

# Risk Factors for Contralateral Progression after Unilateral Burr-Hole Evacuation of Bilateral Chronic Subdural Hematoma

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## Research Article

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# Abstract

## Purpose

Contralateral hematoma progression (CHP) is a common condition among bilateral chronic subdural hematoma (bCSDH) patients after the unilateral evacuation. Investigations focusing on this topic are limited. The author aims to identify risk factors correlated with the CHP.

## Methods

82 patients with bCSDH who underwent the unilateral evacuation in Beijing Tiantan Hospital from 2011 to 2021 were included in this retrospective study. Clinical information and radiological features of these patients were collected and analyzed. Chi Square test, Student t test and Mann-Whitney test was performed to find variables which were statistically significant ( $p < 0.05$ ), then multivariate analysis was applied to identify the independent risk factors.

## Results

In our research, the progression rate was up to 13.41% (11/82). The mean age of CHP patients was significantly higher than non-CHP patients ( $72.45 \pm 12.78$  vs  $62.85 \pm 13.91$ ,  $p = 0.025$ ). Contralateral hematoma locating on the curved side was more likely to progress ( $p = 0.007$ ). The other risk factors including pre- and post-operative volume of hematoma in the non-surgical side and the wide type of contralateral hematoma. The multivariate analysis demonstrated that the wide type of contralateral hematoma was one of the independent risk factors for CHP (OR = 8.769,  $p = 0.020$ , 95%CI 1.410-54.545). Moreover, the opposite hematoma locating on the curved side was also associated with the contralateral progression independently (OR = 7.103,  $p = 0.033$ , 95%CI 1.168–43.213).

## Conclusion

For bCSDH patients, wide contralateral hematoma may increase the risk of CHP. Moreover, non-operative hematoma which locates on the curved side of skull is also an independent risk factor for the enlargement of opposite hematoma. Patients with such radiological characteristic may need additional medical treatment and rigorous follow-up to prevent the progression of contralateral hematoma.

## Introduction

Chronic subdural hematoma (CSDH), a common disease needing neurosurgical operations, is characterized by a slowly accumulating blood products in the cavity between dura mater and arachnoid mater[1]. The incidence of CSDH increasing with age ranges from 3.4/100,000 people per year in patients younger than 65 years to 58.1/100,000 people annually for those aged 65 years and older[2].

Bilateral chronic subdural hematoma (bCSDH), a subtype of chronic subdural hematoma, has been demonstrated as a risk factor associated with postoperative hematoma recurrence[3]. The surgical options for bCSDH largely depends on the hematoma size and patient's symptoms[4]. Many clinicians often perform unilateral evacuation on bCSDH patients for the reason that some contralateral hematoma is small and asymptomatic[5]. However, many previous researches reported that nearly 10%-20% bCSDH patients who underwent unilateral evacuation would be reoperated on the non-surgical side for contralateral progression and accompanying neurological symptoms[6, 7]. Finding risk factors related to contralateral hematoma progression (CHP) can predict the enlargement tendency of contralateral hematoma and decrease the reoperation rate of patients, but few investigations focus on this topic.

In this research, we analyzed the data of 82 patients with bCSDH undergoing unilateral evacuation in our hospital for the purpose of finding some risk factors associated with CHP.

## Methods

### Research population

The present retrospective analysis was approved by the Institutional Review Board of Beijing Tiantan Hospital (KY2020-094-01). The data of patients with bCSDH, who underwent unilateral surgery in the Department of Neurosurgery of Beijing Tiantan Hospital from October,2011 to April,2021, were retrospectively analyzed. The inclusion criteria were as follows: (A) patients who were older than 18 years and younger than 90 years; (B) patients who were diagnosed with bCSDH by the preoperative computed tomography (CT) scan and only one side of the bCSDH met evacuation indications; (C) patients who did not suffer any head trauma event during the 6 months after the initial surgery;(D) patients who had no history of craniotomy and other intracranial lesions.

### Data collection

The research populations' baseline data and clinical manifestations were collected and analyzed. The Glasgow Coma Scale (GCS)[8] on admission day was also recorded in this study. The imaging variables of the routine preoperative CT scan and the last CT scan performed before the removal of drainage tube were measured and analyzed. These variables included hematoma position, hematoma maximal thickness, hematoma volume and volume ratio, hematoma density, midline shift and skull morphology. The location of the contralateral hematoma was classified into wide type (hematoma locates in three lobes or more) and limited type (hematoma only locates in one or two lobes). The hematoma volume was calculated by the XYZ/2 formula[9]. The volume relation ratio (VR-ratio) was defined as the ratio of preoperative non-operated hematoma volume to the operated hematoma volume[10]. Hematoma density shown on the CT scan was divided into four categories according to Nakaguchi's description: homogeneous, laminar, separated and trabecular[11]. The cranial morphology was justified by applying three lines passing the brain midline and both sides of the skull, which had been described in previous researches (Fig. 1.)[12, 13]. If the difference of angles between these lines was more than 2°, the skull would be considered as asymmetrical. The side with a larger angle was defined as the curved side. All the angles were measured by the Intelligent Medical Imaging Information system (NeuSoft, Liaoning, China).

### Surgical options and procedure

For bilateral CSDH, if both the hematomas had significant radiographic sign (eg. maximum hematoma thickness was more than 10 mm) or caused severe neurological symptoms (eg. headache, limb weakness), neurosurgeons would perform bilateral burr hole evacuation[14]. However, if one side of the bilateral hematoma was small and asymptomatic while the other side met the surgical indications, doctors in Beijing Tiantan Hospital would only perform unilateral evacuation. The surgical procedure had been described in detail by Ou et al.[15]. During the operation, one burr hole will be twisted in the side of larger and asymptomatic hematoma. Then a soft catheter will be put under the dura matter for the intraoperative irrigation and postoperative drainage. On the first day after the evacuation, a CT scan will be performed on patients to determine whether the drainage tube can be removed. If the residual hematoma fluid is seldom, then the catheter will be removed. Otherwise, a 5 milliliter of urokinase solution will be injected into the hematoma cavity through the catheter to dissolve the hematoma fluid. This step will be repeated until the CT images revealed that the drainage tube can be removed.

### Definition of CHP and follow-up

CHP was defined as the enlargement of non-operated hematoma, which also caused newly appearing neurological symptoms in six months after the initial burr-hole evacuation. Based on this definition, study populations were classified into CHP group and non-CHP group. The follow-up for patients was performed in the sixth month after the operation. When patients developed new neurological symptoms in 6 months after the initial evacuation, a CT scan would be performed immediately to determine whether the contralateral hematoma progressed.

# Statistical analysis

In this study, Chi Square test were applied to analyze enumeration data and Student t test were used to analyze measurement data. At the beginning, all the quantitative data would be tested for normality by employing the Kolmogorov-Smirnov test. Then Student t test were used for data which distributed normally and Mann-Whitney U test were applied in those non-normally distributed data. *P* value less than 0.05 was considered statistically significant. The variables which were significant in univariate analysis would be selected into multivariate analysis to find the independent risk factors. IBM SPSS Statistic 25 was applied to analyze these data.

## Results

From October 2011 to April, 2021, a total of 279 patients with bilateral CSDH underwent burr hole evacuation in Beijing Tiantan Hospital. 190 patients undergoing bilateral operation were excluded from this research. 5 patients were lost to follow up and 2 patients died in 6 months after the initial evacuation (one patient died of pancreatic cancer and the other patient died of coronary heart disease). Therefore, 82 patients were included in this investigation (Fig. 2). The rate of CHP was 13.41% (11/82). Average hematoma progression interval was 2.11 months (from 0.3 month to 5.7 months). All patients in CHP group underwent another burr-hole evacuation on the hematoma-progressive side. The second surgical procedure was as same as the initial one. Table 1 revealed the clinical characteristics of these patients. The research populations consisted of 59 males and 23 females, with a mean age of  $64.13 \pm 14.07$ . As for the personal history, most patients had the head trauma history before the appearance of neurological symptoms (63/82, 76.8%). The hypertension was the most common comorbidity (31/82, 36.7%). Headache was the most frequent clinical symptom (57/82, 69.5%), followed by dizziness (37, 45.1%), limb weakness (36, 43.9%), vomiting (17, 20.7%). With regarding to the imaging features, the mean value of preoperative contralateral hematoma volume was  $19.61 \pm 10.60$  milliliter (ml) and the postoperative volume was  $18.43 \pm 11.01$  ml. 24 patients had a wide opposite hematoma, and 59 patients had a symmetrical cranial. The analysis of the baseline characteristics, clinical symptoms and radiological characteristics were shown in Table 2. As the data showing, the mean age was significantly higher in CHP group than non-CHP group ( $72.54 \pm 12.78$  vs  $62.85 \pm 13.91$ ,  $p = 0.025$ ). Patients who suffered hypertension or diabetes accounted for more proportions in the CHP group. However, the univariate analysis explored that there was no significant difference in history of hypertension ( $p = 0.316$ ) or diabetes ( $p = 0.162$ ) between the two groups. Differences in sex ( $p = 0.492$ ), anticoagulant/platelet treatment ( $p = 0.617$ ), history of head trauma ( $p = 0.465$ ), history of smoking ( $p = 0.612$ ) and GCS ( $p = 0.130$ ) were not statistically significant as well. Table 2 also showed that the clinical symptoms, including headache ( $p = 0.803$ ), vomiting ( $p = 0.329$ ), dizziness ( $p = 0.762$ ), limb weakness ( $p = 0.444$ ) had no significant difference among the two groups. As for radiological characteristics, the VR-ratio ( $p = 0.254$ ), the preoperative maximal thickness of surgical side and non-surgical side hematoma ( $p = 0.638$  and  $p = 0.407$ , respectively) did not have statistical significance. Considering the small sample size of this research, the CT density of the contralateral hematoma is not suitable to be classified into four groups. In CHP group, homogeneous is the most common type (6/11). Based on this population distribution, the hematoma density was divided into homogeneous group and non-homogeneous group. Chi Square test demonstrated that the homogeneous type was not a significant variable ( $p = 0.307$ ). Compared with the non-CHP group, the volume of pre- and postoperative contralateral hematoma in CHP group was significant larger ( $p = 0.004$ ,  $p = 0.002$ , respectively). The wide type of contralateral hematoma was correlated with CHP significantly ( $p = 0.001$ ), which meant patients with a contralateral hematoma locating on three lobes or more were more likely to suffer CHP. With regarding to the cranial morphology, the skull symmetry had no significant difference between the two groups ( $p = 0.081$ ). However, for the opposite hematoma locating on the curved side, the progression rate was significantly higher ( $p = 0.007$ ).

Table 1

The clinical characteristic of 82 patients with bilateral chronic subdural hematoma

Factors	Patients
Gender (Male: Female)	59:23
Mean Age (years)	64.13 ± 14.07
Personal / Past history <i>n</i> (%)	
Smoking	21 (25.6)
Drinking	16 (19.5)
Hypertension	31 (37.8)
Diabetes	14 (17.1)
History of Head Trauma	63 (76.8)
Anticoagulant/platelet Use	10 (12.2)
Glasgow Coma Scale <i>n</i> (%)	
13–15	73 (89.0)
9–12	7 (8.5)
≤ 8	2 (2.4)
Operative Side <i>n</i> (%)	
Left	47 (57.3)
Right	35 (42.7)
Headache <i>n</i> (%)	57 (69.5)
Dizziness <i>n</i> (%)	37 (45.1)
Vomiting <i>n</i> (%)	17 (20.7)
Limb Weakness <i>n</i> (%)	36 (43.9)
Disturbance of consciousness <i>n</i> (%)	13 (15.8)
Dysphasia <i>n</i> (%)	7 (8.5)
Seizure <i>n</i> (%)	2 (2.4)
Preoperative surgical-side hematoma volume (ml)	81.84 ± 39.01
Preoperative contralateral hematoma volume (ml)	19.61 ± 10.60
Preoperative midline shift (mm)	7.04 ± 3.10
Maximal thickness of preoperative surgical-side hematoma (mm)	21.97 ± 6.15
Maximal thickness of preoperative contralateral hematoma (mm)	10.84 ± 3.82
Density of contralateral hematoma <i>n</i> (%)	
homogeneous	59 (71.9)
non-homogeneous	23 (28.0)

*VR-ratio, volume relation ratio; ml, milliliter; mm, millimeter*

Factors	Patients
Postoperative contralateral hematoma volume (ml)	18.43 ± 11.01
The VR-ratio	0.27 ± 0.19
Location of contralateral hematoma <i>n</i> (%)	
wide type	24 (29.3)
limited type	58 (70.7)
Cranial morphology <i>n</i> (%)	
Symmetry	59 (71.9)
Asymmetry	23 (28.1)
Contralateral hematoma locating on the curved side <i>n</i> (%)	27 (32.8)
<i>VR-ratio, volume relation ratio; ml, milliliter; mm, millimeter</i>	

Table 2

Comparisons of clinical characteristics between the progressing contralateral hematoma and non-progressing contralateral hematoma

Factors	Contralateral Hematoma Progression ( <i>n</i> )		<i>P</i> -value
	Yes (11)	No (71)	
Gender (Male: Female)	7:4	52:19	0.492
Mean Age (years)	72.54 ± 12.78	62.85 ± 13.91	0.025
Personal / Past history <i>n</i> (%)			
Smoking	4(36.4)	17(23.9)	0.612
Drinking	2(18.2)	14(19.7)	0.772
Hypertension	6(54.5)	25(35.2)	0.316
Diabetes	4(36.3)	10(14.1)	0.162
History of Head Trauma	7(63.6)	56(78.9)	0.465
Anticoagulant/platelet Use	2(18.2)	8(11.3)	0.617
Glasgow Coma Scale <i>n</i> (%)			0.130
13–15	8(72.7)	65(91.5)	
9–12	2(18.2)	5(7.0)	
≤ 8	1(9.0)	1(1.4)	
Operative Side <i>n</i> (%)			0.898
Left	7(63.6)	40(56.3)	
Right	4(36.3)	31(43.7)	
Headache <i>n</i> (%)	8(72.7)	49(69.0)	0.803
Dizziness <i>n</i> (%)	5(45.5)	32(45.1)	0.762
Vomiting <i>n</i> (%)	4(36.4)	13(18.3)	0.329
Limb Weakness <i>n</i> (%)	6(54.5)	30(42.2)	0.444
Disturbance of consciousness <i>n</i> (%)	3(27.3)	10(14.1)	0.502
Dysphasia <i>n</i> (%)	2(18.2)	5(7.0)	0.235
Seizure <i>n</i> (%)	1(9.1)	1(1.4)	0.251
Preoperative surgical-side hematoma volume (ml)	96.93 ± 46.32	94.76 ± 38.47	0.125
Preoperative contralateral hematoma volume (ml)	28.91 ± 10.67	18.39 ± 12.79	0.004
Preoperative midline shift (mm)	7.59 ± 2.41	9.03 ± 4.14	0.530
Maximal thickness of preoperative surgical-side hematoma (mm)	22.75 ± 7.40	26.75 ± 6.97	0.638
Maximal thickness of preoperative contralateral hematoma (mm)	10.07(9.87–13.71)	11.59 ± 6.00	0.407
Density of contralateral hematoma <i>n</i> (%)			0.307

*VR-ratio, volume relation ratio; ml, milliliter; mm, millimeter*

Factors	Contralateral Hematoma Progression ( <i>n</i> )		<i>P</i> -value
	Yes (11)	No (71)	
homogeneous	6(54.5)	53(74.6)	
non-homogeneous	5(45.5)	18(25.4)	
Postoperative contralateral hematoma volume (ml)	29.40 ± 10.71	17.48(6.65–20.63)	0.002
The VR-ratio	0.33 ± 0.13	0.20 ± 0.10	0.254
Location of contralateral hematoma <i>n</i> (%)			0.001
wide type	9(81.8)	15(21.1)	
limited type	2(18.2)	56(78.9)	
Cranial morphology <i>n</i> (%)			0.081
Symmetry	6(54.5)	17(20.7)	
Asymmetry	5(45.5)	54(79.3)	
Contralateral hematoma locating on the curved side <i>n</i> (%)	8(72.7)	19(26.8)	0.007
<i>VR-ratio, volume relation ratio; ml, milliliter; mm, millimeter</i>			

After obtaining the statistically significant variables through univariate analysis, multivariate analysis was then performed on these variables. The analysis outcomes were shown in Table 3. The wide type of contralateral hematoma (OR = 8.769, *p* = 0.020, 95%CI 1.410-54.545) was an independent risk factor of contralateral hematoma progression. Furthermore, contralateral hematoma locating on the curved side was also correlated with CHP independently (OR = 7.103, *p* = 0.033, 95%CI 1.168–43.213).

Table 3  
Multivariate analysis of covariates related to contralateral hematoma progression

Variable	OR	95% CI	<i>P</i>
Age	1.058	0.976–1.147	0.173
Preoperative contralateral hematoma volume	1.035	0.883–1.213	0.670
Postoperative contralateral hematoma volume	1.016	0.876–1.180	0.830
Location of contralateral hematoma	8.769	1.410-54.545	0.020
Contralateral hematoma locating on the curved side	7.103	1.168–42.213	0.033
<i>OR, odds ratio; CI, confidence interval.</i>			

We also searched previous articles studying the development of opposite hematoma and five investigations were found to focus on the CHP. The summary of the significant factors of these studies were presented in Table 4. Among these articles, the CHP independent risk factors included use of anticoagulant/platelet, density, thickness, and volume of contralateral hematoma[6, 7, 10, 16, 17].



Table 4

The summary of the significant results of published articles focusing on the contralateral hematoma progression after unilateral evacuation and our current study.

Author/year	Numbers (n)	Mean age (years)	Preoperative contralateral hematoma volume (ml)	Postoperative contralateral hematoma volume (ml)	Wide contralateral hematoma (n)	Other clinical characteristics or imaging characteristics
Fujitani et al.(2017) [15]	CHP:19 non-CHP:74 CHP rate:19%	CHP:75.7 ± 7.3 non-CHP:78.6 ± 11.3 univariate analysis: NS	NR	NR	NR	The iso/hypointense in MRI images (n): CHP (17) vs non-CHP (32)  p = 0.004
Scheichel et al. (2018)[10]	CHP:9 non-CHP:33 CHP rate:21%	NR	CHP:68.4 ± 24.2 non-CHP:27.4 ± 15.9  <i>p &lt; 0.001</i>	NR	NR	VR-ratio: CHP (0.56 ± 0.11) vs non-CHP (0.21 ± 0.12)  <i>p &lt; 0.001</i>
Motiei-Langroudi et al. (2019)[6]	CHP:7 non-CHP:70 CHP rate:9%	CHP:67.9 ± 7.1 non-CHP:73.1 ± 12.1 univariate analysis: NS	NR	NR	NR	Postoperative CHT (mm): CHP (10.2 ± 3.5) vs non-CHP (6.1 ± 2.9) p = 0.001  Postoperative MLF (mm): CHP (1.2 ± 1.6) vs non-CHP (3.5 ± 3.7)  <i>p = 0.008</i>
Shen et al. (2019)[7]	CHP:17 non-CHP:36 CHP rate:32%	CHP:68.8 ± 2.4 non-CHP:70.0 ± 1.5in univariate analysis: NS	CHP:48.27 ± 4.52 non-CHP:35.40 ± 3.36  <i>p = 0.031</i>	CHP:56.74 ± 6.85 non-CHP:34.54 ± 2.85  p = 0.033	CHP:17 Non-CHP:20  <i>p = 0.001</i>	Homogeneous hematoma(n): CHP (10) vs non-CHP (9)  <i>p = 0.017</i>
Zhang et al. (2020)[19]	CHP:4 Non-CHP:94 CHP rate:4%	NR	NR	NR	NR	Use of anticoagulant/platelet  CHP (NR) vs non-CHP (NR)  p = 0.017

*The bold values were significant values in multivariate analysis and the italicized values were only significant in univariate analysis; CHP, contralateral hematoma progression; NS, not significant; NR, no report; CHV, contralateral hematoma volume; VR-ratio, volume relation ratio; CHT, contralateral hematoma thickness*

Author/year	Numbers (n)	Mean age (years)	Preoperative contralateral hematoma volume (ml)	Postoperative contralateral hematoma volume (ml)	Wide contralateral hematoma (n)	Other clinical characteristics or imaging characteristics
Present (2022)	CHP:11 Non-CHP:71 CHP rate:13%	CHP:72.54 ± 12.78 Non-CHP:62.85 ± 13.91 <i>p = 0.025</i>	CHP: 28.91 ± 10.67 non-CHP: 18.39 ± 12.79 <i>p = 0.001</i>	CHP:29.40 ± 10.71 non-CHP:16.69 ± 10.08 <i>p = 0.001</i>	CHP:9 non-CHP:15 <i>p = 0.019</i>	Contralateral hematoma locating on the curved side: CHP (8) vs non-CHP (19) <i>p = 0.030</i>
<i>The bold values were significant values in multivariate analysis and the italicized values were only significant in univariate analysis; CHP, contralateral hematoma progression; NS, not significant; NR, no report; CHV, contralateral hematoma volume; VR-ratio, volume relation ratio; CHT, contralateral hematoma thickness</i>						

## Discussion

For bCSDH patients who underwent unilateral evacuation, the postoperative enlargement of contralateral hematoma is not rare. However, there were a few studies researching the factors associated with CHP. In this current study, the progression rate was 13.41%, which was smaller than most previous studies[6, 7, 10, 16]. Five factors, including pre- and postoperative contralateral hematoma volume, the wide contralateral hematoma, age and opposite hematoma locating on the curved side had statistical significance between the CHP group and non-CHP group. The wide type of opposite hematoma and contralateral hematoma situated on the curved side were independent risk factors for CHP.

Age is an important factor in CSDH patients. Many studies had demonstrated that the age was associated with the incidence and recurrence rate of chronic subdural hematoma[2, 18]. Our investigation explored that among CHP group, the age was significantly higher than non-CHP group. This phenomenon might be explained by the brain atrophy and the increasing fragility of vascular. Blatter et al. described that the volume of brain parenchyma decreased with age, which meant older people would suffer more severe brain atrophy[19]. This severe atrophy was likely to increase the risk of arachnoid tearing which might cause the appearance of subdural effusion[20]. Moreover, Spallone et al. considered that the vascular would be more fragile among older CSDH patients, meaning the vessels in the dura mater was more likely to rupture. Therefore, for bCSDH patients with older age, the subdural effusion might be more common and the bleeding tendency in the subdural space was likely to be more active. The newly appearing blood from the fragile vessels and the subdural effusion might enter into the contralateral hematoma cavity, leading to the development of the non-surgical hematoma. However, none of the five previous investigations reported that the age was associated with CHP. So we consider that research with a large sample size to identify the correlation between CHP and older patients is still needed.

Radiological presentation has always been a central issue in investigations with regard to the progression of chronic subdural hematoma. According to the previous studies, the MRI intense, CT density, hematoma location, volume and maximal thickness of contralateral hematoma, the VR ratio and the midline shift were considered to be significantly correlated with CHP[6, 7, 10, 16]. In this current research, both the pre- and postoperative contralateral hematoma volume of CHP patients are statistically significant in univariate analysis. One possible hypothesis is that a bigger contralateral hematoma is more likely to result a rapid decrease of intracranial pressure in non-surgical side and make a greater postoperative parenchymal shift, which may be correlated with the development of contralateral hematoma. More investigations are needed to verify this hypothesis. As for homogeneous type of contralateral hematoma, although it had no significance in our research, some investigations demonstrated that it was associated with CHP[6, 7]. Shen et al. thought that homogeneous type meant the hematoma had been liquefied totally, making the expansion and enlargement of hematoma more easily. However, some researches revealed that compared with other hematoma density, the bleeding tendency and inflammatory reaction of homogeneous hematoma are milder, suggesting that this type is less active to progress[4, 11, 21]. This finding can be applied to explain the outcome of our study reasonably.

The wide type of contralateral hematoma is an independent risk factor about contralateral hematoma progression. A previous research reported that hematoma location was correlated with the spontaneous resolution of CSDH[22]. However, study exploring the relationship between CHP and hematoma location was rare. Only Shen et al. reported that the hematoma location might be associated with the CHP[7]. According to the description of Shen et al., the contralateral hematoma locating in three lobes was easier to progress, which might be associated with the thickness of hematoma envelope. We considered that this phenomenon was associated with the surface area and the feeding vessels of hematoma membrane. Previous researches demonstrated that the hematoma cavity was enclosed by the inner and external membrane[23]. The inner membrane barely works in the process of CSDH formation, while the external membrane plays an extremely important role in the growth of subdural hematoma[20]. Many studies found that some inflammatory mediators which promote the development of CSDH, for the instance of vascular endothelial growth factor (VEGF), angiopoietin-2 (Ang-2), and thrombomodulin, are originally from the outer membrane[24–27]. Moreover, a large quantity of macro-capillaries which is full of loose gap junction also exist in the outer membrane. The blood may exudate from the capillaries and transfer into the hematoma cavity through these junctions without any hindrance, which is considered as the main reason for the development of contralateral hematoma[20, 25]. Compared with limited type, wide type has a larger area of outer membrane, which may have a greater number of inflammatory factors and macro-capillaries. Therefore, among wide contralateral hematoma, the inflammatory response may be more severe and more blood is likely to transfer from the capillaries into hematoma cavity, causing the contralateral progression. The middle meningeal artery (MMA) was also hypothesized to play a role in the progression of contralateral hematoma. Nakaguchi et al. reported that the hematoma locating on more lobes was fed by more vessels from the MMA, which would suffer a higher bleeding risk[11]. For wide contralateral hematoma, the feeding vessels would be distributed more widely than limited type. So we think that the wide type of contralateral hematoma will have a higher bleeding tendency which may promote the development of non-operated hematoma.

The other independent risk factor is the opposite hematoma which locates on the curved side. As we know, none of the five previous studies researched this variable and our investigation is the first study to explore the relationship between skull morphology and CHP. The cranial morphology is always considered to be correlated with the laterality of hematoma[12]. Lee et al. found that bCSDH were more common among symmetrical cranial[28], which was in accordance with our investigation. In this current study, we found that when the non-operative hematoma occurred on the curved side, the patient was more likely to suffer CHP. This phenomenon was hypothesized to be associated with the subdural space between the two cranial sides. A previous research reported that patients with CSDH preferred to lie on the less curved side[29]. In such condition, the subdural space of the curved side would be enlarged due to the brain gravity, which facilitated the separation of dura-arachnoid interface and increased the risk of arachnoid tearing. This interface separation might influence the arachnoid and vascular permeability[8]. Moreover, Akhadder et al. also demonstrated that the enlarging subdural space would easily result the rupture of bridging veins[30]. Therefore, when the contralateral hematoma locating on the curved side, the appearance of effusion and veins rupture would be more frequent, contributing to the hematoma enlargement.

Our study demonstrated that the hematoma location and the cranial structure, which are ignored by most investigations, may contribute to CHP. These two independent risk factors are intuitive and can be easily obtained from the routine CT scan. The previous studies had reached a consensus that patients with higher CHP risk needed a rigorous follow-up to evaluate the change of non-operative hematoma. In our research, both the independent risk factors are correlated with the vessels existing on the outer membrane or the dura mater. Therefore, we think that the MMA embolization, a surgery method which is less invasive, can be applied for contralateral hematomas which have no surgical indication but are considered to progress easily. This treatment method can shorten the interval from initial surgery to the last follow-up[31], making more benefits for patients. However, the safety and effectiveness of this new treatment strategy is still needed to be investigated by researches with large sample size in the future.

There are some limitations in this investigation. Firstly, our research is a retrospective analysis which may introduce some biases affecting the outcomes unavoidably. Secondly, the statistical analysis about age and the classification of hematoma density are influenced by the small sample size of our research. These variables are worthy to be investigated with a larger research population.

## Conclusion

In the present study, the wide type of contralateral hematoma was one of the independent risk factors associated with CHP. Moreover, contralateral hematoma locating on the curved side was also considered to progress more easily. For patients with such risk factors, additional treatment and rigorous follow-up should be taken into consideration.

## Abbreviations

CHP  
contralateral hematoma progression  
CSDH  
chronic subdural hematoma  
bCSDH  
bilateral chronic subdural hematoma  
CT  
computed tomography  
GCS  
Glasgow Coma Scale  
VR-ratio  
volume relation ratio  
VEGF  
vascular endothelial growth factor  
Ang-2  
angiopoietin-2  
MRI, magnetic resonance image  
MMAE  
middle meningeal artery embolization

## Declarations

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None to report

**Author contribution:**

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication

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**Data availability:**

The datasets used and/or analyzed during the current investigation are available upon reasonable request from the corresponding author.

**Ethics approval and consent to participate**

The studies involving human participants were reviewed and approved by Ethics Committee of the Institutional Review Board of Beijing Tiantan Hospital (KY2020-094-01). Informed consent of the procedure was waived for this retrospective study. Informed consent was waived by the same ethics committee that approved the study.

Consent for publication

Not Applicable.

Competing interests

All authors listed have no conflict of interest, financial or otherwise.

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## Figures

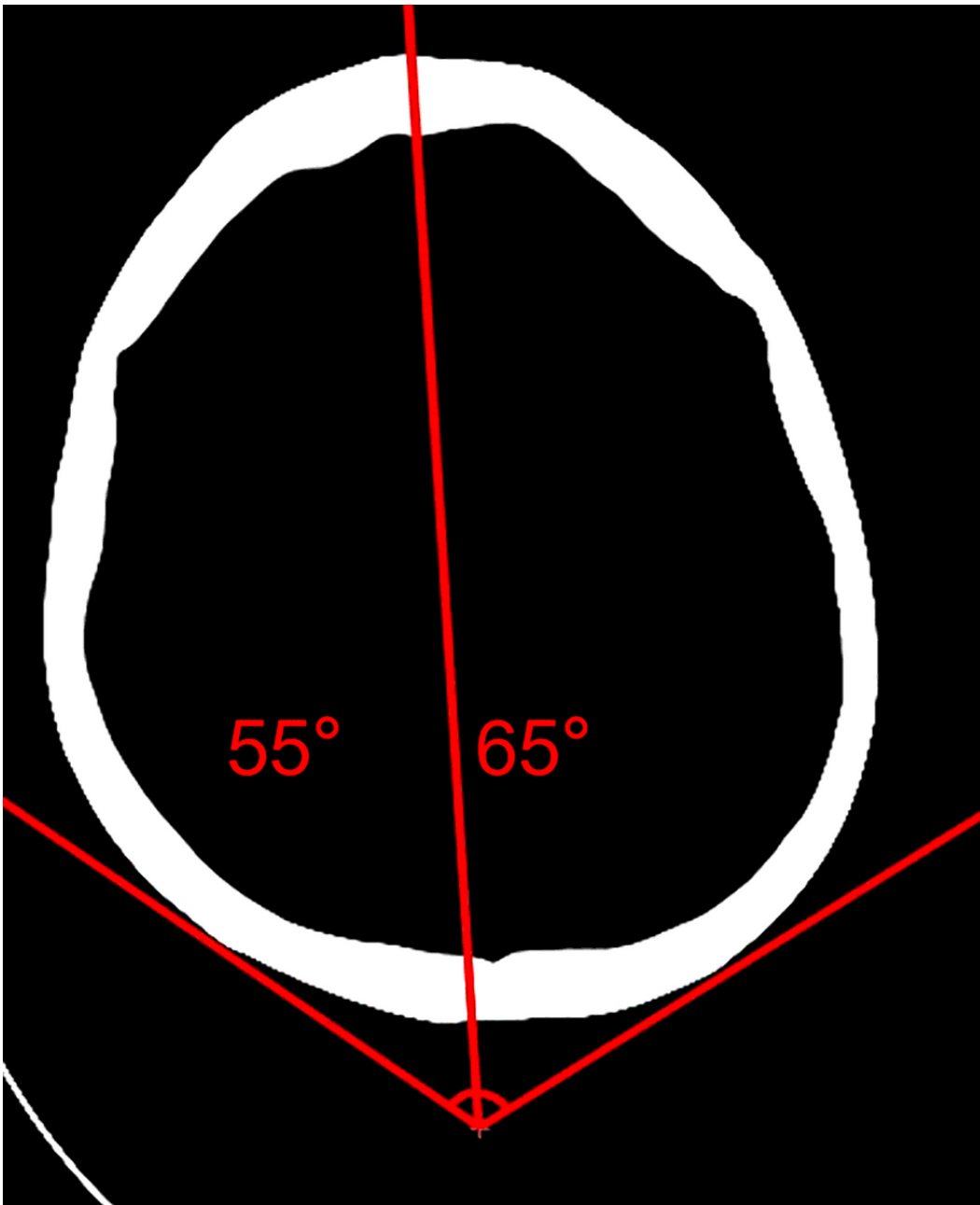
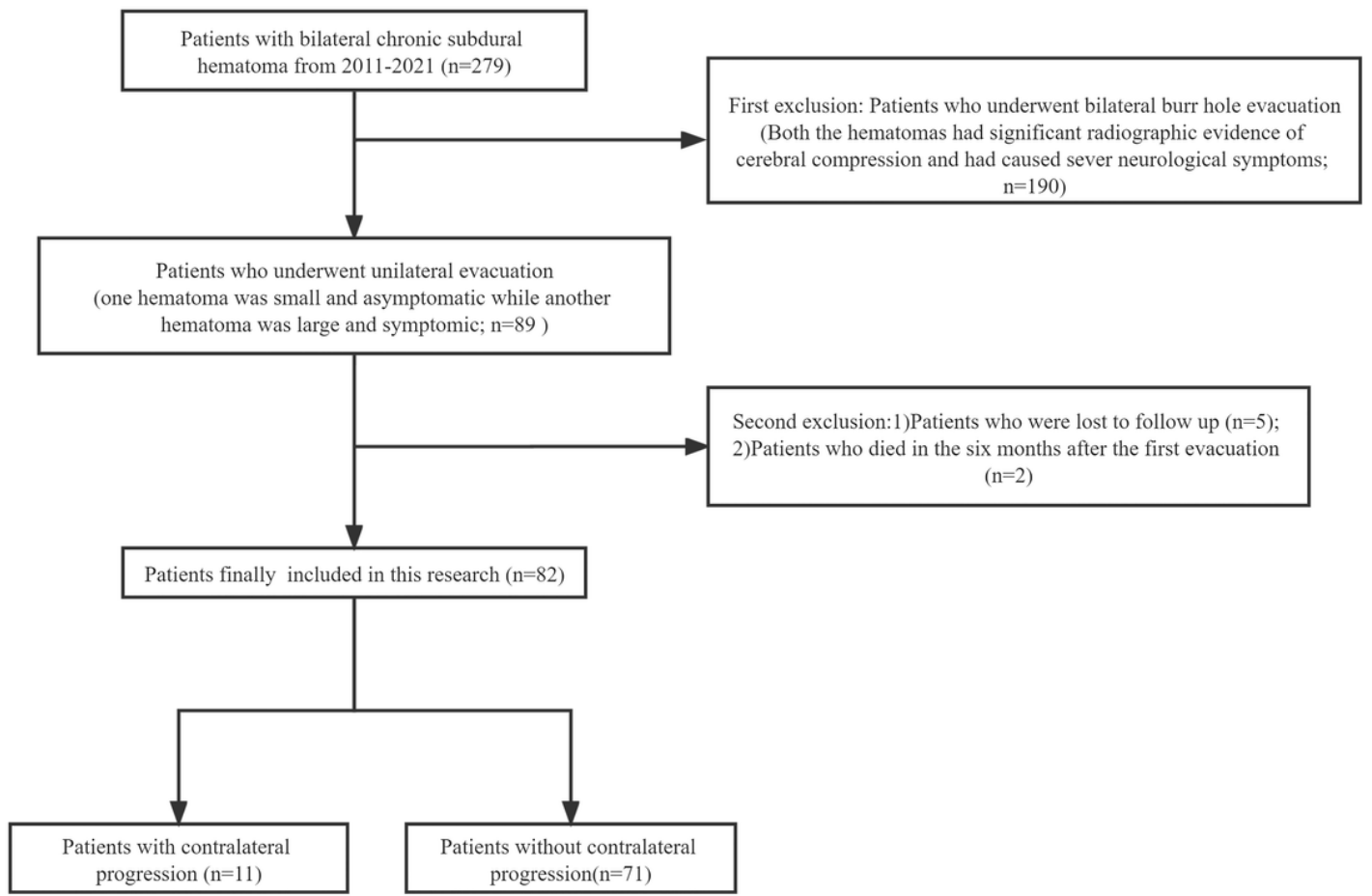


Figure 1

From a single point, three lines were drawn: one line passing the brain midline and two lines touching the outer table on both sides of the cranial. When the differences of the lines were less than  $2^\circ$  the skull would be considered as a symmetrical cranial. The side with a larger angle was considered as the curved side.



**Figure 2**

Flowchart summarizing the enrollment of bilateral chronic subdural hematoma patients who were included in this research