

Surgical Evacuation versus Conservative Treatment in Elderly Patients with Basal Ganglia Hemorrhage: A Propensity Score Matched Study

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Objective: To study and compare the efficacy of surgery and conservative treatment in elderly patients with spontaneous basal ganglia hemorrhage (BGH) using a propensity score matched study.

Materials and Methods: Efficacy research with a retrospective cohort study was conducted by reviewing patients aged 60 and older treated with surgical evacuation or conservative treatment between January 2017 and January 2022. To compare the proportion of favorable outcomes (mRS 0 to 3) at six months, rate of the 30-day mortality, ratio of hospital-acquired pneumonia, and length of hospital stay. Propensity score matching was applied to adjust the confounding factors.

Results: Total of 366 patients were included in the present study. Of these, 204 were matched for analyses (102 with surgical evacuation and 102 with conservative treatment). There was no significant difference in the proportion of favorable outcomes between both groups (adjusted risk difference 11.2%, 95% CI -0.03 to 0.25, $p=0.115$). Surgical evacuation showed significantly lower rates of mortality within 30 days (adjusted risk difference -16.9%, 95% CI -0.3 to -0.1, $p=0.001$). The proportion of hospital-acquired pneumonia and the length of hospital stay showed no significant difference between both groups (adjusted risk difference -3.8%, 95% CI -0.1 to 0.04, $p=0.369$, and mean difference -0.9, 95% CI -2.7 to 1.0, $p=0.358$, respectively).

Conclusion: Surgical evacuation of spontaneous BGH in the elderly patients could reduce the 30-day mortality. However, it did not demonstrate any quantifiable improvement in functional outcome at 6 months, or hospital-acquired pneumonia, and the length of hospital stay.

Keywords: Craniotomy; Conservative treatment; Basal ganglia hemorrhage; Elderly patients; Propensity score matched

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Spontaneous intracerebral hemorrhage (sICH) is the second most common type of stroke⁽¹⁾. Although sICH accounts for 10% to 20% of all strokes, it is associated with high mortality, and the majority of survivors stay with serious neurological sequelae requiring long-term medical and social care^(1,2). Hypertension is the most critical risk factor for sICH, and the basal ganglia is the most common site, representing 60% of hypertensive sICH⁽³⁻⁵⁾. The incidence of basal ganglia hemorrhage (BGH)

increases with advanced age⁽⁶⁾. Management of patients with sICH poses a considerable dilemma because there is no convincing evidence of benefit from any medical or surgical treatment⁽⁷⁾. Theoretically, early hematoma evacuation may decrease the toxic effects of blood products, diminish surrounding edema and ischemia, decrease intracranial pressure, and prevent hematoma expansion^(8,9). Experimental studies have indicated that surgery may help to reduce secondary neuronal damage in sICH⁽¹⁰⁾. On the other side, craniotomy itself could further damage healthy brain parenchyma. Thailand is currently entering the Aging Society. The number of people aged 60 and older is approximately 11.6 million, accounting for 17.6% of the population⁽¹¹⁾. Stroke is a crucial health care problem in Thailand, particularly in aging people. The indication for optimal treatment between surgical and medical is still ambiguous. The present project aimed to study and compare the efficacy of surgery and conservative treatment in the elderly patients with spontaneous BGH.

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Materials and Methods

The present study was a therapeutic study based on a single-center retrospective cohort of elderly patients with spontaneous BGH admitted in Chumphon Khet Udomsakdi Hospital in the southern part of Thailand, between January 2017 and January 2022. In the hospital database, the International Classification of Diseases, Tenth Revision, and Clinical Modification codes (ICD-10) with the code I61.0 were screened. Only diagnosed BGH were recruited in the present study. A patient aged 60 years or older at the time of admittance to the hospital was considered elderly. Because the data were obtained retrospectively and were anonymous, informed consent was not required. The present study was approved by the Institutional Review Board of Chumphon Khet Udomsakdi Hospital (protocol number CPH-EC-009/2564) and the Faculty of Medicine, Thammasat University (protocol number MTU-EC-OO-0-212/64).

Study population and data collection

All admission medical records during the study period were screened for eligibility. The patients aged 60 and older and that had a volume of the hematoma more than 25 mL were included for analyses. Patients were excluded if they were:

1. Coagulopathy or thrombocytopenia,
2. End-stage of underlying diseases,
3. Glasgow coma scale (GCS) less than 6,
4. The extension of basal ganglia hematoma to Thalamic nucleus, and
5. Concurrent intraventricular hemorrhage (IVH)

Included patients were divided into two groups according to their treatment. The first group, surgical hematoma evacuation (standard craniotomy) was performed within 72 hours, whereas the second group received conservative treatment. Other than the surgical evacuation, all patients were provided with standard treatment. The author collected twelve independent variables as age, gender, diabetes mellitus, admission blood glucose, aspirin use, Tranexamic acid intravenously, admission systolic blood pressure (SBP), admission diastolic blood pressure (DBP), left-side BGH, volume of the hematoma (mL), midline shift on computed tomography (CT) scan (cm), and admission GCS. The primary outcome was predefined as the proportion of patients with a favorable functional outcome at six months after BGH using the modified Rankin Scale (mRS), which is range 0 for no functional deficit

to 6 for death. A favorable outcome was defined as a mRS of 0 to 3 with 0 being no deficit to 3 being able to walk independently with a walker or a cane. An unfavorable outcome was defined as a mRS of 4 to 6 with 4 being unable to walk to 6 as death. The secondary outcomes were the rate of 30-day mortality, the average length of hospital stay, and proportion of patients with hospital-acquired pneumonia between both groups.

Propensity score matching methods and statistical analyses

The present study was a non-randomized therapeutic research, selection bias, confounding-by-indication, confounding-by-contraindication, and imbalanced prognostic determinants were likely to occur. The author, therefore, performed a propensity score matching between these two groups before the estimation of the treatment effects. First, the propensity score was calculated to estimate the probability for each patient to be treated with surgical evacuation using a multivariable logistic regression model. In the present study, the propensity score model included:

- The patient's age
- Aspirin use
- Admission GCS
- Left-side BGH
- The volume of the hematoma
- Midline shift on CT scan

The author matched the patients treated with surgical evacuation to the patients treated with conservative treatment with 1:1 ratio, then assessed the balance of baseline characteristics, prognostic factors, and potential confounders between the two groups after matching with a standardized difference (STD), where an absolute STD of less than 10% was considered as no significant difference between groups. The histogram plot showed the propensity score distribution of both groups to illustrate the balance of the score before and after matching. After propensity score matching, the patient characteristics were balanced in the two groups. The data were analyzed using Stata Statistical Software, version 17 (StataCorp LLC, College Station, TX, USA). For all statistical analyses, a two-sided p-value of less than 0.05 was considered significant. The present study described the patient characteristics, number, and percentage for categorical data, and mean (\pm standard deviation) or median and interquartile range (IQR) for numerical data by using descriptive statistics. The author performed a comparative analysis of

Table 1. Clinical characteristics of the original cohort patients (n=366)

Characteristics	Original cohort		STD (%)	p-value
	Surgery (n=137)	Conservative (n=229)		
Age (years); median (IQR)	66 (62, 70)	67 (63, 69)	4.8	0.618 ^a
Sex: male; n (%)	80 (58.4)	109 (47.6)	-21.7	0.045 ^b
Diabetes mellitus; n (%)	23 (16.8)	42 (18.3)	4.1	0.707 ^b
Aspirin use; n (%)	17 (12.4)	34 (14.9)	7.1	0.514 ^b
Admission SBP (mmHg); mean±SD	169.1±12.4	168.3±11.6	-5.8	0.586 ^c
Admission DBP (mmHg); mean±SD	95.3±6.1	94.4±5.9	-15.9	0.141 ^c
Admission blood glucose (mg/dL); mean±SD	147.5±47	147.5±35.9	0	0.998 ^c
Admission GCS; mean±SD	9.2±1.6	8.9±1.3	-19.7	0.061 ^c
Hematoma volume (mL); mean±SD	47.7±10.3	45.1±8.6	-27.6	0.009 ^c
Midline shift(cm); mean±SD	0.63±0.14	0.58±0.1	-40.1	0.001 ^c
Left BGH; n (%)	53 (38.7)	93 (40.6)	3.9	0.716 ^b
Tranexamic acid; n (%)	47 (34.3)	87 (37.9)	7.6	0.479 ^b
Propensity score; mean±SD	0.45±0.19	0.33±0.11	-74.3	0.001 ^c

IQR=interquartile range; SD=standard deviation; STD=standardized difference; SBP=systolic blood pressure; DBP=diastolic blood pressure; GCS=Glasgow coma scale; BGH=basal ganglia hemorrhage

^a The results of the Mann-Whitney U test, ^b The results of the chi-square test, ^c The results of the independent t-test

categorical variables using chi-squared test, whereas continuous variables using the independent t-test for data with normal distribution, and the Mann-Whitney U test for non-normal distribution. The risk difference regression and mean difference were calculated to evaluate any differences between the two groups. To entirely eliminate residual confounding factors all regression models were adjusted for the remaining potential confounders.

Results

Five hundred forty-eight medical charts of hospitalized patients between January 2017 and January 2022 were screened. Of these, 182 did not fulfill the inclusion criteria:

- 52 were GCS less than 6
- 51 were aged less than 60 years
- 35 were concurrent IVH
- 16 had end stage of underlying disease
- 13 had coagulopathy or thrombocytopenia
- 9 were not diagnosed spontaneous BGH
- 6 had incomplete medical records

Three hundred sixty-six patients were included in the present study, 137 were treated with surgical evacuation within 72 hours, and 229 were treated with conservative treatment. After 1:1 matching for propensity score, there were 102 patients included in each treatment group (Figure 1).

Table 1 shows the 366 original cohort patients. There were significant differences in the proportion of gender (male), the mean of hematoma volume,

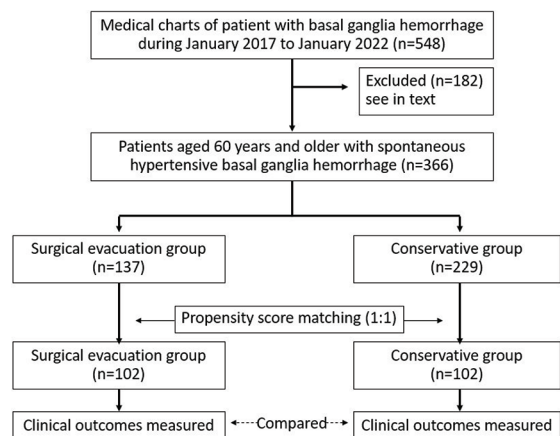


Figure 1. Study flow diagram of the patient cohort.

and midline shift on CT scan between both groups ($p=0.045$, 0.009 , and 0.001 , respectively). The mean of the propensity score in each group was significantly different at 0.45 ± 0.19 versus 0.33 ± 0.11 (STD -74.3 , $p=0.001$)

Table 2 shows the 204 patients after propensity score matching with 102 in the surgical group and 102 in the conservative group. There were no significant differences in all parameters between both groups. The mean of propensity scores in each group became nearly equal at 0.37 ± 0.14 versus 0.36 ± 0.14 (STD -3.4 , $p=0.809$). The balance of propensity scores before and after matching are shown in Figure 2.

Table 3 used a propensity score matched database as the patient's clinical characteristics were similar

Table 2. Clinical characteristics of the patients after propensity score matching (n=204)

Characteristics	Propensity-matched cohort		STD (%)	p-value
	Surgery (n=102)	Conservative (n=102)		
Age (years); median (IQR)	67 (62, 70)	67.5 (63, 70)	10.4	0.431 ^a
Sex: male; n (%)	56 (54.9)	52 (50.9)	-7.8	0.575 ^b
Diabetes mellitus; n (%)	20 (19.6)	18 (17.7)	-5.0	0.719 ^b
Aspirin use; n (%)	14 (13.7)	14 (13.7)	0	0.999 ^b
Admission SBP (mmHg); mean±SD	168.8±11.9	167.8±10.4	-9.2	0.509 ^c
Admission DBP (mmHg); mean±SD	94.9±5.7	93.9±6.3	-17.5	0.211 ^c
Admission Blood glucose (mg/dL); mean±SD	142.3±38.5	148.6±34.9	17.2	0.221 ^c
Admission GCS; mean±SD	8.9±1.4	8.9±1.4	4.3	0.756 ^c
Hematoma volume (mL); mean±SD	46±8.3	46±9.4	1.7	0.902 ^c
Midline shift (cm); mean±SD	0.6±0.1	0.6±0.1	-7.3	0.598 ^c
Left BGH; n (%)	41 (40.2)	46 (45.1)	9.8	0.479 ^b
Tranexamic acid; n (%)	40 (39.2)	38 (37.3)	-4.0	0.773 ^b
Propensity score; mean±SD	0.37±0.14	0.36±0.14	-3.4	0.806 ^c

IQR=interquartile range; SD=standard deviation; STD=standardized difference; SBP=systolic blood pressure; DBP=diastolic blood pressure; GCS=Glasgow coma scale; BGH=basal ganglia hemorrhage

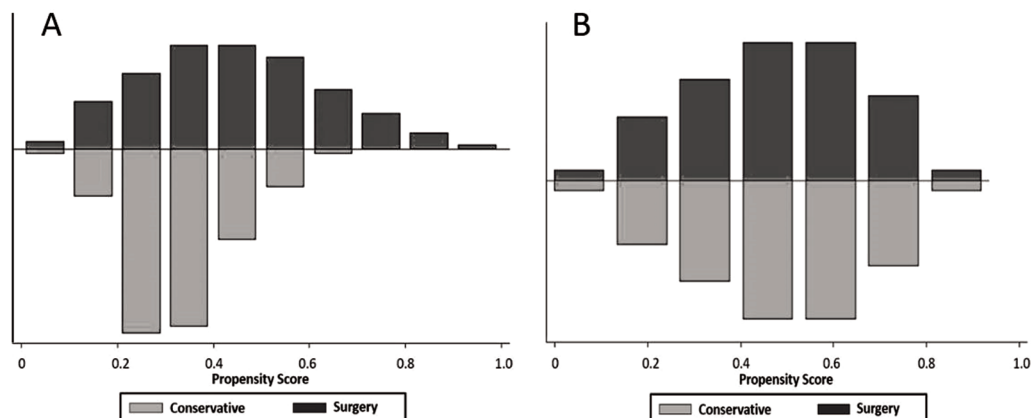
^a The results of the Mann-Whitney U test, ^b The results of the chi-squared test, ^c The results of the independent t-test

Table 3. Clinical outcomes using propensity score-matched database (n=204)

Clinical outcomes	Surgery (n=102)	Conservative (n=102)	Treatment effect (surgical evacuation vs. conservative treatment)				
			Clinical parameters		Adjusted analysis ^a		
					Effect	95% CI	p-value
Favorable outcome; n (%)	55 (53.9)	44 (43.1)	RD (%)		11.2	-0.03 to 0.25	0.115
			OR		1.6	0.9 to 2.7	0.112
30-day mortality; n (%)	7 (6.9)	24 (23.5)	RD (%)		-16.9	-0.3 to -0.1	0.001
			OR		0.23	0.1 to 0.5	0.001
HAP; n (%)	8 (7.8)	12 (11.8)	RD (%)		-3.8	-0.1 to 0.04	0.369
			OR		0.66	0.2 to 1.7	0.398
LOS (days); mean±SD	13.9±7.0	13.1±6.6	Mean difference		-0.9	-2.7 to 1.0	0.358

LOS=length of hospital stay; HAP=hospital acquired pneumonia; RD=risk difference (under risk regression analysis); OR=odds ratio (under logistic regression analysis); SD=standard deviation; CI=confidence interval

^a The results of the multivariable analysis adjusted for potential confounders (double adjustment)

**Figure 2.** Distribution of propensity score. (A) Propensity score before matching and (B) propensity score after matching.

between both groups and the results of all clinical outcomes are presented. The proportion of favorable outcome at six months shows no significant difference between both groups (adjusted risk difference 11.2%, 95% CI -0.03 to 0.25, $p=0.115$, and odd ratio 1.6, 95% CI 0.9 to 2.7, $p=0.112$). The risk of 30-day mortality was lower in patients treated with surgical evacuation (adjusted risk difference -16.9, 95% CI -0.3 to -0.1, $p=0.001$, and odd ratio 0.23, 95% CI 0.1 to 0.5, $p=0.001$). The proportion of hospital-acquired pneumonia shows no significant difference between both groups (adjusted risk difference -3.8, 95% CI -0.1 to 0.04, $p=0.369$, and odd ratio 0.66, 95% CI 0.2 to 1.7, $p=0.398$). Finally, there was no significant difference in length of hospital stay at 13.9 ± 7.0 days in the surgical evacuation group and 13.1 ± 6.6 days in the conservative treatment group (mean difference -0.9, 95% CI -2.7 to 1.0, $p=0.358$).

Discussion

The most common type of hypertensive hemorrhagic stroke is spontaneous basal ganglia bleeding, which is also one of the most dangerous⁽³⁻⁵⁾. Clinical and radiologic factors such as the patient's age, level of consciousness, comorbidity, volume of the hematoma, and midline shift on the initial CT scan appear to be markers of a poor prognosis after BGH⁽¹²⁾. Studies related to the medical and surgical management of BGH have been conducted to overcome its devastating clinical course. Despite these efforts in the past decades, there have been no dramatic advances in the development of interventions to improve the functional outcomes after BGH^(7,13).

In the present study, the author performed a propensity score matching for the balance of baseline characteristics, prognostic factors, and potential confounders between the two groups before estimating the treatment effects. According to the primary outcome, surgical evacuation did not show significant benefit on the favorable outcome at six months in elderly patients with spontaneous BGH. Previous research has similar results^(5,7,14,15). Among these trials, the largest is the STICH trial⁽⁷⁾, an international multicenter prospective randomized clinical trial that concluded the favorable outcome at six months did not significantly differ between surgical and medical treatment groups. In theory, the basal ganglia refer to a group of subcortical nuclei as striatum and globus pallidus, responsible primarily for motor control, as well as other roles such as motor learning, executive functions, behaviors, and

emotions. Basal ganglia lesion would be most likely to result in deficits pertaining to motor, cognitive, associative, limbic functions, and quality of life⁽¹⁶⁾. However, a study published by Pantazis et al⁽¹⁷⁾ showed that patients who underwent craniotomy had a better functional outcome than those received conservative treatment.

According to the secondary outcomes, the surgical evacuation had significantly lowered the 30-day mortality rate. In terms of efficacy, previous studies reported and concluded that surgical evacuation was superior to conservative treatment⁽¹⁸⁻²⁰⁾. In theory, when bleeding occurs, initial tissue injury activates secondary injury pathways, including the release of toxic hemolysis products, oxidative stress, and inflammatory response. Those processes result in neuronal death, development of perihematomal edema, increase in parenchymal volume, and herniation consequence affecting mortality^(8-10,12). Surgical evacuation of intracerebral hematomas reduces the mass effects, thereby reducing intracranial pressure, improving regional blood flow, and limiting the toxicity of blood-breakdown products^(8-10,12). On the other side, surgical evacuation has not been shown to improve mortality in studies^(5,21). However, the patient's clinical characteristics, outcome measurement, and healthcare setting differed from the present study. There was no difference in the proportion of hospital-acquired pneumonia and the average length of hospital stay between both groups, which is similar to the study of Hegde et al⁽¹⁹⁾. According to the theory, hospital-acquired pneumonia is one of the most critical variables in extending the time of hospital stay in stroke patients⁽²²⁾. However, a previous study showed the risk of hospital-acquired pneumonia in the surgical group was higher than in the conservative treatment group⁽²⁰⁾.

Two strengths of the present study should be highlighted. First, this is an observational design that reflects the effect of surgical evacuation use in real-world clinical practice. Thus, it provides a high external validity and can be generalized to other populations with similar circumstances. Second, to estimate the treatment effect between applying surgical evacuation and the favorable outcome from observational data, the author used the propensity score method to minimize selection bias and balance the distribution of measured covariates that give rise to confounding by indication or confounding by contraindication⁽²³⁾. The propensity scores based on six pre-specific characteristics that influence the selection of treatments, either surgical evacuation

or conservative treatment by clinicians were age, aspirin use, admission GCS, left-side BGH, hematoma volume, and degree of midline shift on the initial CT scan. After matching, the differences between groups became smaller; however, the remaining potential confounders were imbalanced with STD of more than 10%. In conclusion, the treatment effect in the presence of a significant imbalance of covariates could compromise the result. Therefore, the author performed double adjustment by multivariable logistic regression model to adjust remaining potential confounders. This approach could eliminate residual confounding bias, increase statistical power, and improve the validity of causal estimates⁽²⁴⁾. There were limitations to be addressed:

1. This was a single-center retrospective study with a lack of randomization, blinding, and measure of surgical success.

2. Propensity score matching to account for confounding may not have compensated entirely for apparent treatment bias.

3. The present study was limited by a lack of standardization in regard to decision-making to opt for surgical evacuation or conservative treatment, and all operations were not performed by the same neurosurgeon.

To further investigate these topics, high-quality, rigorous, randomized controlled trials are needed.

Conclusion

Surgical evacuation of spontaneous BGH in elderly patients could reduce the 30-day mortality. However, there were no discernible changes in functional outcome at six months, hospital-acquired pneumonia, or length of hospital stay.

What is already known on this topic?

Surgical evacuation of spontaneous BGH in the elderly patients did not demonstrate improvement in functional outcome at six months.

What this study adds?

The findings supported that the surgical evacuation of spontaneous BGH in the elderly patients could reduce the 30-day mortality.

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Conflicts of interest

The authors declare no conflict of interest.

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