Intracerebral hemorrhage in young adults: Analysis of etiology, clinical characteristics and discharge outcome

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Summary

Objective: This study evaluated the etiology, clinical characteristics and discharge outcomes of intracerebral hemorrhage (ICH) without trauma in young adults admitted to a comprehensive stroke center. *Subject and method:* This was a retrospective study of patients aged under 46 years with nontraumatic ICH admitted from October 2022 to April 2023. Data was collected on demographics, clinical history, hemorrhage location, possible etiology, and discharge outcome. Categorical data was reported as percentage. Chi-squared test was performed to evaluate association of location of ICH, etiology of ICH with the discharge outcome. *Result:* Forty-five patients met the study criteria, with mean age 35.6 ± 8.1 years including 16 (35.6%) female, 29 (64.4%) male. Headache (86.7%) and hemiparalysis (77.8%) were the most common symptoms. Hematoma was most commonly seen in the deep structures in 21 (46.6%) patients followed by lobar ICH in 17 (37.8%) patients. The most common etiology of ICH was hypertension, which seen in 23 (51.1%) patients, followed by vascular abnormalities in 13 (28.8%) patients. Twenty-two patients (48.9%) had good outcome defined as mRS 0-2. Twenty-three patients (51.1%) had poor outcome with mRS 3-6 at discharge. Location and etiology of hemorrhage were not associated with discharge outcome. *Conclusion:* Hypertension, a modifiable risk factor, is a major cause of nontraumatic ICH in young adults. In primary care settings, hypertension and life styles were important modifiable risk factors for all subtypes of strokes. Considering that hypertension is an independent risk factor for morbidity and mortality in patients with ICH, this comorbidity should be managed aggressively in young patients as part of a primary prevention strategy related to ICH.

Keywords: Intracerebral hemorrhage, young adults, etiology, hypertension.

1. Background

Intracerebral hemorrhage (ICH) in the youthful demographic represents a devastating pathology. Despite its rarity, the condition not only imposes an acute life threatening but also precipitates debilitation, protracted recovery, and socio-economic adversities during the prime years of productivity. While the rate of ICH increases with age, there are also cases of ICH in younger patients, and there have not been many studies investigating the etiologies of ICH in this population group. Sandoval et al described a wide range of risk factors in a study of patients under 40 with ICH with vascular malformation and hypertension being the most common [1]. Given the prevalence and risks of ICH, clarifying the salient characteristics of this entity in the young, with a focus on play an important role in prevention and treatment. In recent studies, the rate of hypertensive ICH in patients under 45 years of age has surpassed vascular malformation as the most common contributor in young adults,

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especially those over 30 years [2], [3]. A novel system has been created to unify the classification system for intracerebral hemorrhage (ICH), known as SMASH-U, which stands for structural lesions, medications, amyloid angiopathy, systemic/other diseases, hypertension, and undetermined causes [4], which was applied in this study. Data pertaining to middle-aged and elderly patients cannot be applied to younger patients because there are differences in clinical features; for example, younger patients with ICH are more likely to be smokers, to have excessive alcohol consumption, to be obese, and to have positive family history of ICH [3], [5]. Thus, it is extremely important that clinical features and outcomes of ICH in young patients be explored to lead to focused management. In this study, *we conducted a retrospective analyse of young adults diagnosed with nontraumatic ICH to elucidate etiologies from 108 Military Central Hospital in Ha Noi, Viet Nam.*

2. Subject and method

From October 2022 to April 2023, our prospective cohort study recruited 45 participants (age under 46 years) who were diagnosed with nontraumatic ICH at the Department of Stroke, 108 Military Central Hospital, Ha Noi, Viet Nam. In all cases included, ICH was defined as a sudden, focal, neurological deficit with intraparenchymal hemorrhage seen on head computed tomography (CT) scans which was available to review and confirm ICH, and ICH was nontraumatic. Patients were excluded from the study if the age was more than 45 years, had any subarachnoid hemorrhage or subdural hemorrhage, or any traumatic intracranial hemorrhage. The medical records of patients meeting the aforementioned study criteria were scrutinized to extract the following data points: (1) demographics, (2) medical history, (3) social history, (4) medication history, (5) presenting symptoms, (6) admission vitals including blood pressure, heart rate and body mass index, and (7) discharge outcome. Classification of each hematoma location was based on the location of lobar (frontal, parietal, temporal, occipital), thalamic, basal ganglia/internal capsule, cerebellar, or brain stem, and intraventricular hemorrhage combination.

The etiology of hemorrhage was determined after thorough review of the chart and reported using SMASH-U etiological classification of ICH previously reported. It refers to structural vascular lesion (S), medication anticoagulants (M), amyloid angiopathy (A), systemic/other disease (S), hypertension (H) and undetermined (U) etiology [3], [4]. Cancer was included under systemic category and amyloid angiopathy was excluded as it does not apply to patients in this study.

Hypertension was determined to be the cause of hemorrhage if they had preexisting history of hypertension or diagnosed to have hypertension during hospitalization for ICH. All young patients underwent CT angiography, cerebral angiogram to determine the etiology of hemorrhage. Some patients had more than 1 etiology for ICH. The most likely single etiology was chosen for reporting the cause of ICH. We evaluated the modified Rankin Scale (mRS) at hospital discharge, splited into two broad categories to simplify the interpretation of outcomes in this study: Good Outcome (mRS 0-2): This category typically includes patients with no symptoms (mRS 0), those with no significant disability (mRS 1), and individuals with slight disability (mRS 2). Patients in this category are generally able to carry out daily activities independently or with minimal assistance; Poor Outcome (mRS 3-6): This category often encompasses patients with moderate disability (mRS 3), moderately severe disability (mRS 4), severe disability (mRS 5), and death (mRS 6). Patients in this category may require varying degrees of assistance, ranging from help with walking to constant nursing care, or they may have succumbed to the condition.

Quantitative variables were represented by mean ± standard deviation. Categorical variables were demonstrated as percentages. Frequency analysis was performed to describe the patient characteristics, presenting symptoms, primary location of hemorrhage, etiology, complications, and discharge disposition. Association of location of ICH and etiology of ICH with the discharge outcome was performed using Chi-squared test. $p<0.05$ was considered statistical significance. Analyses were carried out with SPSS software (version 26; SPSS, Chicago, IL).

3. Result

From October 2022 to April 2023, we enrolled 45 young ICH patients under 46 years. Table 1 shows the characteristics of the study population.

Table 1. Baseline characteristics of young adults with ICH

Variable		No (%)
Sex	Female	16 (35.6)
	Male	29 (64.4)
Age in years, mean ± SD		35.6 ± 8.1
Medical history (No, %)	Hypertension	23 (51.1)
	Diabetes mellitus	1 (2.2)
	Moyamoya	1 (2.2)
	Medication anticogulant	1 (2.2)
Social history (No, %)	Smoking	10 (22.2)
	Alcohol use	12 (26.7)
	Obesity	7 (15.6)
Total		45 (100.0)

Patient demography:

The mean age of the patients was 35.6 ± 8.1 years. It included 16 (35.6%) females, 29 (64.4%) males. Hypertension was the most common medical history present in 23 (51.1%) patients, 3 patients (6.6%) had a history of diabetes mellitus, moyamoya and complication after using medication anticogulant.

In social history, nearly a half of patients had history of smoking and alcohol use, 22.2% and 26.7% respectively. Obesity with BMI over 25 accounted for 15.6% of young patients.

Table 2. Clinical presentation and location of ICH in young adults

Variable		No (%)
Clinical symptoms (No, %)	Headache	39 (86.7)
	Weakness	35 (77.8)
	Nausea/Vomiting	31 (69.8)
	Seizures	3 (6.7)
	Language disorder	28 (62.2)
	Dizziness	20 (44.4)
Primary location of hemorrhage (No, %)	Lobar	17 (37.8)
	Deep	19 (42.2)
	Brainstem/ cerebellum	6 (13.3)
	Intraventricular hemorrhage	3 (6.7)
Total		***45 (100.0)***

Table 2 describes the frequency of each presenting symptoms. Headache was the most common symptoms onset in 39 young patients (86.7%), other symptoms were weakness of one side of the body (77.8%), language disorder was 62.2%, nausea/vomiting and dizziness appeared in 31 (69.8%) patients and 20 (44.4%) patients, respectively. Seizures symptoms was in 3 patients (6.7%) with AVM lesion. Half of

patients had mild hemorrhage stroke with ICH score 0 (51.1%), ICH score 5 was in one patient (2.2%). Most common primary location for hemorrhage was deep structures in 19 patients (42.2%), followed by lobar hemorrhage in 17 (37.8%), and in brainstem and cerebellum in 6 (13.3%). Three patients (6.7%) had primary intraventricular hemorrhage.

Table 3. Etiology, management and discharge outcome of ICH patients

Variable			No (%)
Etiology (No, %)	Structure	AVM	11 (24.4)
		Cavernoma	1 (2.2)
		Moyamoya	1 (2.2)
	Medication - anticogulants		1 (2.2)
	Systemic disease		3 (6.7)
	Hypertensive Angiopathy		23 (51.1)
	Undetermined		5 (11.1)
Management (No, %)	Medical therapy		27 (60.0)
	Decompression surgery		8 (17.8)
	External ventricular drain		1 (2.2)
	Minimal invasive surgery		9 (20.0)
Discharge disposition (No, %)	Good outcome*		22 (48.9)
	Poor outcome*		23 (51.1)
Total			*45 (100.0)*

** Poor (poor outcome group): mRS score 3-6. Good (good outcome group): mRS score 0-2.*

According to the SMASH-U classification, the etiology of ICH was structural abnormalities in 13 (28.8%), medications including anticoagulants in 1 (2.2%), systemic disease in 3 (6.7%), hypertension in 23 (51.1%), and undetermined in 5 (11.1%) patients. Digital subtraction angiography was perfomed in 12 patients and vascular abnormalities on CT angiography were diagnosed in 12 patients: Arteriorvenous malformation in 11 patients, Moyamoya type vasculopathy in 1 patients. In patients with large volume hematoma, 8 patients (17.8%) and 9 patients (20.0%) were performed decompression surgery and minimal invasive surgery, respectively.

Half of patients (n = 22) had good outcome at discharge with mRS 0-2. A half (n = 23) patients had poor outcome with discharge to skilled or long term care facility with mRS 3-6. In detail, 5 patients (11.1%) had mortality at discharge with an mRS score of 6.

Table 4. Discharge outcome of nontraumatic ICH in young adults based on hemorrhage location, etiology, ICH score

Variable		Good outcome* (No, %)	Poor outcome* (No, %)	P
Etiology of ICH (No, %)	Structural	5 (11.1)	8 (17.8)	0.14
	Medication	1 (2.2)	0 (0.0)	
	Systemic	2 (4.4)	1 (2.2)	

	Hypertension	12 (26.7)	11 (24.4)	
	Undetermined	2 (4.4)	2 (4.4)	
Location (No, %)	Lobar	7 (15.6)	10 (22.2)	0.24
	Deep	12 (26.6)	9 (20.0)	
	Brainstem/ cerebellum	4 (8.9)	2 (4.4)	
	IVH	0 (0.0)	3 (6.7)	
Total		***22 (48.9)***	***23 (51.1)***	***45***

** Poor (poor outcome group): mRS score 3-6. Good (good outcome group): mRS score 0-2.*

Table 4 shows the distribution of ICH between good and poor outcome by ICH location and etiology following by SMASH-U classification. The location of ICH was not associated with outcome (p = 0.24). However, patients had hematoma combination with IVH had poor outcome with 6.7%. The etiology of ICH was not associated with discharge outcome (p = 0.14).

4. Discussion

In this study, hypertension, a significant modifiable risk factor implicated in various pathological conditions, stood out as a predominant etiological factor for intracerebral hemorrhage in the young adult population. In our study, 51.1% had ICH due to hypertension. Previous studies in western population have reported hypertension as the etiology of ICH from 11% among those aged 15-40 years in a study published in 1999 [6] to 26.8% among adults aged 18-50 years in 2014 [7]. In comparison to Asian studies, 46.7% of 296 adults aged 15-45 years from Taiwan [8], and 79.2% of 404 adults aged 16-50 years from India had hypertension as an etiology of ICH [9]. Hypertension as a cause of ICH increases with age within the young adult age spectrum. For example, in a study from Finland, 3% (2/62), 21% (14/67) and 33% (68/207) of patients aged 16-29 years, 30-39 years and 40-49 years, respectively, were diagnosed with hypertension as etiology of ICH [10]. In our study, almost patients were not diagnosed with hypertension prior to presentation with ICH. This finding highlights the importance of early screening for hypertension, as it is the most modifiable risk factor for ICH. Moreover, our study showed that only 5.9% of patients with preexisting hypertension were taking antihypertensives at the time of the ICH event. This finding might indicate that hypertension is often underestimated in young individuals and stresses the role of public education and awareness as well. Notably, though not statistically significant, higher number of patients with hypertensive etiology had bad outcomes. In addition, among all patients with a poor outcome, 20.0% had ICH in deep structures of the brain, which is an area highly, correlated with hypertensive etiology. Aggressive blood pressure management in young adults with hypertension could have major impact in this regard to prevent ICH. This is especially important because although ICH has decreased in incidence by 31% amongst all age groups, there has been no appreciable change in mortality rates between 2000 and 2010 [11].

Vascular malformations are a major non-modifiable risk factor for nontraumatic ICH in young adults. Previous studies have reported higher rates of ICH due to vascular malformations, for example 49% in the study by Ruiz- Sandoval et al [6], and 39% by Toffol et al [12]. In our study, structural malformations comprised 28.8% of ICH, a reduction attributed to the escalating prevalence of hypertensive bleeds and potential delays in the earlier treatment or recognition of these anomalies. Given the elevated incidence of vascular malformations as a nontraumatic ICH cause and the potential for adverse outcomes in the absence of timely diagnosis, vascular imaging should be integrated into the diagnostic protocol for all nontraumatic ICH cases in the young adult

population. Diagnostic yield of vessel imaging is higher among patients younger than 50 years with lobar hemorrhage, and without history of hypertension or coagulopathy. Comprehensive workup is essential to prevent future risk of recurrent ICH [13], [14]. One study that had 78 patients with ICH reported 5-year cumulative incidence of recurrent ICH of 8.4% and all 6 patients with recurrent ICH had a vascular malformation, five AVM and one cavernoma [7].

ICH was due to coagulopathy in 2.2% of our patients, which is less than the reported incidence of 4.3% to 5.3% in the literature [8]. None of our patient had ICH due to drug abuse, though it was the cause of young ICH in 7.0% patients in one study [2]. Smoking, alcohol intake and obesity in our study were as frequent as other studies and it may be due to socio-cultural reason [6].

We could not find any correlation between etiology, location of hematoma and discharge outcome, so that is a major limitation of our study. This study is the small sample size, which in future comparative studies can be expanded to more than one center using data repositories. Due to the retrospective nature of the study, we had information on only discharge disposition outcomes and functional scale outcomes were not available.

5. Conclusion

Overall, this study lends support to an enlarging body of evidence that ICH in young adults is modifiable and driven in growing part by hypertension in a population in which chronically elevated blood pressures are not thought to be as prevalent. In primary care settings, hypertension and life styles were important modifiable risk factors for all subtypes of strokes. Considering that hypertension is an independent risk factor for morbidity and mortality in patients with ICH, this comorbidity should be managed aggressively in young patients as part of a primary prevention strategy related to ICH.

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Conflicts of interest.

None.

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