessel images, 22 with aneurysms, 20 with moyamoya disease, 10 with AVMs, four with CMs, three with brain tumors, two with cerebral infarctions, one with a developmental venous anomaly, and one with rete middle cerebral artery. After we excluded 66 patients, 73 were included in the analysis (Fig. 1).

The mean age was 43.5±5.53 years (Table 1). Common characteristics among the 73 study patients were as follows: male sex (83.6%), high BMI (>25 kg/m², 45.8%), smoking history (47.2%), heavy alcohol consumption (30.6%), previously diagnosed hypertension (41.1%), high TG (>150 mg/dL, 33.3%), CMBs (43.6%), WMH (grade 1–3, 46.2%) and cSVD (51.3%). Thirty-eight patients (52.1%) had high GCS scores (14–15) at admission, compared with 16 patients (21.9%) with low GCS scores (3–8) at admission. Twenty-nine patients (39.7%) fully recovered (GOS 5), 14 patients (19.2%) had some deficits but were able to independently carry out activi-

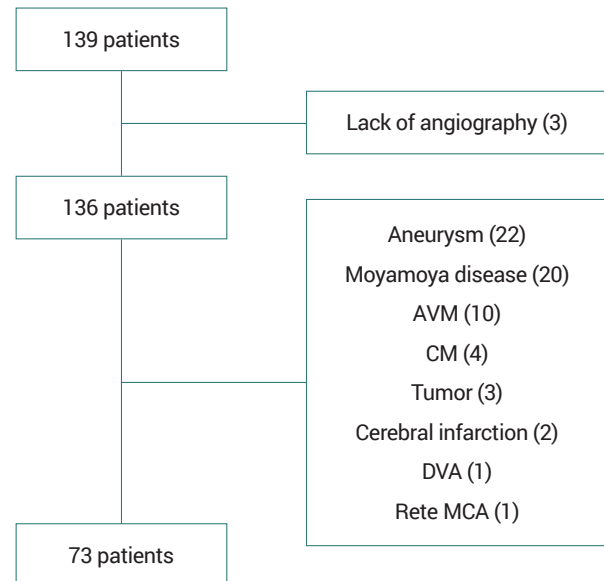


Fig. 1. Seventy-three patients were included in this study after applying the inclusion and exclusion criteria. AVM, arteriovenous malformation; CM, cavernous malformation; DVA, developmental venous anomaly; MCA, middle cerebral artery

ties of daily living (GOS 4), 10 patients (13.7%) required daily support (GOS 3), six patients (8.2%) were in a vegetative state (GOS 2), and fourteen patients (19.2%) died (GOS 1) (Fig. 2, Table 1). The most common

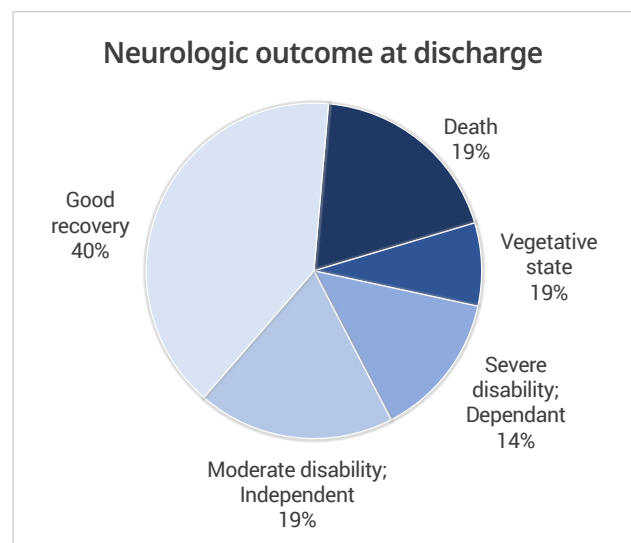


Fig. 2. Neurologic outcomes at discharge: 39.7% fully recovered (GOS 5), 8.2% in a vegetative state (GOS 4), 13.7% required support for daily living (GOS 3), 19.2% had some deficits but were able to independently carry out activities of daily living (GOS 2), and 39.7% died (GOS 1). GOS: Glasgow outcome scale

Table 1. Demographics of all age groups

Age (mean±SD, years)	43.5±5.53
Sex ratio (male : female)	61 (83.6%) : 12 (16.4%)
BMI (mean±SD, kg/m ²)*	25.0±4.27
< 23	22/72 (30.6%)
23~25	17/72 (23.6%)
> 25	50/72 (45.8%)
Smoking (current)*	34/72 (47.2%)
Heavy alcohol consumption*	22/72 (30.6%)
Hypertension	30/73 (41.1%)
On medication	15/73 (20.5%)
DM	10/73 (13.7%)
Total cholesterol (mean±SD, mg/dL) [†]	193.4±43.40
Low level (< 160 mg/dL) [†]	14/69 (20.3%)
TG (mean±SD, mg/dL) [†]	149.0±106.58
High level (> 150 mg/dL)	23/69 (33.3%)
LDL (mean±SD, mg/dL) [†]	116.1±29.40
HDL (mean±SD, mg/dL) [†]	50.3±14.29
HbA1c (%)	5.79±1.201
GCS in admission	
3~8	16/73 (21.9%)
9~13	19/73 (26.0%)
14~15	38/73 (52.1%)
GOS at discharge	
1(Expired)	14/73 (19.2%)
2	6/73 (8.2%)
3	10/73 (13.7%)
4	14/73 (19.2%)
5(Fully recovered)	29/73 (39.7%)
Location	
Deep brain	40/73 (54.8%)
Lobar	19/73 (26.0%)
Brain stem	8/73 (11.0%)
Cerebellum	6/73 (8.2%)
Microbleeds [‡]	17/39 (43.6%)
White matter hyperintensity [‡]	
Grade 0	21/39 (53.8%)
Grade 1	6/39 (15.4%)
Grade 2	6/39 (15.4%)
Grade 3	6/39 (15.4%)
Grade 1-3	18/39 (46.2%)
Small vessel disease [‡]	20/39 (51.3%)
Surgery	15/73 (34.1%)
Volume of hematoma (mean±SD, cc)	27.7±29.71

* Those data was not available in 1 patients

† Those data was not available in 4 patients

‡ The radiographic changes related to small vessel disease were assessed on MRI images, which were available in 39 patients.

SD, standard deviation; BMI, body mass index; DM, diabetes mellitus; TG, triglyceride; LDL, low density lipoprotein; HDL, high density lipoprotein; HbA1c, hemoglobin A1c; GCS, Glasgow coma scale; GOS, Glasgow outcome scale

hematoma location was the deep brain (n=40, 54.8%), followed by lobar (n=19, 26.0%), brain stem (n=8, 11.0%), and cerebellum (n=6, 8.2%) (Fig. 3). The mean hematoma volume was 27.7±29.71 mL (Table 1).

There were 21 patients aged 30–40 years and 52 patients aged 41–50 years (Table 2). In the older group, there were significantly more patients with heavy alcohol consumption than in the younger group (40.4% versus 5.0%, $P=0.004$). There were significantly more patients with admission GCS scores of 14–15 in the younger group than in the older group (76.2% versus 42.3%, $P=0.009$), and there were significantly fewer patients with poor outcomes (GOS of 3 or less) at discharge in the younger group than in the older group (19.0% versus 50%, $P=0.019$). The mean hematoma volume was significantly higher in the older group than in the younger group (32.0 mL versus 16.9 mL, $P=0.048$). There were no significant differences between the older and younger groups in sex ratio, BMI, smoking history, hypertension prevalence, DM prevalence; level of total cholesterol, TG, LDL, HDL, or HbA1c; mortality, hematoma location, or evidence of cSVD on MRI.

There were 39 patients who had MRI data available for analysis. Among them, 20 patients (51.3%) had cSVD evident on MRI (Table 3). In the cSVD group, 60% (12 patients) were diagnosed with hypertension before the

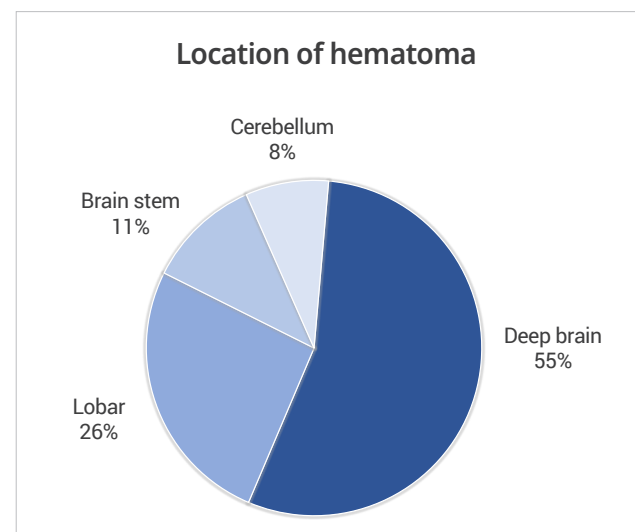


Fig. 3. Hematoma locations. 54.8% in the deep brain, 26.0% in the lobar location, 11.0% in the brain stem, and 8.2% in the cerebellum.

Table 2. Group comparison between patients 30-40 versus those 41-50 years of age

	30-40 years (n=21)	41-50 years (n=52)	p-value
Age (mean±SD, years)	36.1±3.30	46.5±2.63	
Sex ratio (male : female)	15 : 6 (71.4%)	46 : 6 (88.5%)	0.075
BMI (mean±SD, kg/m ²)*	26.4±5.88	24.5±3.39	0.193
High BMI (> 25 kg/m ²)	11/20 (55%)	22/52 (42.4%)	0.333
Smoking (current)*	10/20 (50%)	24/52 (46.2%)	0.77
Heavy alcohol consumption*	1/20 (5%)	21/52 (40.4%)	0.004
Hypertension	6/21 (28.6%)	24/52 (46.2%)	0.167
On medication	3/21 (14.3%)	12/52 (23.1%)	0.53
DM	3/21 (14.3%)	7/52 (13.5%)	1
Total cholesterol (mean±SD, mg/dL) [†]	193.2±31.70	193.5±47.38	0.979
TG (mean±SD, mg/dL) [†]	128.1±99.12	157.0±109.18	0.319
LDL (mean±SD, mg/dL) [†]	121.4±25.63	114.1±30.71	0.359
HDL (mean±SD, mg/dL) [†]	47.6±7.63	51.3±16.06	0.195
HbA1c (mean±SD, %)	6.1±1.79	5.7±0.85	0.401
GCS at admission	13.2±3.64	11.4±3.87	0.08
GOS at discharge ≤ 3	4/21 (19.0%)	26/52 (50%)	0.019
Expired	3/21 (14.3%)	13/52 (25%)	0.37
Location of hematoma			0.631
Deep brain	10/21 (27.6%)	30/52 (57.7%)	
Lobar	6/21 (28.6%)	13/52 (25%)	
Brain stem	2/21 (9.5%)	6/52 (11.5%)	
Cerebellum	3/21 (14.3%)	3/52 (5.8%)	
Volume of hematoma (mean±SD, cc)	16.9±29.02	32.0±29.13	0.048
Small vessel disease [‡]	5/12 (41.7%)	15/27 (55.6%)	0.423

* Those data was not available in 1 patients

[†] Those data was not available in 4 patients

[‡] The radiographic changes related to small vessel disease were assessed on MRI images, which were available in 39 patients.

SD, standard deviation; BMI, body mass index; DM, diabetes mellitus; TG, triglyceride; LDL, low density lipoprotein; HDL, high density lipoprotein; HbA1c, hemoglobin A1c; GCS, Glasgow coma scale; GOS, Glasgow outcome scale

ICH event, and this was a significantly higher percentage than the 26.4% (five patients) in the non-cSVD group ($P=0.034$). DM was diagnosed in five patients in the non-cSVD group, compared with 0 in the cSVD group ($P=0.02$), and HbA1c was higher in the non-cSVD group than cSVD group (6.0% versus 5.4%, $P=0.03$). There were no significant differences between the cSVD and non-cSVD groups in terms of age, sex ratio, BMI, smoking history, heavy alcohol consumption; level of TG, LDL, or HDL; GCS at admission, GOS at discharge, or hematoma location or volume.

Variables for multivariate logistic regression analysis included hypertension, DM, and HbA1c which were

the variables with P value <0.1 in univariate analysis. In multivariate analysis, previously diagnosed hypertension was independently associated with cSVD (OR, 7.769; 95% CI, 1.21–50.02; $P=0.031$) (Table 4).

There was significant variation among the hematoma-location groups in terms of the proportions of patients with poor outcomes ($P=0.025$) (Table 5). ICH in the brain stem was associated with the highest proportion (87.5%) of patients with poor outcomes, and there was a significant difference in this regard between brain stem and non-brain-stem ICH ($P=0.007$). The mean age of the poor-outcome group was 45.1 ± 4.49 years and that of the favorable-outcome group was 42.4 ± 5.95

Table 3. Group comparison between patients with cerebral small vessel disease versus those without cerebral small vessel disease

	30-40 years (n=21)	41-50 years (n=52)	p-value
Age (mean±SD, years)	42.4±6.47	44.3±4.94	0.3
Sex ratio (male : female)	15 : 4 (78.9%)	16 : 4 (80%)	1
BMI (mean±SD, kg/m ²)	25.2±3.73	25.7±3.59	0.679
High BMI (> 25 kg/m ²)	10/19 (52.6%)	10/20 (50%)	1
Smoking (current)*	7/19 (36.8%)	10/20 (50%)	0.408
Heavy alcohol consumption	5/19 (26.3%)	7/20 (35%)	0.557
Hypertension	5/19 (26.3%)	12/20 (60%)	0.034
On medication	4/19 (21.1%)	5/20 (25%)	1
DM	5/19 (26.3%)	0/20 (0%)	0.02
Total cholesterol (mean±SD, mg/dL)*	194.2±31.74	200.8±37.39	0.563
TG (mean±SD, mg/dL)*	140.1±99.42	148.6±88.84	0.783
LDL (mean±SD, mg/dL)*	114.8±23.65	117.3±23.93	0.752
HDL (mean±SD, mg/dL)*	54.0±12.79	52.9±12.69	0.783
HbA1c (mean±SD, %)	6.0±0.89	5.4±0.58	0.03
GCS at admission	13.7±2.57	13.3±2.90	0.584
GOS at discharge ≤3	4/19 (21.1%)	7/20 (35%)	0.48
Expired	1/19 (5.3%)	2/20 (10%)	1
Location of hematoma			0.219
Deep brain	10/19 (52.6%)	9/20 (45%)	
Lobar	6/19 (31.6%)	4/20 (20%)	
Brain stem	0/19 (0%)	4/20 (20%)	
Cerebellum	3/19 (15.8%)	3/20 (15%)	
Volume of hematoma (mean±SD, cc)	22.1±27.44	17.1±22.17	0.53

* Those data was not available in 1 patients

SD, standard deviation; BMI, body mass index; DM, diabetes mellitus; TG, triglyceride; LDL, low density lipoprotein; HDL, high density lipoprotein; HbA1c, hemoglobin A1c; GCS, Glasgow coma scale; GOS, Glasgow outcome scale

Table 4. Logistic regression analysis of risk factors for cerebral small vessel disease in young patients with spontaneous intracerebral hemorrhage

	OR	95% CI	p-value
Hypertension	7.769	1.206-50.024	0.031
DM	< 0.0001		0.999
HbA1c	0.569	0.093-3.464	0.54

OR, odd ratio; CI, confidence interval; DM, diabetes mellitus; HbA1c, hemoglobin A1c

years ($P=0.03$). In the poor-outcome group, the mean GCS score at admission was 8.9 ± 4.05 , which is significantly lower than that of the favorable-outcome group (14.0 ± 1.80 , $P<0.001$). In the poor-outcome group, 23.3% of patients had a GCS score ≥ 14 at admission; this was significantly lower than the proportion in the favorable-outcome group ($P<0.001$). The poor-outcome group (44.3 ± 35.05 mL) also had a significantly higher

mean hematoma volume than the favorable-outcome group (16.1 ± 18.18 mL, $P<0.001$).

DISCUSSION

Establishing a cutoff age for “young age” in the field of stroke is difficult and has not yet been clearly defined.

Table 5. Factors associated with poor outcome

	Poor outcome (GOS≤3)	Favorable outcome (GOS 4 or 5)	p-value
Age (mean±SD, years)	45.1±4.49	42.4±5.95	0.03
Location of hematoma			0.025
Deep brain (40)	16 (40%)	24 (60%)	0.834*
Lobar (19)	6 (31.6%)	13 (68.4%)	0.327 [†]
Brain stem (8)	7 (87.5%)	1 (12.5%)	0.007[‡]
Cerebellum (6)	1 (16.7%)	5 (83.3%)	0.39 [§]
GCS at admission	8.9±4.05	14.0±1.80	<0.001
Volume of hematoma (mean±SD, cc)	44.3±35.05	16.1±18.18	<0.001

* Deep brain vs non-deep brain

[†] Lobar vs non-lobar

[‡] Stem vs non-stem

[§] Cerebellum vs non-cerebellum

GOS, Glasgow outcome scale; SD, standard deviation; GCS, Glasgow coma scale

Previous studies and registries commonly set the age limit at 45 or 50 years.^{4,18)} The decision to focus our study on individuals aged 30–50 was driven by two main considerations: (1) the intention to compare the characteristics between patients in their 30s and 40s, and (2) the observation that the number of non-lesional spontaneous ICH patients below the age 30 was very low, at just around two individuals, which would likely introduce bias if included, thus leading us to narrow the age range 30–50 for our research.

Few studies have investigated the causes of spontaneous ICH in young adults. Ruiz-Sandoval et al.¹⁷⁾ investigated 200 patients diagnosed with spontaneous ICH before reaching 40 years of age, and found that 54.5% had identifiable causative lesions: AVM (33.5%), CM (16%), and CVT (5%). In a study conducted by Chen et al.⁶⁾, among 259 spontaneous ICH patients <45 years of age, 28.6% had structural vasculopathy, and 62.7% of patients between 16 and 30 years old had structural causes. Elmegiri et al.⁸⁾ investigated 116 spontaneous ICH patients 15–49 years old, including only patients who had undergone MR scanning within 3 months of experiencing ICH, and found 50% of the patients to have lesional causes detected by MRI: 23.3% with CMs, 12.9% with AVMs, 7.8% with CVT, 5.2% with tumors, and 0.9% with moyamoya disease. Similar to these previous studies, 63 of 136 patients in our study had

lesional causes. In other words, more than half of the patients diagnosed with ICH (73 of 136) had non-lesional pathology that might have been associated with vascular risk factors.

In other studies investigating spontaneous ICH in young adults, the most common hematoma location has been the cerebral lobes.^{8,17)} In our study, however, the most common location was the deep brain (54.8%) followed by the cerebral lobes (26.0%). This difference may be explained by the fact that previous studies included ICH with lesional causes, unlike our study. Nevertheless, the proportion of lobar ICH in our study was still notably high at 26%, suggesting the need for further research with a larger cohort to validate these findings. The following potential biases could have contributed to the increased proportion of lobar ICH in our study. Firstly, in cases of extensive hemorrhage affecting both deep brain and lobar areas, some of them could be classified to lobar ICH. Secondly, in deceased patients, some vascular causes might be masked in initial CT angiography with no further workup, leading to their enrollment. Since lesional ICH typically has a higher proportion of lobar ICH, this could have consequently influenced the elevated proportion of lobar ICH observed in our study.

After we excluded lesions commonly associated with spontaneous ICH, well-known risk factors for ICH, such

as male sex, hypertension, heavy alcohol consumption, and smoking, were also commonly identified among young patients who were treated for ICH. It is remarkable that the mean BMI (25.0 kg/m^2 , indicating obesity according to the Asia-Pacific BMI classification) was high and that 45.8% of patients were classified as obese ($\text{BMI} > 25 \text{ kg/m}^2$) in this cohort of young patients with spontaneous ICH, diverging from previously determined proportions of older patients with obesity and ICH.

We investigated whether the associations between some factors vary with increasing age. Compared with younger patients in this cohort ($n=21$, age 30–40 years), the older group ($n=52$, age 41–50 years) had more individuals with heavy alcohol consumption, a higher mean hematoma volume, a lower GCS at admission, and poorer outcomes. Half of the older group had poor outcomes. There were no significant differences between the age groups in terms of the sex ratio or proportions of patients with high BMI, smoking histories, hypertension, or cSVD. In the younger group, 41.7% of the patients had cSVD, compared with 55.6% in the older group, with cSVD detectable on imaging as early as the fourth decade of life.

Various pathological processes affecting small vessels of the brain—such as small arteries, arterioles, capillaries, and small veins—are collectively referred to as cSVD.¹⁵⁾ Several neuroimaging markers should be evaluated to determine whether a patient has cSVD: WMH, CMBs, lacunae, and perivascular space.¹⁴⁾ In our study, the MRI findings of 20 patients included WMH or CMBs but few lacunae and minimal perivascular space. Notably, about half of the patients had evidence of cSVD on MRI. Considering the representative cSVDs, namely amyloid cSVD and hypertensive cSVD,^{5,7)} and given that previously diagnosed hypertension and deep-lying hematomas were common in the cSVD group (60% and 45%, respectively), young patients with ICH in our study exhibited evidence of non-amyloid cSVD.

Hypertension has been suggested as the leading risk factor for cardiovascular disease and mortality in many studies, and hypertension at a young age is associated

with an increased incidence and earlier onset of heart failure, coronary heart disease, stroke, and transient ischemic attacks.¹⁰⁾¹⁹⁾²¹⁾ Early-onset uncontrolled hypertension in young adults seems to disrupt the blood-brain barrier and evoke endothelial dysfunction in small cerebral vessels. Our study demonstrated that hypertension was the independent risk factor for cSVD in young ICH patients. Early management and detection of hypertension may be beneficial in preventing cSVD among young adults.

In several studies investigating neurologic outcomes after spontaneous ICH, lower GCS scores at admission, medical comorbidities, high hematoma volume, and rebleeding or expansion after primary bleeding have been associated with poorer outcomes.^{1–3)} Broderick et al.²⁾ found hematoma volume to be the most powerful predictor of 30-day mortality and demonstrated that we can predict 91% of the 30-day mortality using the criteria of hematoma volume $>60 \text{ mL}$ and GCS score >8 . We observed similar results: low GCS at admission and high hematoma volume were associated with poor outcomes in our study. Additionally, hematoma location in the brain stem and age were associated with poor outcomes.

Favorable outcomes (GOS 4 or 5) were observed in 58.9% of patients who were able to live independently, while 41.1% had poor outcomes (with 19.2% dying and 21.9% requiring assistance in their daily living). This substantial proportion of patients reflected worse outcomes than those determined by other studies. Ruíz-Sandoval et al.,⁴⁾ in their study of ICH patients younger than 40 years, 8% died, and 60% had favorable outcomes; however, when only hypertension-related ICH was considered, 27.3% died, and only 31.8% had favorable outcomes.¹⁷⁾ We can speculate that hypertension-associated ICH may generally lead to worse outcomes than lesional ICH. Considering the poor outcomes associated with non-lesional spontaneous ICH, more attention should be paid to primary prevention through lifestyle modifications and hypertension treatment in younger patients.

This study had several limitations. First, we were

unable to determine risk factors for ICH in young adults due to the absence of a control group. Further comparative studies with appropriate control groups will be needed. Second, among the patients who died, it is possible that structural lesions were missed owing to a lack of investigation with imaging studies, such as MRI or transfemoral cerebral angiography. There might also have been a selection bias against MRI because it was highly likely that patients who died or ended up in a vegetative state did not undergo MRI. Third, we might have underestimated the prevalence of hypertension because many young people would not have been screened for high blood pressure before experiencing ICH.

CONCLUSIONS

Although this study had a small sample size and limited patient group, we found that hypertension, obesity, smoking, and cSVD were important factors associated with ICH among patients aged 30–50 years. Deep-lying ICH was most common. Patients as young as those in their 30s exhibited imaging evidence of cSVD, which was associated with previously diagnosed hypertension.

Disclosure

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REFERENCES

1. An SJ, Kim TJ, Yoon BW. Epidemiology, risk factors, and clinical features of intracerebral hemorrhage: An update. *J Stroke*. 2017 Jan;19(1):3-10.
2. Broderick JP, Brott TG, Duldner JE, Tomsick T, Huster G. Volume of intracerebral hemorrhage. A powerful and easy-to-use predictor of 30-day mortality. *Stroke*. 1993 Jul;24(7):987-93.
3. Brott T, Broderick J, Kothari R, Barsan W, Tomsick T, Sauerbeck L, et al. Early hemorrhage growth in patients with intracerebral hemorrhage. *Stroke*. 1997 Jan;28(1):1-5.
4. Bukhari S, Yaghi S, Bashir Z. Stroke in young adults. *J Clin Med*. 2023 Jul 29;12(15):49999.
5. Charidimou A, Jäger HR. Developing biomarkers for cerebral amyloid angiopathy trials: do potential disease phenotypes hold promise? *Lancet Neurol*. 2014 Jun;13(6):538-40.
6. Chen CY, Lin PT, Wang YH, Syu RW, Hsu SL, Chang LH, et al. Etiology and risk factors of intracranial hemorrhage and ischemic stroke in young adults. *J Chin Med Assoc*. 2021 Oct;84(10):930-6.
7. Cuadrado-Godia E, Dwivedi P, Sharma S, Ois Santiago A, Roquer Gonzalez J, Balcells M, et al. Cerebral small vessel disease: A review focusing on pathophysiology, biomarkers, and machine learning strategies. *J Stroke*. 2018 Sep;20(3):302-20.
8. Elmegiri M, Koivunen RJ, Tatlisumak T, Putaala J, Martola J. MRI characterization of non-traumatic intracerebral hemorrhage in young adults. *Front Neurol*. 2020 Oct 29;11:558680.
9. Fazekas F, Chawluk JB, Alavi A, Hurtig HI, Zimmerman RA. MR signal abnormalities at 1.5 T in Alzheimer's dementia and normal aging. *AJR Am J Roentgenol*. 1987 Aug;149(2):351-6.
10. Hinton TC, Adams ZH, Baker RP, Hope KA, Paton JFR, Hart EC, et al. Investigation and treatment of high blood pressure in young people: Too much medicine or appropriate risk reduction? *Hypertension*. 2020 Jan;75(1):16-22.
11. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet*. 1975 Mar;1(7905):480-4.
12. Kothari RU, Brott T, Broderick JP, Barsan WG, Sauerbeck LR, Zuccarello M, et al. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke*. 1996 Aug;27(8):1304-5.
13. Mailles A, De Broucker T, Costanzo P, Martinez-Almoyna L, Vaillant V, Stahl JP. Long-term outcome of patients presenting with acute infectious encephalitis of various causes in France. *Clin Infect Dis*. 2012 May;54(10):1455-64.
14. Norrving B. Evolving concept of small vessel disease through advanced brain imaging. *J Stroke*. 2015 May;17(2):94-100.
15. Pantoni L. Cerebral small vessel disease: from pathogenesis and clinical characteristics to therapeutic challenges. *Lancet Neurol*. 2010 Jul;9(7):689-701.
16. Qureshi AI, Tuhim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. *N Engl J Med*. 2001 May;344(19):1450-60.
17. Ruiz-Sandoval JL, Cantú C, Barinagarrementeria F. Intracerebral hemorrhage in young people: analysis of risk factors, location, causes, and prognosis. *Stroke*. 1999 Mar;30(3):537-41.

18. Smajlović D. Strokes in young adults: epidemiology and prevention. *Vasc Health Risk Manag*. 2015 Feb;11:157-64.
19. Sundström J, Neovius M, Tynelius P, Rasmussen F. Association of blood pressure in late adolescence with subsequent mortality: Cohort study of Swedish male conscripts. *BMJ*. 2011 Feb 22;342:d643.
20. van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol*. 2010 Feb;9(2):167-76.
21. Yano Y, Reis JP, Colangelo LA, Shimbo D, Viera AJ, Allen NB, et al. Association of blood pressure classification in young adults using the 2017 American college of cardiology/American heart association blood pressure guideline with cardiovascular events later in life. *JAMA*. 2018 Nov 6;320(17):1774-82.