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Original articles

Factors influencing therapeutic strategy for patients with basal ganglia hemorrhage – could age play a potential role in final treatment decision?

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Abstract

Background: Hypertension-associated intracerebral hemorrhage, when compared with cerebral infarction and subarachnoid hemorrhage, is associated with worse clinical outcomes or major disability. Worse clinical outcomes have been observed in the elderly population though age as a factor influencing physicians' final treatment decision is not well determined.

Materials and Methods: We studied 199 patients diagnosed with intracerebral hemorrhage (ICD code: ICD-9-CM-431) who visited a tertiary medical center from January 2003 to March 2006. Baseline characteristics, major medical histories (including co-morbidities), vital signs, neurological assessment (evaluated by the Glasgow Coma Scale), location of the hemorrhage, and the amount of hemorrhaging were all included as variables. A multivariate logistic regression model was chosen to evaluate the significant independent factors that could influence the physician's choice of treatment approach.

Results: There were totally 110 patients meeting the inclusion criteria for enrollment. We observed that worse neurological function on-arrival ($\chi^2 = 8.57$, $p = .01$) and larger amount of bleeding ($\chi^2 = 9.29$, $p = .01$) were more likely to receive surgery. Multivariate logistic regression revealed that age, neurological function on-arrival, and the amount of hemorrhage were significant independent factors influencing the physicians' treatment decision (all $p < .05$).

Conclusion: Age, after adjustment for clinical variables representative of clinical severity, was an important factor in the final therapeutic decision. Our data suggest that a comprehensive evaluation of the patients' on-arrival status may be made and that advanced age should not be a determining factor in the choice of final treatment methods.

Key words: Intra-cerebral hemorrhage; surgical intervention; medical treatment; Glasgow Coma Scale.

Introduction

Intracerebral hemorrhage (ICH) is the most serious and least treatable form of stroke, accounting for 10%-30% of strokes, with greater relative frequencies observed among elderly Chinese and Japanese patients, posing a large social and economic burden (1). Hypertensive ICH is the most frequent type of ICH with the most common location of occurrence at the basal ganglia (2, 3). When patients presenting with hypertensive ICH arrive at the emergency department, physicians generally assess the severity of the stroke based on several factors, including: the level of consciousness on arrival (e.g., by applying the Glasgow Coma Scale, GCS), the side of the brain where the bleeding has occurred, the amount and location of the bleeding, the patient's blood pressure and other baseline characteristics, such as age, sex, race and associated co-morbidities (2, 4-8). However, the factors that may affect the therapeutic decision-making and ultimate strategy of approach, whether medical or surgical, remain complicated and not well-documented (2, 5, 9-12). Results from recent randomized, prospective studies comparing early surgical and conservative medical treatment were controversial and vary considerably (13-15). Therefore, clarifying the important factors influencing a physician's therapeutic choices and analyzing the degree of influence of such factors is of much clinical interest and significance.

Recently, issues have been raised about how aging may exacerbate brain injury and lead to greater neurological defects after ICH (16-17). It has further been mentioned that an elderly population with ICH tends to suffer worse outcomes than a younger population with ICH regardless the types of treatment (9, 10). Whether this difference in clinical outcome may stem from physicians' biased decision in the types of treatment has not yet been fully explored in daily practice. The present study seeks to assess whether the patients' aging itself, after adjusting for other clinical variables, influences the physicians' choice of clinical treatment approach during the hospitalization of their patients after basal ganglia hemorrhage.

Materials and Methods

Study Population

This retrospective study involved a detailed chart review of all the patients' clinical records. Patients in this study were identified among those who visited the emergency department of a tertiary medical center in Taipei, Taiwan, presenting with hypertensive ICH of the basal ganglia between 1 January 2003 to 31 March 2006. Patients were hospitalized and treated either by medical or surgical methods, and then discharged after treatment. Using the definition of ICH of the International Classification of Diseases (ICD) diagnostic code for ICH (ICD-9-CM-431), a total of 199 cases were identified in this period, of which 110 patients with basal ganglia hemorrhage were reviewed for this study.

Independent variables assessed in the present study were classified into three categories: individual patient characteristics, on-arrival neurological function, and disease progression during hospitalization. Individual patient characteristics included age (< 44 years old, 45-64 years old, and > 65 years old), sex, and the presence of known co-morbidities from chart review, such as hypertension, diabetes, heart diseases, and stroke. Heart diseases were defined as presence of any previous heart morbidities including documented coronary arterial disease, heart failure, significant valvular diseases with or without intervention. On-arrival clinical presentations included blood pressure level on admission (hypertension was defined as current usage of anti-hypertensive medication or a history of hypertension based on the chart review with cut-off levels of > 140 mm Hg for systolic blood pressure and > 90 mm Hg for diastolic blood pressure), GCS score on admission (minor: ≥ 13 points; moderate: 9-12 points; severe: ≤ 8 points), the side of bleeding in the brain (left, right, bilateral), and the amount of hemorrhaging (< 20 cc, 20-30 cc, > 30 cc) estimated by computed tomography (CT) scan-based volume quantification (estimated as 1/2 length × width × height based on CT measure) less than one hour after the patient's arrival.

CT images in our study were all performed at the emergency department under the clinical suspicion of stroke within one to two hours of the patient's arrival. The necessity of an immediate neurological surgical approach during the acute phase was judged by the surgeons based on the clinical presentation, pupil size (whether anisocoric or not), and the degree of impaired consciousness assessed by the coma scale (minor, moderate, or severe, as described above).

Patients initially presenting with suspected elevated intra-cranial pressure (ICP) with an accompanying deterioration of consciousness (coma scale ≤ 8) were potential candidates for more aggressive treatment, including neurosurgical approaches. The method of neurosurgical approach was determined by the amount of intra-cranial bleeding and degree of mid-line shift between the brain hemispheres as demonstrated by the CT imaging study. Either a total amount of bleeding > 30 cc or a mid-line shift > 0.5 cm was considered to be clinical criteria for aggressive surgical intervention. Surgical intervention consisted of an open craniotomy plus a hematoma evacuation with subsequent ICP monitoring (extraventricular drainage). Deteriorating clinical neurological manifestations such as changing bilateral pupil size, and a worsening GCS during hospitalization (defined as GCS discrepancy score > 2 points) would lead to repeated CT follow up with surgeons re-assessment for possible surgical intervention if necessary. Subjects who were not initially assigned to the aggressive neurological treatment surgery group underwent re-assessment for possible surgical intervention would then receive CT-guided stereotactic evacuation.

Dependent variables were categorized by treatment methods – surgical or medical treatment. The surgically-treated group included patients who underwent neurosurgery during their hospitalization. Patients who did not undergo neurosurgery were classified in the medically-treated group.

Statistical Analysis

Data were analyzed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics included frequency or percentage for categorical variables and expressed as mean and standard deviation for continuous variables. Inferential statistical tests included the chi-square test, Fisher exact test for categorical and Mann-Whitney test or *t*-test for continuous variables as appropriate.

Data regarding patients' information including baseline patient characteristics, clinical features, GCS score on arrival, the amount of bleeding and the change in disease condition during hospitalization at the hospital were all entered into a multivariate logistic regression model to determine the independent factors that may play significant roles in the final treatment decision. All p were set at two-tailed probability with p value less than 0.05 considered to be statistical significant.

Results

Descriptive Baseline Characteristics

A total of 110 patients were enrolled in this study of whom 49 (44.5%) received surgical treatment and 61 (55.5%) received medical treatment. Chi-square tests on the demographic data and the physicians' choices of treatment were performed on the basis of independent variables, including age, sex, co-morbidities (hypertension, diabetes, heart disease and stroke history), blood pressure on-arrival, GCS score on-arrival, the side of bleeding, the amount of bleeding (Table 1).

There was no obvious difference in the age and gender distribution between these two treatment groups (p = 0.26 & 0.138, respectively). The differences in on-arrival GCS ($p < 0.001$) and the amount of bleeding ($p = 0.03$) between two treatment groups were statistically significant with the surgically treated group having lower GCS and higher amount of bleeding. The differences on-arrival GCS and bleeding amount between these two groups based on a categorical classification were also listed in Table 1. There was a tendency for the more hypertensive patients to be assigned to the medically-treated group, although this tendency did not reach statistical significance ($p = 0.073$).

Blood pressures on-arrival were similar in distribution between groups. Lower GCS on-arrival was associated with higher probabilities of receiving surgical treatment (p = 0.014). Larger amount of bleeding especially those of more than 30 cc when assessed by CT, were more possible to receive surgical intervention (p = 0.01) while the site of bleeding were similar between groups (p = 0.846). Among the surgically treated patients during hospitalization, 75.5% of patients stabilized (GCS discrepancy score was < 1 point) and 24.5% had clinical deterioration (GCS discrepancy score was > 2 points) while in the medically treated patients, 90.2% of the patients stabilized (GCS discrepancy score was < 1 point), and 9.8% had clinical deterioration (GCS discrepancy score was > 2 points).

The Association between On-arrival GCS score, Amount of bleeding and Changes in Disease Condition

Chi-square analysis of the on-arrival GCS score, the amount of bleeding and the changes in disease condition was listed in Table 2. These results showed that patients with higher on-arrival GCS scores had significantly less bleeding amount ($p < 0.001$) assessed by CT. The GCS score on-arrival and change in disease condition was also presented in Table 2 and showed a borderline increase in the incidence of worsening GCS during hospitalization in patients with higher on-arrival GCS ($p = 0.083$, $\chi^2 = 4.646$).

Multivariate Statistical Analysis – Logistic Regression Analysis of the Influence of Factors Affecting Physician Choice of Treatment

Logistic regression analysis was performed on the variables that were statistically significant in the bivariate analysis, including the on-arrival GCS score, the amount of bleeding, and changes in disease condition during hospitalization. Although analysis of age, sex, and co-morbidity did not reach statistical significance in the present study, these variables have been recognized as important risk factors for stroke in other studies (10, 22-24). Therefore, we chose to subject these variables to multivariate analysis (Table 3). To facilitate the analyses, the reference age group was those older than 65 years old, the reference amount of bleeding was < 20 cc, and the reference for the on-arrival GCS score was ≥ 13 points. For the analysis of GCS score discrepancy during hospitalization, the reference was set for < 1 point (stabilized). For the Hosmer-Lemeshow goodness-of-fit test, the estimated value was X^2.

The multivariate analysis of on-arrival patient information indicated that age, amount of bleeding, on-arrival GCS score, and physician's choice of treatment were statistically significant (Table 3). There was a 2.832-fold difference in choosing surgical treatment in patients of 45 to 64 years old while compared to those over 65 years old ($p = 0.031$) and a 25.374-fold difference in choosing surgical treatment in patients showing > 30 cc of bleeding compared to those showing < 20 cc of bleeding ($p = 0.020$). There was a 3.559-fold difference in choosing surgical treatment between patients with an on-arrival GCS score of 9 to 12 points and patients with an on-arrival GCS score ≥ 13 points ($p = 0.017$).

When change in disease condition during hospitalization was included in the multivariate model, there was a 2.887-fold difference in choosing

Table 1

Chi-square test of patient demographic data and physicians' choice of treatment

Item	Surgical	Medical		
	Number (%) or Average	Number (%) or Average	χ^2	p value
Age (years)	61.12 (11.71)	64.05 (15.36)	–	0.26
< 44	3 (6.1)	5 (8.2)	3.127	0.228
45-64	30 (61.2)	27 (44.3)		
> 65	16 (32.7)	29 (47.5)		
Sex			2.197	0.138
Male	27 (55.1)	42 (68.8)		
Female	22 (44.9)	19 (31.2)		
Comorbidities				
Hypertension	48 (98)	54 (88.6)		0.073
Diabetes	7 (14.3)	8 (13.1)		0.859
Heart diseases	2 (4.1)	7 (11.5)		0.294
Stroke	5 (10.2)	6 (9.8)		1.000
Blood pressure				1.000
Nonhypertensive	5 (10.2)	6 (9.8)		
Hypertensive	44 (89.8)	55 (90.2)		
On-arrival GCS	10.96 (2.7)	12.62 (2.89)	–	< 0.001
≤ 8 points	9 (18.4)	6 (9.8)	8.571	0.014
9-12 points	24 (49)	18 (29.5)		
≥ 13 points	16 (32.6)	37 (60.7)		
Bleeding side			0.384	0.846
Right	19 (38.8)	26 (42.6)		
Left	26 (53)	29 (47.5)		
Bilateral	4 (8.2)	6 (9.9)		
Amount of bleeding	16.2 (18.57)	8.84 (15.46)	–	0.03
< 20	37 (75.5)	56 (91.8)	9.291	0.010
20-30	3 (6.1)	4 (6.6)		
> 30	9 (18.4)	1 (1.6)		
Change in condition			4.263	0.039
Stabilized	37 (75.5)	55 (90.2)		
Deteriorated	12 (24.5)	6 (9.8)		
Total	49	61		

* Analyses of age and amount of bleeding were performed by independent *t*-test. The Mann-Whitney-Wilcoxon test was used to analyze on-arrival GCS.

GCS, Glasgow Coma Scale; SD, standard deviation.

surgical treatment in patients of 45 to 64 years old when compared to those over 65 years old ($p = 0.031$). There was a 25.185-fold difference in choosing surgical treatment in patient showing > 30 cc of bleeding when compared to those showing < 20 cc of bleeding ($p = 0.017$) and a 3.287-fold difference in choosing surgical treatment in patients with an on-arrival GCS score of 9 to 12 points when compared to those with an on-arrival GCS score ≥ 13 points ($p = 0.017$). Finally, there was a borderline difference in choosing surgical treatment in deteriorated patients (3.255-fold, $p = 0.055$) during hospitalization. Hosmer-Lemeshow goodness-of-fit analysis showed no significant difference between the actual

Table 2

Chi-square analysis of on-arrival GCS score and amount of bleeding

Item	On-arrival GCS (points)			*p*-value
Bleeding Amount	≥ 13	9-12	≤ 8	< .001
< 20 cc	48	37	8	
20-30 cc	5	2	0	
> 30 cc	0	3	7	
GCS discrepancy score				0.083 (χ^2 = 4.646)
< 1 point (n = 92)	45	32	15	
> 2 points (n = 18)	8	10	0	

GCS, Glasgow Coma Scale.

Table 3

Logistic regression analyses of physician choice of treatment

Item	Model 1 Estimated value β (*p* value)	Success ratio Odds ratio	Model 2 Estimated value β (*p* value)	Success ratio Odds ratio
Intercept	–4.106 (0.005)	0.016	–4.120 (0.006)	0.016
Sex				
Male	0.878 (0.069)	2.405	0.864 (0.081)	2.373
Age[1]				
< 44	1.311 (0.168)	3.709	1.200 (0.228)	3.321
45-64	1.041 (0.031)	2.832	1.060 (0.031)	2.887
Comorbidity				
Yes	2.227 (0.108)	9.272	2.056 (0.150)	7.814
Bleeding[2]				
20-30 cc	0.045 (0.962)	1.046	–0.117 (0.899	0.890)
> 30 cc	3.234 (0.020)	25.374	3.226 (0.017)	25.185
On-arrival GCS[3]				
9-12 points	1.270 (0.009)	3.559	1.190 (0.017)	3.287
≤ 8 points	0.351 (0.674)	1.421	0.532 (0.527)	1.702
Discrepancy				
Deteriorated			1.180 (0.055)	3.255
Hosmer-Lemeshow goodness-of-fit[5]	5.256		12.271	

1. The reference group was set for over 65 years of age.
2. The reference group was set for < 20 cc of bleeding.
3. The reference group was set for on-arrival GCS score ≥13.
4. The reference group was set for on-arrival GCS score ≥13 and stabilized.
5. The estimated value was X^2.

and estimated distributions of the medically or surgically treated groups.

Discussion

In this study, we demonstrated that age itself could be an important factor influencing the final treatment decision after adjusting for other clinical confounding variables. Our analysis used similar baseline demographics with some differences in the amount of hemorrhaging and initial neurological function at presentation. We showed an independent shift in the physicians' clinical approach from surgery to conservative medical treatment, regardless of the variables entered and models used, if the patient being treated was older.

McKissock *et al.*, reported the first prospective, randomized control trial comparing the outcomes of neurosurgery and conservative treatment, with worse results observed in the surgical group (18). This study has had a tremendous effect on the management of most such patients in the past half century. Currently, the clinical criteria now widely used to help predict patient outcomes was proposed by Kanaya *et al.*, in a large observational study (19). A more recent multicenter randomized trial of 1 033 patients, the International Surgical Trial in Intracerebral Hemorrhage (STICH), which tried to clarify the role of surgery compared with medical therapy alone in ICH still failed to show any overall benefit from an early surgical approach (13). Though plenty of research has investigated the clinical predictors of ICH patients and the beneficial effects of different treatment modalities (20), few studies discussed the factors influencing the physicians' clinical therapeutic decision in real world practice.

In line with previous studies, the results of our bivariate analysis showed that the on-arrival GCS score was significantly affected by the amount of bleeding; the more total bleeding there was, the lower the on-arrival GCS score. Further results relating to the on-arrival GCS score were obtained by multivariate analyses. Therefore, the on-arrival GCS score was also a critical factor affecting the physician's decision to choose between medical or surgical treatment (21). Our results also showed that when physicians considered the therapeutic methods for stroke, the main factors were the amount of bleeding, the on-arrival GCS score, and age. A novel aspect of the present study was our distinction of GCS scores according to on-arrival GCS score and GCS discrepancy score (stabilized or deteriorated). This allowed us to perform a cross-evaluation and regression analyses of patient characteristics and their clinical presentation. Hence, our results could be systematically compared. On this basis, we believe that specific guidelines should be provided for physicians to adjust, at any time, the medical or surgical treatment of patients with hemorrhagic stroke in the basal ganglia.

Many previous studies have indicated that patient age is one of the most critical causative risk factors for ICH (2, 5, 12, 22-23). In addition, advanced age was ever consistently recognized to be associated with worse outcomes (24, 25). However, to our best knowledge, none has aimed at pointing out whether age itself may play a determining factor influencing physicians' treatment strategy. The results of our present study showed that age was statistically significant by multivariate analysis ($p = .031$) in the therapeutic decision making process. These results confirmed the higher probability that surgical treatment was chosen for patients between 45 and 64 years old while compared to patients older than 65 years old. In other words, for patients aged 45 to 64 years old, their age was critical in their physician's choice of surgical treatment. This finding might imply that subconsciously, physicians may attempt a more aggressive rather than conservative approach in the management for ICH in younger populations in the real world practice. Interestingly, there was no significance associated with patients younger than 44 years old, probably because of the few number of cases.

Stereotactic instrumentation has been mentioned by Hattori et al to provide the rapid access with great accuracy to virtually any intracranial lesion (28). The rationale for applying CT-guided stereotactic neurosurgical procedures in our practice is thus to accurately access those targets initially not assigned (either due to a smaller intra-cranial lesion or a more difficult anatomy) to ordinary craniotomy with minimal spatial error and a high reproducibility in order to reduce added operation risks once clinical condition worsened and may mandate surgical approach after re-assessment.

According to our study, we categorized the amount of bleeding into groups: < 20 cc, 20-30 cc and > 30 cc. Some studies divided their patients groups as more or less than 30 cc (26) or 20 cc (27). Our results indicated that this variable was statistically significant in monovariate, bivariate and multivariate analyses in selecting treatment approaches. Therefore, the amount of bleeding, with a cut-off of whether > 30 cc or < 20 cc, was a critical factor affecting the physicians' choice preferring for surgical treatment.

Limitations

A major limitation of the present study was that the data were obtained from a single center. This permitted the evaluation of the GCS scores in the emergency department as well as during hospitalization to be performed by a consistent group of medical personnel under relatively stable conditions.

Furthermore, patient care and physician choice of treatment are affected by many factors, such as physician attitudes, the wishes of the patient and their family members, and the limitations of medical resources and equipment, among other factors. Because this study was retrospective, we were unable to include this other related information in our analyses.

Conclusion

The amount of bleeding and the GCS score in patients with ICH are sound guidelines for choosing treatment methods. In the present study, we further investigated other potential therapeutic determining factors in patients with basal ganglia hemorrhage in the real-world practice. Our data demonstrated that age may potentially play as an important factor affecting physicians' subconscious selection of medical or surgical treatment beyond the amount of bleeding and on-arrival GCS score. Results of the present study may help medical personnel in selecting and adjusting appropriate therapeutic options which may also potentially reflect the observed outcomes relating to the aging population.

Declarations

There was no conflict of interest for any of the contributing authors with regard to the publication of these results.

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