ORIGINAL WORK



Clinical, Imaging Characteristics and Outcome of Intracerebral Hemorrhage Caused by Structural Vascular Lesions

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Abstract

Background: The objective of this study was to investigate the clinical, imaging, and outcome characteristics of intracerebral hemorrhage (ICH) caused by structural vascular lesions.

Methods: We retrospectively analyzed data from a prospective observational cohort study of patients with spontaneous ICH admitted to the First Affiliated Hospital of Chongqing Medical University between May 2016 and April 2021. Good outcome was defined as modified Rankin Scale score of 0–3 at 3 months. The clinical and imaging characteristics were compared between primary ICH and ICH caused by structural vascular lesions. Multivariable logistic regression analysis was performed to test the associations of etiology with clinical outcome.

Results: All patients enrolled in this study were Asian. Compared with patients with primary ICH, those with structural vascular lesions were younger (48 vs. 62 years, P < 0.001), had a lower incidence of hypertension (26.4% vs. 81.7%, P < 0.001) and diabetes (7.4% vs. 16.2%, P = 0.003), and had mostly lobar hemorrhages (49.1% vs. 22.8%). ICH from structural vascular lesions had smaller baseline hematoma volume (8.4 ml vs. 13.8 ml, P = 0.010), had lower mortality rate at 30 days and 3 months (5.8% vs. 12.0%, P = 0.020; 6.7% vs. 14.8%, P = 0.007), and are associated with better functional outcome at 3 months (88% vs.70.3%, P < 0.001).

Conclusions: Compared with primary ICH, ICH due to vascular lesions has smaller hematoma volume and less severe neurological deficit at presentation and better functional outcomes.

Keywords: Intracerebral hemorrhage, Structural vascular lesion, Hematoma, Outcome

Introduction

Intracerebral hemorrhage (ICH) is a devastating type of stroke characterized by hemorrhage in the brain parenchyma [1]. ICH accounts for 10-15% of all strokes in the United States [2, 3], but is more prevalent in China [4, 5]. ICH can be caused by different etiologies [6, 7]. The Structural lesion, Medication, Amyloid angiopathy, Systemic/other disease, Hypertension, Undetermined

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The clinical, imaging, and prognosis have been extensively studied in patients with primary ICH without a demonstrated structural or traumatic cause [10]; however, analyses of secondary ICH associated with vascular lesions are sparse. Emerging studies suggested that ICH due to structural vascular lesion have better functional outcomes and lower mortality [9, 11, 12], but the specific mechanism and hematoma characteristics are poorly



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understood. The main purpose of this study was to compare the clinical, imaging, and prognosis of primary ICH and ICH associated with structural vascular lesion, so as to better understand the clinical and imaging features of ICH with different etiologies.

Methods

Standard Protocol Approvals, Registrations, and Patient Consents

This study was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. Informed consent was obtained from all participants or their legal representatives.

Patient Selection

We retrospectively analyzed data from a prospective observational cohort study of consecutive patients presenting with ICH at the First Affiliated Hospital of Chongqing Medical University between May 2016 and April 2021. Patients were eligible for our study if they were diagnosed with spontaneous ICH and had completed computed tomography (CT) examination. All patients were classified etiologically according to the SMUSH-U method [8], as described in Fig. 1. We included in this analysis those with ICH from a structural vascular lesion and those with primary ICH. Patients with ICH due to secondary causes (e.g., anticoagulants, systemic diseases) were excluded.

Data Collection

The demographic and clinical data including age, sex, the status of smoking and alcohol, past medical history and drug use, the admission blood pressure (BP), and blood test results were obtained. The admission Glasgow Coma Scale (GCS) score and the admission National Institute of Health stroke scale (NIHSS) score were prospectively collected. All CT, CT angiography, or magnetic resonance imaging (MRI) examinations were independently reviewed by two trained neurologists who were blinded to clinical data and outcome. The hematoma volume was calculated by the semiautomated, computer-assisted volumetric analysis (Analyze 12.0, Mayo Clinic, Rochester, MN) as described [13, 14]. The primary outcome was assessed using modified Rankin Scale (mRS) score at 3 months after discharge. Good outcome was defined as an mRS score of 0-3 [15]. Functional independence was defined as an mRS score of 0-2 [16]. In addition, 30-day and 3-month mortality rates were recorded.

Statistical Analysis

Statistical analyses were performed using SPSS (version 25.0, IBM Corp, Armonk, NY). Continuous variables were expressed as medians with interquartile ranges

due to the nonnormal distribution. Categorical variables were provided as percentages (%). The nearest neighbor propensity score matching (caliper = 0.02, ratio = 2) was used to reduce selection bias by matching patients with primary ICH and those with structural vascular lesions. Confounding factors, including age, sex, current smoking, alcohol consumption, hypertension, systolic BP (mm Hg), diastolic BP (mm Hg), diabetes, coronary heart disease, antiplatelet, and statin, were chosen for matching. The propensity score matching was conducted by R software. The baseline demographic, clinical, and imaging characteristics were compared between primary ICH and vascular lesion group, using Kruscal Whallis H tests or χ^2 tests, as appropriate. We used multivariable logistic regression analysis to investigate factors associated with good outcome and functional independence at 3 months after discharge. All P values presented are two-sided, and a P value of 0.05 or less is considered statistically significant.

Results

Between May 2016 and April 2021, a total of 1,515 patients with spontaneous ICH who had complete imaging data were included in our database at the First Affiliated Hospital of Chongqing Medical University. Of these, 1,318 (87%) were primary ICH and 163 (10.76%) were diagnosed as ICH due to structural vascular lesion. Of 163 patients diagnosed with ICH due to vascular lesions, 73 (44.79%) were arteriovenous malformation (AVM), 38 (23.31%) were cavernous angioma, 19 (11.66%) were cerebral aneurysm, 19 (11.66%) were moyamoya disease, 8 (4.91%) were venous malformations, and 6 (3.68%) were arteriovenous fistula.

Compared with patients with primary ICH, those with structural vascular lesions were younger (48 vs. 62 years, *P*<0.001), less likely to smoke (33.7% vs. 43.1%, P=0.022) and consume alcohol (19.0% vs. 30.7%, P = 0.001), had lower incidence of hypertension (26.4% vs. 81.7%, P<0.001) and diabetes (7.4% vs. 16.2%, P = 0.003), and were more likely to have seizures (9.2%) vs. 3.0%, P < 0.001). Notably, patients with ICH who had vascular lesions were more likely to have a prior history of ICH events (16.6% vs. 7.2%, P<0.001) and the blood pressure levels were significantly lower than those with primary ICH (systolic BP 131.5 mm Hg vs. 169 mm Hg, P<0.001; diastolic BP 80 mm Hg vs. 96 mm Hg, P < 0.001). The baseline hematoma volume was significantly smaller in patients with ICH who had structural vascular lesions than those with primary ICH (8.4 ml vs. 13.8 ml, P = 0.010), but there were no differences in the prevalence of intraventricular hemorrhage (IVH) (37.0% vs. 33.6%, *P*=0.389) and IVH volume (2.41 ml vs. 2.14 ml, P = 0.281).



Patients with ICH who had vascular lesions were more prone to have a longer median time from symptom onset to hospital admission (24 h vs. 6.5 h, P < 0.001) compared with patients with primary ICH. However, there were no differences in the incidence of wake-up ICH (5.5% vs. 7.4%, P=0.390). Furthermore, ICH from structural vascular lesions had higher admission GCS (14 vs. 13, P=0.009), lower admission NIHSS (3 vs. 12, P < 0.001), and lower mortality rates at 30 days (5.8% vs. 12.0%, P=0.020) and 3 months (6.7% vs. 14.8%, P=0.007). The proportion of patients who had good outcome (mRS 0–3) were significantly more in structural vascular lesions than primary ICH (88.0% vs. 70.3%, P < 0.001).

The most common bleeding site for primary ICH is basal ganglia (45.8%), followed by cerebral lobes (22.8%) and thalamus (16.0%) (Table 1). However, lobar hemorrhage (49.1%) is the most common type of bleeding for patients with vascular structural lesions, followed by basal ganglia (15.3%) and then brain stem (12.3%). Compared with primary ICH, cerebellar or primary IVH were more common in vascular structure lesions (11.7% vs. 6.5%, 4.9% vs. 1.6%, P < 0.001).

Primary ICH (n = 1318) vascular lesion (n = 103) Pvalue (n = 103) Pvalue (n = 103) Pvalue (n = 103) Pvalue (n = 103) Race Asian Asian Asian Male sex 914 (69.3) 90 (55.2) <0001 104 (58.8) 50 (65.7) 0.74 Onset-to-admission 65 (3 - 24) 24 (5 - 96) <0001 13 (7.3) 6 (58.7) 0.74 Vaske-up ICH 97 (7.4) 9 (55.5) 0.390 13 (7.3) 6 (58.7) 0.724 Vaske-up ICH 97 (7.4) 9 (55.7) 0.300 13 (7.3) 6 (58.7) 0.724 Vaske-up ICH 97 (7.4) 9 (55.7) 0.301 3 (2.03) 2 (2.1) 0.724 Vaske-up ICH 97 (7.4) 9 (52.1) 0.001 3 (2.03) 2 (2.1) 0.724 Vaske-up ICH 97 (7.8) 3 (1.9) 0.001 3 (2.03) 2 (2.1) 0.724 Systake BP (mm Hg) 96 (83-110) 80 (7.2) 2.216 6.34 4 (3.8) 0.822 Dabstofe BP (mm Hg) <t< th=""><th rowspan="2">Variables</th><th colspan="3">Before matching</th><th colspan="3">After matching</th></t<>	Variables	Before matching			After matching		
Race Asian Asian Age 62 (50–70) 48 (29–54) < 0001 50 (39–64) 51 (46.5–63) 0.051 Male sox 914 (69.3) 90 (55.2) < 0.001 104 (58.8) 59 (56.7) 0.740 OnSetto-admission 65 (3–24) 24 (5–96) < 0.001 55 (3–14) 10.54 (4–60) 0.011 tme (b) 97 (7.4) 9 (5.5) 0.390 13 (7.3) 6 (5.8) 0.613 Valke-up (CH 97 (7.4) 9 (5.5) 0.390 13 (7.3) 6 (5.8) 0.051 Alcohol consumption 405 (30.7) 31 (19.0) 0.001 36 (20.3) 23 (2.1) 0.724 Hypertension 107 (81.7) 43 (26.4) <0.001 81 (21.16.9) 0.322 Diabetes 213 (16.2) 12 (7.4) 0.003 18 (17.2) 0.425 Coronary heart disease 69 (5.2) 3 (1.8) 0.57 84 (3.9) 0.435 Statin 44 (3.3) 2 (1.2) 0.143 4 (2.3) 2 (1.9) 0.850		Primary ICH (<i>n</i> = 1318)	vascular lesion (n = 163)	<i>P</i> value	Primary ICH (<i>n</i> = 177)	vascular lesion (n = 104)	<i>P</i> value
Age 62 (50-70) 48 (29-54) < 000 50 (39-64) 51 (46.5-63) 0.051 Male sex 91 (69.3) 90 (55.2) < 0.001	Race	Asian			Asian		
Male sex 914 (69.3) 90 (55.2) < 0001 104 (58.8) 59 (56.7) 0.740 Onsert-oradmission time (n) 6.5 (3–24) 24 (5–96) < 0001	Age	62 (50–70)	48 (29–54)	< 0.001	50 (39–64)	51 (46.5–63)	0.051
Onsett-oadmission time (h) 6.5 (3–24) 24 (5–96) <0.001 5.5 (3–14) 10.54 (4–60) 0.011 time (h) 9 (7.4) 9 (5.5) 0.309 13 (7.3) 6 (5.8) 0.612 Current smoking 56 (3.1) 5 (33.7) 0.022 68 (38.4) 40 (38.5) 0.994 Alcohol consumption 405 (30.7) 31 (19.0) 0.011 36 (20.3) 23 (21.1) 0.724 Systolic BP (mm Hg) 169 (151–190) 131.5 (121–151) <0.001 142 (131–169) 142.5 (125–163.5) 0.382 Diabetes 213 (16.2) 12 (7.4) 0.001 81 (72–102) 855 (76.5–100) 0.852 Coronary heart disease 69 (5.2) 31 (18.0) 0.057 8 (4.5) 3 (2.9) 0.455 Coronary heart disease 69 (5.2) 31 (19.0) 0.18 23 (13.0) 25 (24.0) 0.035 Coronary heart disease 69 (5.2) 31 (21.2) 0.14 4 (2.3) 20 (19.2) 0.001 Stripic dist 44 (3.3) 21 (16.0 32 (19.6) 0.025	Male sex	914 (69.3)	90 (55.2)	< 0.001	104 (58.8)	59 (56.7)	0.740
Wake-up ICH 97 (7.4) 9 (5.5) 0.390 13 (7.3) 6 (5.8) 0.612 Current smoking 568 (43.1) 55 (3.7) 0.02 68 (34.3) 23 (2.1) 0.724 Alcohol consumption 405 (0.7) 31 (19.0) 0.001 86 (45.2) 23 (2.1) 0.724 Hypertension 107 (81.7) 43 (26.4) <.0001	Onset-to-admission time (h)	6.5 (3–24)	24 (5–96)	< 0.001	5.5 (3–14)	10.54 (4–60)	0.011
Current smoking 56 (84.1) 55 (33.7) 0.022 68 (84.) 40 (38.5) 0.994 Alcohol consumption 405 (30.7) 31 (19.0) 0.001 36 (20.3) 23 (2.1) 0.724 Hypertension 1077 (81.7) 43 (26.4) <0.001	Wake-up ICH	97 (7.4)	9 (5.5)	0.390	13 (7.3)	6 (5.8)	0.612
Alcohol consumption 405 (30.7) 31 (19.0) 0.001 36 (20.3) 23 (22.1) 0.724 Hypertension 1077 (81.7) 43 (26.4) <.0001 80 (20.2) 43 (41.3) 0.530 Systolic BP (mm Hg) 169 (151-190) 131.5 (121-151) <.0001 142 (131-169) 142.5 (125-163.5) 0.382 Diabetes 213 (16.2) 12 (7.4) 0.003 19 (10.7) 10 (9.6) 0.766 Coronary heart disease 69 (5.2) 3 (18) 0.057 8 (45) 3 (2.9) 0.842 Statin 44 (3.3) 21 (12.0) 0.18 23 (13.0) 25 (2.40) 0.081 Previous Storke 20 (5 1.5) 32 (19.5) 0.18 23 (13.0) 25 (2.40) 0.018 Previous Storke 95 (7.2) 27 (16.6) <.001 11 (6.2) 20 (19.2) 0.010 Breading site (central-point Hord) 15 (8.2) 31 (12.0) 20 (19.2) 20 (10.2) 20 (10.2) Breading site (central-point Hord) 11 (6.7) 16 (9.0) 43 (2.7) 4 (3.8) 20 (10	Current smoking	568 (43.1)	55 (33.7)	0.022	68 (38.4)	40 (38.5)	0.994
Hypertension 1077 (81.7) 43 (26.4) < 0.001 80 (45.2) 43 (41.3) 0.530 Systolic BP (mm Hg) 169 (151-190) 131.5 (121-151) < 0.001	Alcohol consumption	405 (30.7)	31 (19.0)	0.001	36 (20.3)	23 (22.1)	0.724
Systolic BP (mm Hg) 169 (151–190) 131.5 (121–151) <0.001	Hypertension	1077 (81.7)	43 (26.4)	< 0.001	80 (45.2)	43 (41.3)	0.530
Diastolic BP (mm Hg) 96 (83-110) 80 (70-89) < 0.001 81 (72-102) 85 5 (76.5-100) 0.852 Diabetes 213 (16.2) 12 (7.4) 0.003 19 (10.7) 10 (9.6) 0.766 Coronary heart disease 69 (5.2) 3 (1.8) 0.057 8 (4.5) 3 (2.9) 0.495 Athiplatelet 59 (4.5) 4 (2.5) 0.27 6 (3.4) 4 (3.8) 0.852 Statin 44 (3.3) 2 (1.2) 0.143 4 (2.3) 2 (1.9) 0.018 Previous Stroke 205 (15.6) 32 (19.6) 0.18 23 (13.0) 25 (24.0) 0.018 Previous ICH 95 (7.2) 27 (16.6) 0.001 11 (6.2) 20 (19.2) 0.001 Thrombocytes (E9/L) 181 (140-22.5) 192 (166-231) 0.002 6 (3.4) 8 (7.7) 0.109 Beading site (central-pointmethed) <<0.001	Systolic BP (mm Hg)	169 (151–190)	131.5 (121–151)	< 0.001	142 (131–169)	142.5 (125–163.5)	0.382
Diabetes 213 (16.2) 12 (7.4) 0.003 19 (10.7) 10 (9.6) 0.766 Coronary heart disease 69 (5.2) 3 (1.8) 0.057 8 (4.5) 3 (2.9) 0.4495 Antiplatelet 59 (4.5) 4 (2.5) 0.227 6 (3.4) 4 (3.8) 0.842 Statin 4 (3.3) 2 (1.2) 0.143 4 (2.3) 2 (1.9.0) 0.808 Previous Stroke 205 (1.5.6) 3 (1.9.0) 11 (6.2) 2 (1.9.0) 0.001 Thombocytes (E9/L) 181 (140-225) 192 (166-231) 0.025 183 (141-224) 182.5 (162-230.5) 0.245 Seizures 40 (3.0) 15 (9.2) <0.001	Diastolic BP (mm Hg)	96 (83–110)	80 (70–89)	< 0.001	81 (72–102)	85.5 (76.5–100)	0.852
Coronary heart disease 69 (5.2) 3 (1.8) 0.057 8 (4.5) 3 (2.9) 0.495 Antiplatelet 59 (4.5) 4 (2.5) 0.227 6 (3.4) 4 (3.8) 0.842 Statin 44 (3.3) 2 (1.2) 0.143 4 (2.3) 2 (1.9) 0.850 Previous Stroke 205 (15.6) 32 (19.6) 0.18 23 (13.0) 25 (24.0) 0.018 Previous CH 95 (7.2) 27 (16.6) <0.001	Diabetes	213 (16.2)	12 (7.4)	0.003	19 (10.7)	10 (9.6)	0.766
Antiplatelet 59 (4.5) 4 (2.5) 0.227 6 (3.4) 4 (3.8) 0.842 Statin 44 (3.3) 2 (1.2) 0.143 4 (2.3) 2 (1.9) 0.850 Previous Stroke 205 (1.5.6) 32 (19.6) 0.18 23 (13.0) 25 (24.0) 0.018 Previous ICH 95 (7.2) 27 (16.6) <0.001	Coronary heart disease	69 (5.2)	3 (1.8)	0.057	8 (4.5)	3 (2.9)	0.495
Statin 44 (3.3) 2 (1.2) 0.143 4 (2.3) 2 (1.9) 0.850 Previous Stroke 205 (15.6) 32 (19.6) 0.18 23 (13.0) 25 (24.0) 0.018 Previous ICH 95 (7.2) 27 (16.6) <0.001	Antiplatelet	59 (4.5)	4 (2.5)	0.227	6 (3.4)	4 (3.8)	0.842
Previous Stroke 205 (15.6) 32 (19.6) 0.18 23 (13.0) 25 (24.0) 0.018 Previous ICH 95 (7.2) 27 (16.6) <0.001	Statin	44 (3.3)	2 (1.2)	0.143	4 (2.3)	2 (1.9)	0.850
Previous ICH 95 (7.2) 27 (16.6) < 0.001 11 (6.2) 20 (19.2) 0.001 Thrombocytes (E9/L) 181 (140-225) 192 (166-231) 0.025 183 (141-224) 182.5 (162-230.5) 0.245 Seizures 40 (3.0) 15 (9.2) < 0.001	Previous Stroke	205 (15.6)	32 (19.6)	0.18	23 (13.0)	25 (24.0)	0.018
Thrombocytes (E9/L) 181 (140–225) 192 (166–231) 0.025 183 (141–224) 182.5 (162–230.5) 0.245 Seizures 40 (3.0) 15 (9.2) <0.001	Previous ICH	95 (7.2)	27 (16.6)	< 0.001	11 (6.2)	20 (19.2)	0.001
Seizures 40 (3.0) 15 (9.2) < 0.001 6 (3.4) 8 (7.7) 0.109 Bleeding site (central-point method) < 0.001	Thrombocytes (E9/L)	181 (140–225)	192 (166–231)	0.025	183 (141–224)	182.5 (162–230.5)	0.245
Bleeding site (central-point method) < 0.001	Seizures	40 (3.0)	15 (9.2)	< 0.001	6 (3.4)	8 (7.7)	0.109
Basal ganglia 603 (45.8) 25 (15.3) 80 (45.2) 20 (19.2) Thalamus 211 (16.0) 11 (6.7) 16 (9.0) 4 (3.8) Lobar 301 (22.8) 80 (49.1) 48 (27.1) 47 (45.2) Brainstem 96 (7.3) 20 (12.3) 11 (6.2) 14 (13.5) Cerebellar 86 (6.5) 19 (11.7) 15 (8.5) 13 (12.5) Primary IVH 21 (1.6) 8 (4.9) 7 (4.0) 6 (5.8) ICH volume (mL) 13.8 (5.3–37.2) 8.4 (2.7–24.3) 0.010 15.3 (5.28–37.32) 5.64 (2.0–15.72) 0.004 Existing IVH* 443/1,317 (33.6) 60/162 (37.0) 0.389 50/177 (28.2) 35/103 (34.0) 0.314 VH volume (mL) 2.14 (0–10.15) 2.41 (0.27–12.97) 0.281 1.89 (0–10.47) 2.70 (0–15.88) 0.487 Admission GCS 13 (8–15) 14 (9–15) 0.009 12 (7–15) 14 (8.5–15) 0.350 Admission NIHSS 12 (4–26) 3 (1–17) <0.001	Bleeding site (central-poi	nt method)		< 0.001			< 0.001
Thalamus 211 (16.0) 11 (6.7) 16 (9.0) 4 (3.8) Lobar 301 (22.8) 80 (49.1) 48 (27.1) 47 (45.2) Brainstem 96 (7.3) 20 (12.3) 11 (6.2) 14 (13.5) Cerebellar 86 (6.5) 19 (11.7) 15 (8.5) 13 (12.5) Primary IVH 21 (1.6) 8 (4.9) 7 (4.0) 6 (5.8) ICH volume (mL) 13.8 (5.3–37.2) 8.4 (2.7–24.3) 0.010 15.3 (5.28–37.32) 5.64 (2.0–15.72) 0.004 Existing IVH* 443/1,317 (33.6) 60/162 (37.0) 0.389 50/177 (28.2) 35/103 (34.0) 0.314 VH volume (mL) 2.14 (0–10.15) 2.41 (0.27–12.97) 0.281 1.89 (0–10.47) 2.70 (0–15.88) 0.487 Admission GCS 13 (8–15) 14 (9–15) 0.009 12 (7–15) 14 (8.5–15) 0.350 Admission NIHSS 12 (4–26) 3 (1–17) <0.001	Basal ganglia	603 (45.8)	25 (15.3)		80 (45.2)	20 (19.2)	
Lobar 301 (22.8) 80 (49.1) 48 (27.1) 47 (45.2) Brainstem 96 (7.3) 20 (12.3) 11 (6.2) 14 (13.5) Cerebellar 86 (6.5) 19 (11.7) 15 (8.5) 13 (12.5) Primary IVH 21 (1.6) 8 (4.9) 7 (4.0) 6 (5.8) ICH volume (mL) 13.8 (5.3–37.2) 8.4 (2.7–24.3) 0.010 15.3 (5.28–37.32) 5.64 (2.0–15.72) 0.004 Existing IVH* 443/1,317 (33.6) 60/162 (37.0) 0.389 50/177 (28.2) 35/103 (34.0) 0.314 IVH volume (mL) 2.14 (0–10.15) 2.41 (0.27–12.97) 0.281 1.89 (0–10.47) 2.70 (0–15.88) 0.487 Admission GCS 13 (8–15) 14 (9–15) 0.009 12 (7–15) 14 (8.5–15) 0.350 Admission NIHSS 12 (4–26) 3 (1–17) <0.001	Thalamus	211 (16.0)	11 (6.7)		16 (9.0)	4 (3.8)	
Brainstem 96 (7.3) 20 (12.3) 11 (6.2) 14 (13.5) Cerebellar 86 (6.5) 19 (11.7) 15 (8.5) 13 (12.5) Primary IVH 21 (1.6) 8 (4.9) 7 (4.0) 6 (5.8) ICH volume (mL) 13.8 (5.3–37.2) 8.4 (2.7–24.3) 0.010 15.3 (5.28–37.32) 5.64 (2.0–15.72) 0.004 Existing IVH* 443/1,317 (33.6) 60/162 (37.0) 0.389 50/177 (28.2) 35/103 (34.0) 0.314 NH volume (mL) 2.14 (0–10.15) 2.41 (0.27–12.97) 0.281 1.89 (0–10.47) 2.70 (0–15.88) 0.487 Admission GCS 13 (8–15) 14 (9–15) 0.009 12 (7–15) 14 (8.5–15) 0.350 Admission NIHSS 12 (4–26) 3 (1–17) <0.001	Lobar	301 (22.8)	80 (49.1)		48 (27.1)	47 (45.2)	
Cerebellar86 (6.5)19 (11.7)15 (8.5)13 (12.5)Primary IVH21 (1.6)8 (4.9)7 (4.0)6 (5.8)ICH volume (mL)13.8 (5.3–37.2)8.4 (2.7–24.3)0.01015.3 (5.28–37.32)5.64 (2.0–15.72)0.004Existing IVH*443/1,317 (33.6)60/162 (37.0)0.38950/177 (28.2)35/103 (34.0)0.314IVH volume (mL)2.14 (0–10.15)2.41 (0.27–12.97)0.2811.89 (0–10.47)2.70 (0–15.88)0.487Admission GCS13 (8–15)14 (9–15)0.00912 (7–15)14 (8.5–15)0.350Admission NIHSS12 (4–26)3 (1–17)<0.001	Brainstem	96 (7.3)	20 (12.3)		11 (6.2)	14 (13.5)	
Primary IVH21 (1.6)8 (4.9)7 (4.0)6 (5.8)ICH volume (mL)13.8 (5.3-37.2)8.4 (2.7-24.3)0.01015.3 (5.28-37.32)5.64 (2.0-15.72)0.004Existing IVH*443/1,317 (33.6)60/162 (37.0)0.38950/177 (28.2)35/103 (34.0)0.314IVH volume (mL)2.14 (0-10.15)2.41 (0.27-12.97)0.2811.89 (0-10.47)2.70 (0-15.88)0.487Admission GCS13 (8-15)14 (9-15)0.00912 (7-15)14 (8.5-15)0.350Admission NIHSS12 (4-26)3 (1-17)<0.001	Cerebellar	86 (6.5)	19 (11.7)		15 (8.5)	13 (12.5)	
ICH volume (mL) 13.8 (5.3–37.2) 8.4 (2.7–24.3) 0.010 15.3 (5.28–37.32) 5.64 (2.0–15.72) 0.004 Existing IVH* 443/1,317 (33.6) 60/162 (37.0) 0.389 50/177 (28.2) 35/103 (34.0) 0.314 IVH volume (mL) 2.14 (0–10.15) 2.41 (0.27–12.97) 0.281 1.89 (0–10.47) 2.70 (0–15.88) 0.487 Admission GCS 13 (8–15) 14 (9–15) 0.009 12 (7–15) 14 (8.5–15) 0.350 Admission NIHSS 12 (4–26) 3 (1–17) <0.001	Primary IVH	21 (1.6)	8 (4.9)		7 (4.0)	6 (5.8)	
Existing IVH* 443/1,317 (33.6) 60/162 (37.0) 0.389 50/177 (28.2) 35/103 (34.0) 0.314 IVH volume (mL) 2.14 (0-10.15) 2.41 (0.27-12.97) 0.281 1.89 (0-10.47) 2.70 (0-15.88) 0.487 Admission GCS 13 (8-15) 14 (9-15) 0.009 12 (7-15) 14 (8.5-15) 0.350 Admission NIHSS 12 (4-26) 3 (1-17) <0.001	ICH volume (mL)	13.8 (5.3–37.2)	8.4 (2.7–24.3)	0.010	15.3 (5.28–37.32)	5.64 (2.0–15.72)	0.004
WH volume (mL) 2.14 (0–10.15) 2.41 (0.27–12.97) 0.281 1.89 (0–10.47) 2.70 (0–15.88) 0.487 Admission GCS 13 (8–15) 14 (9–15) 0.009 12 (7–15) 14 (8.5–15) 0.350 Admission NIHSS 12 (4–26) 3 (1–17) <0.001	Existing IVH*	443/1,317 (33.6)	60/162 (37.0)	0.389	50/177 (28.2)	35/103 (34.0)	0.314
Admission GCS 13 (8–15) 14 (9–15) 0.009 12 (7–15) 14 (8.5–15) 0.350 Admission NIHSS 12 (4–26) 3 (1–17) <0.001	IVH volume (mL)	2.14 (0-10.15)	2.41 (0.27–12.97)	0.281	1.89 (0-10.47)	2.70 (0-15.88)	0.487
Admission NIHSS 12 (4–26) 3 (1–17) < 0.001 12 (3–35) 3 (1–16.5) < 0.001 Mortality at 30 days ^a 151/1256 (12.0) 9/156 (5.8) 0.020 16/165 (9.7) 6/101 (5.9) 0.280 good outcome at 3 months ^a 869/1237 (70.3) 132/150 (88.0) < 0.001	Admission GCS	13 (8–15)	14 (9–15)	0.009	12 (7–15)	14 (8.5–15)	0.350
Mortality at 30 days ^a 151/1256 (12.0) 9/156 (5.8) 0.020 16/165 (9.7) 6/101 (5.9) 0.280 good outcome at 3 months ^a 869/1237 (70.3) 132/150 (88.0) <0.001	Admission NIHSS	12 (4–26)	3 (1–17)	< 0.001	12 (3–35)	3 (1–16.5)	< 0.001
good outcome at 3 months ^a 869/1237 (70.3) 132/150 (88.0) < 0.001	Mortality at 30 days ^a	151/1256 (12.0)	9/156 (5.8)	0.020	16/165 (9.7)	6/101 (5.9)	0.280
Functional independ- 734/1232 (59.6) 125/150 (83.3) < 0.001 102/162 (63.0)	good outcome at 3 months ^a	869/1237 (70.3)	132/150 (88.0)	< 0.001	124/162 (76.5)	86/98 (87.8)	0.026
Mortality at 3 months ^a 183/1238 (14.8) 10/150 (6.7) 0.007 17/162 (10.5) 7/98 (7.1) 0.366	Functional independ- ence at 3 months ^a	734/1232 (59.6)	125/150 (83.3)	< 0.001	102/162 (63.0)	80/98 (81.6)	0.001
	Mortality at 3 months ^a	183/1238 (14.8)	10/150 (6.7)	0.007	17/162 (10.5)	7/98 (7.1)	0.366

Table 1 Characteristics of patients with primary ICH and those with structural vascular lesions before and after propensity score matching

All values are median (interquartile range) or n (%)

BP blood pressure, ICH intracerebral hemorrhage, IVH intraventricular hemorrhage, GCS Glasgow Coma Scale, NIHSS National Institutes of Health Stroke Scale

 $^{\rm a}\,$ There are missing values in this item, and the exact data are listed in the table

Significant covariates from univariate analyses with P < 0.1 and other variables chosen for their potential clinical relevance (etiology, age, sex, hypertension, diabetes, previous ICH, admission GCS, ICH volume, and IVH volume) were included in multivariable models.

We found that ICH from vascular structure lesions was associated with good outcome (odds ratio [OR] 4.460; 95% confidence interval [CI] 1.724-11.536, P=0.002; Table 2) and more likely to be functionally independent (OR 6.893; 95% CI 2.677-17.746, P < 0.001; Table 2) at 3 months.

Variables	Good outcome (mRS 0–3)		Functional independence (mRS 0–2)		
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value	
Vascular lesion ^a	4.460 (1.724–11.536)	0.002	6.893 (2.677–17.746)	< 0.001	
Age (per year)	0.958 (0.942–0.974)	< 0.001	0.964 (0.949–0.980)	< 0.001	
Male sex	0.809 (0.507–1.291)	0.374	0.940 (0.595–1.484)	0.790	
Hypertension	1.576 (0.889–2.795)	0.120	1.253 (0.711–2.210)	0.435	
Diabetes	1.052 (0.585–1.891)	0.865	1.016 (0.565–1.827)	0.959	
Previous ICH	0.373 (0.171–0.812)	0.013	0.308 (0.135–0.704)	0.005	
Admission GCS	1.401 (1.305–1.505)	< 0.001	1.411 (1.302–1.530)	< 0.001	
ICH volume (ml)	0.982 (0.973–0.992)	< 0.001	0.972 (0.960–0.984)	< 0.001	
IVH volume (ml)	0.980 (0.962–0.999)	0.038	0.983 (0.963–1.004)	0.108	

Table 2 Multivariable regression analysis of factors associated with good outcome (mRS 0–3) and functional independence (mRS 0–2) at 3 months before propensity score matching

GCS Glasgow Coma Scale, ICH intracerebral hemorrhage, IVH intraventricular hemorrhage

^a Compared with primary ICH

To further verify the association between ICH etiology and outcomes, we created a cohort with a comparable baseline using the nearest neighbor propensity score matching method (1:2). After propensity score matching, we included 177 and 104 patients with primary ICH and structural vascular lesions, respectively (Table 1). We also found that ICH from vascular structure lesions was associated with good outcome (OR 8.418; 95% CI 2.090–33.901, P=0.003; Table 3) and more likely to be functionally independent (OR 25.220; 95% CI 4.202–151.358, P<0.001; Table 3) at 3 months.

Discussion

This observational study found that ICH due to structural vascular lesions may have a distinct clinical phenotype as compared with primary ICH. ICH due to structural vascular lesions were associated with a higher rate of functional independence and a lower 3-month mortality than primary ICH.

In our study, about half of the patients with ICH due to structural vascular lesions had bleeding sites in cerebral lobes, whereas more than half of the patients with primary ICH had a basal ganglia or thalamus hematoma. A possible explanation would be that hypertensive ICH predominantly affects deep brain structures such as basal ganglia and thalamus, whereas secondary ICH caused by AVM arteriovenous malformation usually occurs in cerebral lobes [17]. Unlike deep ICH, which was associated with poor functional outcome [18, 19], ICH due to vascular lesions are mostly lobar hemorrhages that is associated with better functional outcome.

We found that ICH due to structural vascular lesions had relatively smaller hematomas than primary ICH. The reasons for this may be related to lower BP [20, 21] and venous or capillary bleeding [3, 22, 23]. Consistent with

Table 3 Multivariable regression analysis of factors associated with good outcome (mRS 0–3) and functional independence (mRS 0–2) at 3 months after propensity score matching

Variables	Good outcome (mRS 0–3)		Functional independence (mRS 0–2)	
	OR (95% CI)	P value	OR (95% CI)	<i>P</i> value
Vascular lesion ^a	8.418 (2.090-33.901)	0.003	25.220 (4.202–151.358)	< 0.001
Age (per year)	0.961 (0.921–1.002)	0.064	0.975 (0.934–1.018)	0.253
Male sex	0.755 (0.234–2.432)	0.638	1.338 (0.362–4.952)	0.663
Hypertension	1.771 (0.567–5.531)	0.325	1.787 (0.492–6.493)	0.378
Diabetes	1.024 (0.155–6.761)	0.980	3.380 (0.349–32.753)	0.293
Previous ICH	0.081 (0.012–0.543)	0.010	0.083 (0.010-0.721)	0.024
Admission GCS	1.391 (1.152–1.680)	0.001	1.589 (1.222–2.066)	0.001
ICH volume (ml)	0.991 (0.967–1.015)	0.457	0.972 (0.938–1.007)	0.114
IVH volume (ml)	0.990 (0.952–1.030)	0.619	0.987 (0.942-1.034)	0.584

CI confidence interval, GCS Glasgow Coma Scale, ICH intracerebral hemorrhage, IVH intraventricular hemorrhage, mRS modified Rankin Scale, OR odds ratio

^a Compared with primary ICH

previous reports, we found that patients with ICH due to structural vascular lesions were younger and had lower admission NIHSS, and higher admission GCS [24–26].

Furthermore, it was interesting to observe that the time from symptom onset to hospitalization was significantly longer in patients with ICH due to vascular lesions than primary ICH. A possible explanation would be that ICH due to vascular lesions had less severe neurological deficits and the hematomas were mostly located within the nidus or in the venous side with sparing the healthy brain parenchyma [24, 27]. In addition, we noticed that patients with ICH due to structural vascular lesions were more likely to have epileptic symptoms, probably because of the lobar location of the hemorrhage, which may increase the chances of cortical irritation with gliosis, leading to epileptic seizures [28].

Our findings highlight that etiological classification of ICH is important for individualized risk stratification, management, and outcome prediction. SMASH-U and H-ATOMIC are representatives of the etiologic classifications of ICH that have been proposed and shown high interrater reliability [9]. Unlike the H-ATOMIC classification, which is relatively complex and time-consuming [29], the SMUSH-U classification is an easy-to-use system that can be quickly used by experienced emergency physicians or neurologists to classify etiologies and has been widely used in clinical practice. In previous reports, most studies focused on primary ICH. Data are sparse on the etiology and spectrum of secondary ICH, especially ICH due to structural vascular lesions. In our study, we have investigated the clinical and imaging characteristics of different types of hematomas according to the SMASH-U classification. Our findings have shed light on the etiological constituents of ICH. We found that the most common cause of ICH due to structural lesions was AVM, followed by cavernous angioma, cerebral aneurysm, and moyamoya disease. Intracranial aneurysms occur in approximately 2-5% in the general population [30] and are more common than brain AVMs [31]. Because a ruptured aneurysm typically presents with subarachnoid hemorrhage [32], ICH due to ruptured intracranial aneurysm is less common than ICH secondary to AVM. We found that ICH due to cavernous angioma is not uncommon in patients with ICH who had vascular lesions, suggesting that brain MRI might be useful in elucidating the underlying cause of ICH.

Limitations

Our study has several limitations. First, this is a singlecenter study, and the natural history of ICH in this population may not be representative of other populations. Second, not all patients received a brain MRI scan in the cohort, which may underestimate the real prevalence of ICH due to structural lesions. Third, the sample size of some subtypes of vascular lesions is relatively small, so all kinds of vascular structural lesions were analyzed uniformly.

Conclusions

Our study concluded that the patients with ICH due to vascular lesions have smaller hematoma volume and less severe neurological deficit at presentation and better functional outcomes than those with primary ICH. It is of great significance to complete multimodal imaging examination to identify secondary ICH associated with vascular lesions.

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Author contributions

QL, X-FW: study concept and design. X-FW, LD, X-NL, Z-QL, Z-JW, XH, M-JP, CC and L-BZ: acquisition of data. X-FW: statistical analysis. Analysis and interpretation of data: all authors. X-FW: drafting of the manuscript. QL, X-FW: critical revision of the manuscript for important intellectual content. QL: obtained funding. QL: study supervision. The authors approved the final manuscript.

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Conflicts of interest

The authors declare no competing interests.

Ethical Approval/Informed Consent

The Ethics Committee of the First Affiliated Hospital of Chongqing Medical University approved the study protocol.

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