Clinical Characteristics, Management, and Functional Outcomes in Chinese Patients Within the First Year After Intracerebral Hemorrhage: Analysis from China National Stroke Registry

Wen-Juan Wang,¹ Jing-Jing Lu,¹ Yong-Jun Wang,¹ Chun-Xue Wang,¹ Yi-Long Wang,¹ Kolin Hoff,² Zhong-Hua Yang,¹ Li-Ping Liu,¹ An-Xin Wang,¹ Xing-Quan Zhao¹ & on behalf of the investigators for the China National Stroke Registry (CNSR)

¹ Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

² Division of Endocrinology, Diabetes and Metabolism Perelman School of Medicine, The University of Pennsylvania, Philadelphia, PA, USA

Keywords

Complications; functional outcomes; intracerebral hemorrhage; medical management; risk factors.

Correspondence

Xing-Quan Zhao, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, No.6 Tiantanxili, Chongwen District, Beijing 100050, China.
Tel.: +86-10-6709-8891;
Fax: +86-10-6701-9968;
E-mail: zxq@vip.163.com
Received 10 March 2012; revision 21 May 2012; accepted 25 May 2012.

SUMMARY

Aims: The aim of this study was to understand the association between clinical characteristics, medical management, and functional outcomes in Chinese patients with nontraumatic intracerebral hemorrhage (ICH). **Methods:** The China National Stroke Registry (CNSR) was a prospective cohort study that included 132 Chinese hospitals. Logistic regression was used to determine the risk factors associated with poor outcomes at 3, 6, and 12 months, post-ICH onset. **Results:** Three thousand two hundred fifty five ICH patients with follow-up information up to 1 year post-ICH were included in this study. 49.1%, 47.1%, and 46.0% of ICH patients had poor outcomes at 3, 6, and 12 months, respectively. Age, admission systolic blood pressure, admission Glasgow Coma Score, hematoma volume, withdrawal of support, and complication of gastrointestinal hemorrhage were associated with poor outcomes at 3 and 12 months. Stroke unit care was associated with good outcome at 3 months. Intensive care unit (ICU)/Neurology ICU care was associated with poor outcome at 3 months. **Conclusion:** This is the first report of long-term functional outcomes in ICH patients from mainland China. Our study elucidates the risk factors that may influence functional outcomes post-ICH and therefore facilitate the development of management strategies to improve ICH care in China.

doi: 10.1111/j.1755-5949.2012.00367.x

The first two authors contributed equally to this work.

Introduction

Nontraumatic intracerebral hemorrhage (ICH) is the second most common cause of stroke and is associated with disproportionately catastrophic outcomes [1,2]. Only 33% and 12–26% of patients have an independent life at 6 and 12 months post-ICH onset, respectively [3,4]. Much less data on ICH epidemiology are available from developing countries where a higher ICH incidence has been documented [5]. This highlights the urgent need to obtain more data on functional outcomes after ICH, as well as to gain better understanding of potential risk factors that may impact functional outcomes.

In China, 17.1–55.4% of strokes are because of ICH [6,7], which is higher than those in Western countries [8,9]. The impact

of ICH on long-term functional outcomes, however, remains poorly studied. The requirement for supportive care after the initial hospital stay is another relatively unexplored area. To date, only one study has examined the current management of ICH in China, but this study did not evaluate the association between management patterns and long-term functional outcomes after ICH [10]. Given the rapid economic development, progressive aging of the population, a westernized lifestyle, and healthcare reformation in China, a study that investigates these major health issues is desperately needed.

To provide new insights into the burden of post-ICH care in China, we systematically studied the current management and functional outcomes of all ICH patients within 1 year in China National Stroke Registry (CNSR).

Methods

Study Design

The CNSR is a multi-center, prospective nationwide registry of patients with acute cerebrovascular events. Data on vascular risk factors, clinical characteristics, diagnosis, treatment, prevention, and clinical outcomes for patients with cerebrovascular events were collected and analyzed. A total of 132 hospitals representing all 27 provinces and 4 municipalities (including Hong Kong) in China were selected as study sites [11].

Patient Eligibility

ICH was diagnosed according to World Health Organization criteria [12] and combined with brain axial computerized tomography (CT) confirmation. ICH patients were eligible to be enrolled in the analysis if they met the following criteria: ≥ 18 years of age and presented to hospital within 14 days after the onset of symptoms. Patients were excluded if they met any criterion below: ICH was caused by tumor, data of ICH hematoma volume was not available, they had primary intraventricular hemorrhage (IVH), their prestroke modified Rankin Scale (mRS) was >2 , they disagreed to participate in the study, or they were lost to follow-up. The ethics committees at all participating hospitals approved this study, and all patients or their designated relatives gave informed consents.

Image Analysis

The CT protocol and data were performed as follows: (1) Initial noncontrast CT (NCCT) scans were performed with a section thickness of 9 mm supratentorially and 4.5 mm infratentorially; and (2) ICH hematoma volume was measured on the initial head NCCT scan using the *ABC/2* method, in which *A* is the greatest diameter on the largest hemorrhage slice, *B* is the diameter perpendicular to *A*, and *C* is the approximate number of axial slices with hemorrhage multiplied by the slice thickness [13]; (3) Hematoma locations were classified as lobar, basal ganglia, thalamus (supratentorial), cerebellum, and brainstem (infratentorial). The presence or absence of intraventricular extension (IVE) was also noted on the initial head NCCT.

All images were prospectively viewed by a neuroradiologist blinded to clinical data at different study centers. The neuroradiologists of the study centers were trained centrally with the CT protocol.

Risk Factors Definition

Patient characteristics (e.g., gender, age, height, weight, marital status) were collected on admission. Baseline vascular risk factors included history of stroke (defined as confirmed from a medical chart), diabetes mellitus (history of diabetes mellitus or hypoglycemic drug use), hypertension (history of hypertension or antihypertensive drug use), dyslipidemia (history of dyslipidemia or lipid-lowering drug use), atrial fibrillation (history of atrial fibrillation confirmed by at least one electrocardiogram, or presence of the arrhythmia during hospitalization), cardiovascular disease,

current smoking, moderate or heavy alcohol consumption (≥ 2 standard alcoholic beverages per day), body mass index (BMI, calculated as weight [kg] divided by the square of height [m^2]), and medication history including antihypertensive, antiplatelet, anticoagulants, lipid-lowering, and hypoglycemic agents.

The severity of neurological impairment was evaluated by the National Institute of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS) within 24 h after admission. Data of routine laboratory tests were recorded.

Stroke units were defined as areas in a hospital where physicians, nurses, and other ancillary staff had training and experience on stroke management and provided care for acute stroke patients. Management by stroke unit, neurology intensive care unit (NICU), and intensive care unit (ICU) was defined as when a patient was admitted to a stroke unit, NICU, or ICU at any point during the hospitalization. Surgical interventions for ICH included hemispherectomy, craniotomy for hematoma removal, or stereotactic drainage of a hematoma. The complications during hospitalization were also recorded. Length of stay (LOS) was defined as the number of days from admission to discharge or case fatality.

Patient Follow-Up and Assessment of Endpoints

At 3, 6, and 12 months after ICH onset, the functional outcomes of all patients were assessed through telephone follow-up interview to obtain information on mRS, death (or mRS = 6), and the corresponding dates of outcomes. Poor outcome was defined as death or dependency (mRS = 3–6), and good outcome was defined as mRS ≤ 2 [14]. The telephone follow-up was centralized for all included patients and based on a shared standardized interview protocol. The interviewers were trained with the interview protocol.

Statistical Analysis

Data were reported as median with interquartile range (IQR) for nominal variables or as percentage of patients with nonmissing values for categorical variables. The nonparametric Kruskal–Wallis one-way analysis of variance was used for nominal variables. The chi-squared test was used to compare categorical variables. A logistic model was developed to identify risk factors associated with poor functional outcomes at 3 months and 1 year post-ICH. Variables were selected using stepwise regression. All variables with a $P < 0.2$ (equivalent to maximizing the information criteria) in the univariate analysis were considered in the multivariable regression model. We estimated the discrimination of the selected model to predict in-hospital case fatality using the c-statistic. We used 1000 bootstrap samples to estimate the 95% confidence interval (95% CI) for each c-statistic. All tests were 2-tailed, and $P < 0.05$ was considered statistically significant. All analyses were conducted using SAS version 9.2 statistical software (SAS Institute Inc., Cary, NC, USA).

Results

From September 2007 to August 2008, this project consecutively recruited 22,216 hospitalized patients with acute cerebrovascular events. Among them, 5136 patients were diagnosed as

acute ICH. The following patients were excluded from this study: (1) 881 patients without data of hematoma volume; (2) 138 with primary IVH; (3) 12 patients whose ICH caused by intracranial tumor; (4) 261 with a prestroke mRS > 2; (5) 308

who were unwilling to participate in this study; and (6) 281 lost to follow-up. The remaining 3255 patients completed the 1-year follow-up and were included in the final statistical analysis (Figure 1).

Figure 1 Flow diagram defining the potentially eligible patients with intracerebral haemorrhage.

Table 1 Demographics and risk factors of intracerebral hemorrhage patients for 3-month and 1-year functional outcomes

	All	3-month outcome			1-year outcome		
		Good	Poor	P	Good	Poor	P
N	n = 3255	n = 1656	n = 1599		n = 1758	n = 1497	
Demographics							
Age, years, median (IQR)	62 (53–72)	60 (52–69)	65 (54–75)	0.00	59 (51–68)	67 (56–76)	0.00
18–45	357 (11%)	222 (13.4%)	135 (8.4%)	0.00	239 (13.6%)	117 (7.8%)	0.00
46–65	1554 (47.7%)	887 (53.6%)	667 (41.7%)		973 (55.4%)	581 (38.8%)	
66–75	782 (24%)	362 (21.9%)	420 (26.3%)		376 (21.4%)	406 (27.1%)	
≥ 76	562 (17.3%)	185 (11.2%)	377 (23.6%)		169 (9.6%)	393 (26.3%)	
Gender (Male), n (%)	1995 (61.3)	1060 (64.0)	935 (58.5)	<0.01	1110 (63.2)	884 (59.1)	0.02
Marital status	361 (11.1%)	147 (8.9%)	214 (13.5%)	0.00	144 (8.2%)	217 (14.6%)	0.00
(Single/divorced/widowed)							
Education, n%							
Elementary or below	1573 (48.3)	736 (44.4)	837 (52.3)	0.00	771 (43.9)	802 (53.6)	0.00
Middle school	888 (27.3)	453 (27.4)	435 (27.2)		488 (27.8)	399 (26.7)	
High school or above	794 (24.4)	467 (28.2)	327 (20.5)		498 (28.3)	296 (19.8)	
BMI, (kg/m ²), median (IQR)	23.9 (21.5–26.1)	23.9 (21.7–26.1)	23.7 (21.5–26.3)	0.24	24.0 (22.0–26.1)	23.7 (21.3–26.2)	0.01
<25	1865 (63.7)	944 (63.0)	921 (64.4)	0.51	989 (62.2)	875 (65.3)	0.22
25–30	896 (30.6)	472 (31.5)	424 (29.6)		507 (31.9)	389 (29.0)	
≥ 30	169 (5.8)	83 (5.5)	86 (6.0)		93 (5.9)	76 (5.7)	
Current smoking, n (%)	1228 (37.7)	656 (39.6)	572 (35.8)	0.02	694 (39.5)	534 (35.7)	0.03
Current heavy drinking, n (%)	367 (11.3)	208 (12.6)	159 (9.9)	0.02	224 (12.7)	143 (9.6)	<0.01
Medical history, n (%)							
Stroke	889 (27.3)	379 (22.9)	510 (31.9)	0.00	377 (21.5)	512 (34.2)	0.00
Diabetes	290 (8.9)	127 (7.7)	163 (10.2)	0.01	132 (7.5)	158 (10.6)	<0.01
Hypertension	2210 (67.9)	1119 (67.6)	1091 (68.2)	0.69	1191 (67.8)	1018 (68.0)	0.90
Dyslipidemia	230 (7.1)	133 (8.0)	97 (6.1)	0.03	141 (8.0)	89 (5.9)	0.02
Cardiovascular disease	273 (8.4)	114 (6.9)	159 (10.0)	<0.01	123 (7.0)	150 (10.1)	<0.01
Atrial fibrillation	54 (1.7)	19 (1.1)	35 (2.2)	0.02	21 (1.2)	33 (2.2)	0.03
Medication history, n (%)							
Antihypertensive	1388 (42.6)	708 (42.8)	680 (42.5)	0.90	755 (43.0)	632 (42.2)	0.67
Antiplatelet	291 (8.9)	136 (8.2)	155 (9.7)	0.14	143 (8.1)	148 (9.9)	0.08
Anticoagulants	32 (1)	1520 (91.8)	1444 (90.3)	0.65	15 (0.9)	17 (1.1)	0.42
Lipid lowering	37 (1.1)	18 (1.1)	19 (1.2)	0.28	18 (1.0)	19 (1.3)	0.76
Hypoglycemic	50 (1.5)	18 (1.1)	32 (2.0)	0.06	17 (1.0)	33 (2.2)	<0.01

IQR, interquartile range; BMI, body mass index.

The case fatality rate was 20.0%, 22.5%, and 26.1%.; and the proportion of all ICH patients with poor outcome was 49.1%, 47.1%, and 46.0% at 3 months, 6 months, and 1 year, respectively.

The demographics and clinical characteristics of ICH patients are presented in Tables 1 and 2. The median age was 62 years, and 61.3% were men. When compared with the ICH patients with good functional outcomes at 3 months and 1 year after ICH,

Table 2 Clinical characteristics of intracerebral hemorrhage patients for 3-month and 1-year functional outcomes

	All	3-month outcome			1-year outcome		
		Good	Poor	<i>P</i>	Good	Poor	<i>P</i>
N	n = 3255	n = 1656	n = 1599		n = 1758	n = 1497	
NIHSS at hospital admission, median (IQR)	9 (3–16)	4 (2–9)	15 (9–25)	0.00	5 (2–10)	15 (8–25)	0.00
0–4	1084 (33.3%)	871 (52.6%)	213 (13.3%)	0.00	849 (48.3%)	235 (15.7%)	0.00
5–14	1196 (36.7%)	636 (38.4%)	560 (35.0%)		702 (40.0%)	494 (33.0%)	
≥ 15	975 (30%)	149 (9.0%)	826 (51.7%)		206 (11.7%)	768 (51.3%)	
GCS at hospital admission, median (IQR)	14 (9–15)	15 (14–15)	11 (6–15)	0.00	15 (14–15)	11 (6–15)	0.00
13–15	1873 (60.3%)	1281 (82.4%)	592 (38.1%)	0.00	1312 (79.5%)	561 (38.5%)	0.00
9–12	479 (15.4%)	152 (9.8%)	327 (21.1%)		186 (11.3%)	293 (20.1%)	
3–8	755 (24.3%)	121 (7.8%)	634 (40.8%)		152 (9.2%)	603 (41.4%)	
Blood pressure, (mmHg), median (IQR)							
Systolic blood pressure	160 (148–180)	160 (145–180)	165 (150–186)	0.00	160 (145–180)	165 (150–186)	0.00
Diastolic blood pressure	95 (87–106)	94 (86–105)	95 (87–108)	0.11	95 (87–105)	95 (87–107)	0.34
Laboratory, median (IQR)							
Hemoglobin, g/DL	139 (126–150)	139 (128–150)	138 (125–151)	0.08	139 (128–150)	138 (124–151)	0.04
White cell count, 10 ⁹ /L	8.7 (6.7–11.4)	7.8 (6.3–9.95)	9.7 (7.42–13)	0.00	7.9 (6.3–10.2)	9.63 (7.42–12.9)	0.00
Platelet, 10 ⁹ /L	186 (145–230)	188 (150–229)	184 (141–233)	0.16	189 (149–230)	184 (141–232)	0.15
Serum glucose, mmol/L	6.34 (5.73–7.49)	6.16 (5.42–6.9)	6.59 (5.93–8.1)	0.00	6.2 (5.47–7)	6.57 (5.93–8.1)	0.00

NIHSS, National Institutes of Health stroke Scale; IQR, interquartile range; GCS, Glasgow Coma Score.

Table 3 Imaging characteristics of intracerebral hemorrhage patients for 3-month and 1-year functional outcomes

	All	3-month outcome			1-year outcome		
		Good	Poor	<i>P</i>	Good	Poor	<i>P</i>
N	n = 3255	n = 1656	n = 1599		n = 1758	n = 1497	
Hematoma location							
Location 1, n (%)							
Supratentorial	2862 (87.9)	1478 (89.3)	1384 (86.6)	0.02	1570 (89.4)	1291 (86.2)	<0.01
Infratentorial	393 (12.1)	178 (10.7)	215 (13.4)		187 (10.6)	206 (13.8)	
Location 2, n (%)							
Basal ganglia	1878 (57.7)	913 (55.1)	965 (60.4)	<0.01	1011 (57.5)	866 (57.8)	0.86
Lobar	704 (21.6)	368 (22.2)	336 (21.0)	0.40	368 (20.9)	336 (22.4)	0.30
Thalamus	631 (19.4)	292 (17.6)	339 (21.2)	0.01	306 (17.4)	325 (21.7)	<0.01
Brainstem	258 (7.9)	97 (5.9)	161 (10.1)	0.00	109 (6.2)	149 (10.0)	0.00
Cerebellum	184 (5.7)	99 (6.0)	85 (5.3)	0.41	95 (5.4)	89 (5.9)	0.51
Hematoma volume, median (IQR)	12.6 (5.46–28)	9 (4–18)	20 (8.75–42)	0.00	9 (4.2–18.6)	20 (8.1–45)	0.00
Supratentorial, n (%)				0.00			0.00
≤ 30 mL	2368 (72.7)	1391 (84.0)	977 (61.1)		1469 (83.6)	898 (60.0)	
30–60 mL	288 (8.8)	63 (3.8)	225 (14.1)		75 (4.3)	213 (14.2)	
>60 mL	206 (6.3)	24 (1.4)	182 (11.4)		26 (1.5)	180 (12.0)	
Infratentorial, n (%)							
≤ 10 mL	280 (8.6)	140 (8.5)	140 (8.8)		144 (8.2)	136 (9.1)	
10–20 mL	61 (1.9)	20 (1.2)	41 (2.6)		26 (1.5)	35 (2.3)	
>20 mL	52 (1.6)	18 (1.1)	34 (2.1)		17 (1.0)	35 (2.3)	
Intraventricular extension, n (%)	962 (29.6)	315 (19.0)	647 (40.5)	0.00	345 (19.6)	617 (41.2)	0.00
Midline shift, n (%)	676 (23.5)	199 (12.9)	477 (35.8)	0.00	240 (14.7)	436 (35.2)	0.00

IQR, interquartile range.

patients with poor outcomes were older, more likely to be women, and had a level of education at elementary school or below. More patients in the poor outcome group were single, widowed, or remarried, but fewer were smokers or moderate or heavy alcohol drinkers. Patients with poor functional outcomes at 3 months and 1 year post-ICH also presented with higher frequency of medical histories of stroke, diabetes, cardiovascular disease, and atrial fibrillation, whereas dyslipidemia was presented less frequently. More ICH patients with poor functional outcome were with higher NIHSS score and lower GCS on admission. Mean values of systolic blood pressure (SBP), white cell count, and serum glucose on admission were also significantly higher in patients with poor functional outcomes at 3 months and 1 year post-ICH.

Table 3 shows that the frequency of bleeding sites for all ICH patients was 57.7% for basal ganglia, 21.6% for lobar, 19.4% for thalamus, 7.9% for brainstem, and 5.7% for cerebellum, respectively. Thalamus and brainstem hemorrhage occurred more frequently in patients with 3-month and 1-year poor functional outcomes, whereas the basal ganglia hemorrhage presented more frequently only in patients with 3-month poor functional outcome. Larger hematoma volume, IVE, and midline shift also presented more frequently in patients with poor outcomes at both 3 months and 1 year post-ICH.

Table 4 demonstrates that patients with good functional outcomes at 3 months and 1 year post-ICH had significantly longer LOS and used antihypertensive therapy more frequently than those with poor outcomes. In contrast, NICU/ICU care, treatment with intravenous mannitol, withdrawal of support, and complications during hospitalization occurred more frequently in ICH patients with 3-month and 1-year poor functional outcomes.

Further, the multivariate logistic regression analyses (Table 5) suggested that age, admission SBP, admission GCS, hematoma volume, withdrawal of support, and complication of gastrointestinal hemorrhage were associated with poor outcomes at 3 months and 1 year. NICU/ICU care was associated with poor outcome, but stroke unit care was associated with good outcome at 3 months.

Discussion

The overall incidence of ICH was 24.6 per 100,000 person-years, which was unchanged between 1980 and 2008 in the world [5]. In China, the age-adjusted ICH incidence in people ≥ 55 years of age was 167.1–454.3 per 100,000 person-years, which was the highest among other regions reported in the world, specifically higher than those in western countries (46.1–121.7 per 100,000 person-years) [15]. However, less data were available on long-term functional outcomes of ICH patients in China. CNSR is a national registry that contains the largest data bank on ICH patients from every region in China compared with other stroke registries [10,16,17]. To our knowledge, this is the largest cohort of long-term functional outcome study of ICH patients in China. In this study, patient baseline characteristics, current management in hospital, and functional outcomes within the first year after ICH onset in Chinese patients were analyzed.

Several previous studies have reported on the long-term functional outcomes but with relatively smaller sample sizes of 57–69 [3,4]. In their results, only 31% of patients were functionally independent at 3 months, 33% at 6 month, and 12–26% at 1 year post-ICH onset [3,4,18]. In contrast, we found that more than half of the ICH patients included in our study achieved inde-

Table 4 Management and outcomes at discharge of intracerebral haemorrhage patients for 3-month and 1-year functional outcomes

	All	3-month outcome			1-year outcome		
		Good	Poor	<i>P</i>	Good	Poor	<i>P</i>
N	n = 3255	n = 1656	n = 1599		n = 1758	n = 1497	
Treated in, n (%)							
Neurology ward/Ward	2022 (62.1)	1142 (69.0)	880 (55.0)	0.00	1165 (66.3)	857 (57.2)	0.00
Stroke unit	554 (17)	294 (17.8)	260 (16.3)		326 (18.6)	227 (15.2)	
Neurosurgical/Intervention Ward	94 (2.9)	40 (2.4)	54 (3.4)		48 (2.7)	46 (3.1)	
NICU/ICU	585 (18)	180 (10.9)	405 (25.3)		218 (12.4)	367 (24.5)	
Medical treatment, n (%)							
Antihypertensive therapy	1910 (58.7)	1045 (63.1)	865 (54.1)	0.00	1113 (63.3)	796 (53.2)	0.00
Intravenous traditional Chinese medicine	1139 (38)	593 (37.4)	546 (38.8)	0.42	642 (38.1)	497 (38.0)	0.95
Intravenous mannitol	2799 (92.8)	1438 (89.9)	1361 (96.0)	0.00	1538 (90.7)	1260 (95.5)	0.00
Neurosurgical intervention	81 (2.7)	21 (1.3)	60 (4.2)	0.00	28 (1.6)	53 (4.0)	0.00
Withdraw of support	404 (12.4)	109 (6.6)	295 (18.4)	0.00	118 (6.7)	286 (19.1)	0.00
Complications in hospital, n (%)							
Recurrent stroke	103 (3.2)	23 (1.4)	80 (5.0)	0.00	21 (1.2)	82 (5.5)	0.00
Myocardial infarction	25 (0.8)	2 (0.1)	23 (1.4)	0.00	6 (0.3)	19 (1.3)	<0.01
Pneumonia	585 (18)	144 (8.7)	441 (27.6)	0.00	159 (9.0)	426 (28.5)	0.00
GI hemorrhage	179 (5.5)	23 (1.4)	156 (9.8)	0.00	28 (1.6)	151 (10.1)	0.00
Seizure	63 (1.9)	14 (0.8)	49 (3.1)	0.00	17 (1.0)	46 (3.1)	0.00
Total length of stay, median (IQR)	18 (11–26)	19 (13–25)	16 (5–27)	0.00	19 (13–26)	15 (5–26)	0.00

NICU, neurology intensive care unit; ICU, intensive care unit; GI hemorrhage, gastrointestinal hemorrhage; IQR, interquartile range.

Table 5 Adjusted odds ratio of poor outcomes in intracerebral hemorrhage patients at 3 and 12 months

	3-month poor outcome OR(95% CI)	1-year poor outcome OR(95% CI)
Age, years		
18–45	1	1
46–65	2.12 (1.42–3.16)	1.92 (1.30–2.84)
66–75	4.18 (2.70–6.46)	4.31 (2.84–6.54)
≥ 76	7.03 (4.42–11.2)	10.2 (6.5–15.9)
Stroke	1.36 (1.05–1.75)	1.83 (1.46–2.31)
Systolic blood pressure	1.06 (1.01–1.14)	1.04 (1.00–1.08)
GCS at admission		
13–15	1	1
9–12	1.97 (1.44–2.68)	1.61 (1.22–2.14)
3–8	2.82 (2.03–3.91)	2.10 (1.57–2.81)
Hematoma volume		
Supratentorial		
≤ 30 mL	1	1
30–60 mL	1.90 (1.23–2.94)	2.09 (1.42–3.06)
>60 mL	1.90 (0.97–3.70)	2.70 (1.49–4.87)
Infratentorial		
≤ 10 mL	1.54 (1.02–2.32)	1.38 (0.95–2.00)
10–20 mL	4.62 (2.02–10.6)	1.36 (0.58–3.16)
>20 mL	3.87 (1.54–9.69)	3.66 (1.49–8.99)
Treated in		
Neurology ward/Ward	1	–
Stroke unit	0.69 (0.47–0.96)	–
NICU/ICU	1.69 (1.23–2.30)	–
Withdraw of support	1.59 (1.11–2.28)	2.14 (1.56–2.94)
Complications in hospital		
Gastro-intestinal hemorrhage	3.53 (1.90–6.56)	3.24 (1.92–5.48)

OR, odds ratio; CI, confidence interval; GCS, Glasgow Coma Score; NICU/ICU, neurology intensive care unit/intensive care unit. The poor outcomes OR are expressed per 10 mmHg of admission SBP and per 1 mL of hematoma volume. Adjusted by age, marital status, stroke history, history of cardiovascular disease, atrial fibrillation history, unit of admission, admission National Institutes of Health stroke Scale, admission GCS, admission systolic blood pressure, hematoma volume, infratentorial hematoma, intraventricular extension, complications of recurrent stroke, myocardial infarction, gastrointestinal hemorrhage, and seizure in hospital, antihypertensive therapy, intravenous traditional Chinese medicine, intravenous mannitol and withdraw of support.

pendency at 3 months, 6 months, and 1 year. This could in part be explained by differences in target population and study designs. For example, we only included ICH patients who were admitted to the selected urban hospitals, and more intense and systematic medical care in urban hospitals may contribute to the better outcomes for patients in our study. In addition, only 16.2% of patients in our study registry were older than 65 years old. The better outcomes achieved by our study are consistent with previous findings that there was correlation between age and poor long-term (1 or 2 years) outcomes [19].

Clinical trials have shown that any of these risk factors, such as age, infratentorial ICH origin, and ICH severity measured either by clinically (level of consciousness on admission GCS) or by

imaging modalities (initial hematoma volume, IVE), have been most consistently proven to be poor prognostic factors [20,21]. A study performed by J. Claude Hemphill III *et al.* in an Asian population has shown that the ICH score (age, infratentorial ICH origin, admission GCS, hematoma volume, and IVE as predictors) is a valid clinical grading scale for predicting long-term functional outcomes after acute ICH [19]. Similarly, age, admission GCS, and hematoma volume were proved to be associated with poor functional outcomes at 3 months and 1 year post-ICH in our study.

Hypertension is one of the most important risk factors for stroke [22]. In an analysis of 45,330 ICH patients, 75% of patients had SBP with greater than 140 mmHg and 20% of patients had SBP with greater than 180 mmHg at presentation [23]. High blood pressure post-ICH is associated with poor outcome; however, the exact cause remains unclear [24]. Our study showed that patients with higher SBP were associated with poor functional outcome within the first year post-ICH, supporting the previous finding that higher SBP was associated with poor long-term functional outcome. Consistent with this result, outcomes from another study suggested that there was a greater therapeutic benefit with aggressively lower blood pressure [25]. The Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) trial and the Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage (INTERACT) trial reported that aggressive reduction in blood pressure to less than 140 mmHg probably decreased the rate of hematoma enlargement [26,27], although no difference was observed for 3-month death and disability between patients treated with aggressive and conservative lowering of blood pressure in both trials. Both American Stroke Association Stroke Council and The European Stroke Initiative guidelines suggested that aggressive SBP lowering should be considered in patients without clinical signs of high intracranial pressure or chronic hypertension [28,29]. Although antihypertensive therapy during hospitalization was not proved to be associated with good outcome within 1 year post-ICH (Table 5), our study results supported that a greater percentage of patients with antihypertensive therapy during hospitalization in the good outcome group at 3 months and 1 year post-ICH than that in the poor outcome group (Table 4).

18%, 5.5%, 3.2%, 1.9%, and 0.8% of ICH patients in CNSR had complications of pneumonia, gastrointestinal hemorrhages, recurrent stroke, seizure, and myocardial infarction, respectively. Our results showed that patients with 3-month and 1-year poor outcomes had more complications than patients with good outcomes. Other researches have found the same tendency. For example, 4.2–20% of patients were reported to have a complication of seizure after acute ICH; and seizure was associated with epilepsy development, expanding hemorrhage, and poor outcome [1,30,31]. A randomized placebo-controlled trial of ranitidine versus sucralfate in patients with ICH for prevention of gastric hemorrhage showed that 23% of patients with ICH had gastric hemorrhage with a higher in-hospital case fatality than patients treated with ranitidine or sucralfate [32]. Although the incidence of complication in CNSR was lower than what had been reported, complications of gastrointestinal hemorrhage and recurrent stroke were proved to be associated with 3-month and 1-year poor outcomes. These findings have important implications in our daily clinical practice, such as identifying and treating the complications in hospital early. Thus, well organized and multimodal therapy

addressing each of the modifiable factors might be needed to improve patient outcomes after ICH.

Stroke unit care is one of the most effective interventions to improve clinical outcomes after acute stroke and proved to be associated with 3-month good outcome in our study. But most ICH patients (62.1%) are cared in general medical wards instead of stroke units (17%) in CNSR. In a review of 1421 patients with ICH, care limitation or withdrawal of life-sustaining interventions was the most common cause of death (68%) [33,34]. These provide indirect evidence that aggressive medical management and specialist care can improve the overall outcomes in ICH patients. In our study, 18% of patients were cared in NICU/ICU and 12.4% of patients withdrew from support. Furthermore, NICU/ICU care during hospitalization was associated with 3-month and 1-year poor outcomes just as one study that had reported a significant high case fatality with NICU/ICU care [35], which suggested the possibility of confounding factors. For example, it is likely that the patients who were treated in NICU/ICU had severe strokes and they were treated with supportive care rather than active clinical care. These factors would be associated with a poorer outcome in this group of patients.

The management of ICH in China is also characterized by high rates of nonevidence based on medical treatments, intravenous osmotic diuretics (such as mannitol), and traditional Chinese medicines (TCMs) in the acute phase in particular. Randomized trials showed no benefit in functional outcomes from regular use of intravenous mannitol [36]. Therefore, only short-term use of mannitol in patients with ICH under special circumstances, such as transtentorial herniation or acute neurological deterioration associated with high intracranial pressure or mass effect, should be considered. Stroke guidelines advocate restricting osmotic diuretics use in patients with clear evidence of increased intracranial pressure because of inconclusive evidence regarding the benefit of the routine use [28]. In our study, most patients (92.8%) got intravenous osmotic diuretics use in acute phase, and osmotic diuretics use could not improve the functional outcomes post-ICH. TCMs have a long tradition of therapeutic benefit for a wide variety of conditions in China, and 38% of ICH patients obtained intravenous TCM therapy in CNSR. TCM use was not proven to be different in ICH patients with 3-month and 1-year good or poor functional outcomes. Intravenous osmotic diuretics and TCM use in ICH patients during hospitalization were overly aggressive and should be limited according to treatment guidelines.

There are some caveats in our study that deserve comments. First, ICH patients in CNSR are younger than those in some other regions of the world. They therefore potentially had fewer comorbidities, and this may have led to better survival or functional outcomes. Second, we did not record and analyze the blood pressure before and after antihypertensive treatment during hospitalization. Third, the association between functional outcomes and interventions, such as NICU/ICU care, may be confounded and reflect the fact that patients with very severe ICH may die before receiving NICU/ICU cares, or they may not be offered these interventions because the severity of ICH makes a palliative approach more appropriate. Thus, the absence of certain interventions may be a reason for more severe patients resulting to poor functional outcome.

In this largest national registry study in China, characteristics, management in hospital, and long-term functional outcomes of ICH patients have been tabulated. The overall long-term functional outcomes in these ICH patients appear to be better than previously published reports from other regions in the world. This may be related to differences in selected population and study designs. Having a better understanding of the characteristics of ICH patients and risk factors that are associated with the functional outcomes can help developing strategies to improve the healthcare process for patients with ICH in China.

Acknowledgments

The authors thank all participating relevant clinicians and imaging and laboratory technicians. This study was sponsored by the Ministry of Science and Technology and the Ministry of Health of the People's Republic of China and Beijing Municipal Health Bureau. The Grant numbers are National S & T Major Project of China (2008ZX09312 -008) and State Key Development Program of (for) Basic Research of China (2009CB521905); Beijing Public Health System Special Projects of High-level Training for Medical Technologist (2009-3-27).

Conflict of Interest

The authors declare no conflict of interest.

References

- Balami JS, Buchan AM. Complications of intracerebral haemorrhage. *Lancet Neurol* 2012;**11**: 101–118.
- Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol* 2009;**8**: 355–369.
- Vibo R, Korv J, Roose M. The third stroke registry in tartu, estonia, from 2001 to 2003. *Acta Neurol Scand* 2007;**116**: 31–36.
- Vibo R, Korv J, Roose M. One-year outcome after first-ever stroke according to stroke subtype, severity, risk factors and pre-stroke treatment. A population-based study from tartu, estonia. *Eur J Neurol* 2007;**14**: 435–439.
- van Asch CJ, Luitse MJ, Rinkel GJ, et al. 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;**9**: 167–176.
- Yang QD, Niu Q, Zhou YH, et al. Incidence of cerebral hemorrhage in the Changsha community. A prospective study from 1986 to 2000. *Cerebrovasc Dis* 2004;**17**: 303–313.
- Zhang LF, Yang J, Hong Z, et al. Proportion of different subtypes of stroke in china. *Stroke* 2003;**34**: 2091–2096.
- Lovelock CE, Molyneux AJ, Rothwell PM. Change in incidence and aetiology of intracerebral haemorrhage in Oxfordshire, UK, between 1981 and 2006: a population-based study. *Lancet Neurol* 2007;**6**: 487–493.
- Islam MS, Anderson CS, Hankey GJ, et al. Trends in incidence and outcome of stroke in perth, western australia during 1989 to 2001: the perth community stroke study. *Stroke* 2008;**39**: 776–782.
- Wei JW, Huang Y, Wang JG, et al. Current management of intracerebral haemorrhage in china: a national, multi-centre, hospital register study. *BMC Neurol* 2011;**11**: 16.
- Wang Y, Cui L, Ji X, et al. The china national stroke registry for patients with acute cerebrovascular events: design, rationale, and baseline patient characteristics. *Int J Stroke* 2011;**6**: 355–361.
- Goldstein M, Barnett HJM, Orgogozo JM, et al. Recommendations on stroke prevention, diagnosis, and therapy. Report of the WHO task force on stroke and other cerebrovascular disorders. *Stroke* 1989;**20**: 1407–1431.

13. Kothari RU, Brott T, Broderick JP, et al. The abcs of measuring intracerebral hemorrhage volumes. *Stroke* 1996;**27**: 1304–1305.
14. Quinn TJ, Dawson J, Walters MR, et al. Exploring the reliability of the modified rankin scale. *Stroke* 2009;**40**: 762–766.
15. Jiang B, Wang WZ, Chen H, et al. Incidence and trends of stroke and its subtypes in china: results from three large cities. *Stroke* 2006;**37**: 63–68.
16. Liu X, Xu G, Wu W, et al. Subtypes and one-year survival of first-ever stroke in chinese patients: the nanjing stroke registry. *Cerebrovasc Dis* 2006;**22**: 130–136.
17. Heeley E, Anderson CS, Huang Y, et al. Role of health insurance in averting economic hardship in families after acute stroke in china. *Stroke* 2009;**40**: 2149–2156.
18. Ferro JM. Update on intracerebral haemorrhage. *J Neurol* 2006;**253**: 985–999.
19. Hemphill JC, 3rd, Farrant M, Neill TA Jr. Prospective validation of the ICH score for 12-month functional outcome. *Neurology* 2009;**73**: 1088–1094.
20. Rost NS, Smith EE, Chang Y, et al. Prediction of functional outcome in patients with primary intracerebral hemorrhage: the func score. *Stroke* 2008;**39**: 2304–2309.
21. Ruiz-Sandoval JL, Chiquete E, Romero-Vargas S, et al. Grading scale for prediction of outcome in primary intracerebral hemorrhages. *Stroke* 2007;**38**: 1641–1644.
22. Yu JG, Zhou RR, Cai GJ. From hypertension to stroke: mechanisms and potential prevention strategies. *CNS Neurosci Ther* 2011;**17**: 577–584.
23. Qureshi AI, Ezzeddine MA, Nasar A, et al. Prevalence of elevated blood pressure in 563,704 adult patients with stroke presenting to the ed in the united states. *Am J Emerg Med* 2007;**25**: 32–38.
24. Qureshi AI. Acute hypertensive response in patients with stroke: pathophysiology and management. *Circulation* 2008;**118**: 176–187.
25. Anderson CS, Huang Y, Wang JG, et al. Intensive blood pressure reduction in acute cerebral haemorrhage trial (interact): a randomised pilot trial. *Lancet Neurol* 2008;**7**: 391–399.
26. Qureshi AI, Tariq N, Divani AA, et al. Antihypertensive treatment of acute cerebral hemorrhage. *Crit Care Med* 2010;**38**: 637–648.
27. Anderson CS, Huang Y, Arima H, et al. Effects of early intensive blood pressure-lowering treatment on the growth of hematoma and perihematomal edema in acute intracerebral hemorrhage: the intensive blood pressure reduction in acute cerebral haemorrhage trial (interact). *Stroke* 2010;**41**: 307–312.
28. Morgenstern LB, Hemphill JC 3rd, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the american heart association/american stroke association. *Stroke* 2010;**41**: 2108–2129.
29. Steiner T, Kaste M, Forsting M, et al. Recommendations for the management of intracranial haemorrhage—part i: spontaneous intracerebral haemorrhage. The european stroke initiative writing committee and the writing committee for the EUSI executive committee. *Cerebrovasc Dis* 2006;**22**: 294–316.
30. Szaflarski JP, Rackley AY, Kleindorfer DO, et al. Incidence of seizures in the acute phase of stroke: a population-based study. *Epilepsia* 2008;**49**: 974–981.
31. Claassen J, Jette N, Chum F, et al. Electrographic seizures and periodic discharges after intracerebral hemorrhage. *Neurology* 2007;**69**: 1356–1365.
32. Misra UK, Kalita J, Pandey S, et al. A randomized placebo controlled trial of ranitidine versus sucralfate in patients with spontaneous intracerebral hemorrhage for prevention of gastric hemorrhage. *J Neurol Sci* 2005;**239**: 5–10.
33. Naidech AM, Bernstein RA, Bassin SL, et al. How patients die after intracerebral hemorrhage. *Neurocrit Care* 2009;**11**: 45–49.
34. Zahuranec DB, Brown DL, Lisabeth LD, et al. Early care limitations independently predict mortality after intracerebral hemorrhage. *Neurology* 2007;**68**: 1651–1657.
35. Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. *Lancet* 2009;**373**: 1632–1644.
36. Misra UK, Kalita J, Ranjan P, et al. Mannitol in intracerebral hemorrhage: a randomized controlled study. *J Neurol Sci* 2005;**234**: 41–45.