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-  Zeynep Karakaya<sup>1</sup>  
 Ayhan Saritas<sup>2</sup>  
 Pınar Yesim Akyol<sup>1</sup>  
 Fatih Esad Topal<sup>1</sup>  
 Umut Payza<sup>1</sup>  
 Serkan Bilgin<sup>1</sup>

<sup>1</sup> Katip Çelebi University,  
Atatürk Training and Research  
Emergency Medicine, Izmir,  
Turkey

<sup>2</sup> Düzce University, Medical  
Faculty, Department of  
Emergency Medicine, Düzce,  
Turkey

**Corresponding Author:**

Ayhan Saritas  
Düzce University, Medical Faculty,  
Department of Emergency Medicine,  
Düzce, Turkey  
Tel: +90 531 904 1000  
E-mail: a\_saritas\_@hotmail.com

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www.konuralptipdergi.duzce.edu.tr

**Evaluation of Chronic Subdural Hematoma Volume Calculated via Cavalieri's Principle****ABSTRACT**

**Objective:** Chronic subdural hematoma (CSDH) is a frequently encountered entity in neurosurgery. The objective of this study was to describe the use of unbiased Cavalieri principle to assess CSDH volume to total brain volume fraction (Percentage) and compare it with the clinical features of the patients.

**Methods:** A total of 33 patients were included in the study. Computed tomography (CT) was acquired from the hospital-imaging database. The ratio of hematoma volume, brain volume, and hematoma volume to brain volume were measured via CT by two clinicians. Measurements were compared with clinical findings.

**Results:** The sample consisted of 22 males and 11 females and mean age 67,27±12,63 years. The measured hematoma volume was 89,78 ± 54,13 cm<sup>3</sup>, the brain volume was 1329,91 ± 2098,35 cm<sup>3</sup> and the percentage volume was 8,14 ± 4,92 cm<sup>3</sup>. The brain volume values of the cases with impaired consciousness were found to be statistically significant (p <0.05).

**Conclusions:** It should be kept in mind that the bleeding volume of patients with vomiting may be higher.

**Keywords:** Chronic Subdural Hematoma, Cavalieri's Principle, Emergency Medicine.

**Cavalieri Prensibi İle Hesaplanan Kronik Subdural Hematom Hacminin Değerlendirilmesi****ÖZET**

**Amaç:** Kronik subdural hematom (KSDH) beyin cerrahisinde sıklıkla karşılaşılan durumlardan biridir. Bu çalışmanın amacı, KSDH hacminin total beyin hacmine oranı fraksiyonu (yüzdesi) değerlendirmek için bias taşımayan Cavalieri prensibinin kullanımını anlatmak ve bunu hastaların klinik özellikleri ile karşılaştırmaktır.

**Gereç ve Yöntem:** Çalışmaya toplam 33 hasta alındı. Bilgisayarlı tomografi (BT) hastane görünürleme verilerinden elde edildi. Hematom hacmi, beyin hacmi ve hematom hacminin beyin hacmine oranı iki klinisyen tarafından BT'den ölçüldü.

**Bulgular:** Hastalar 22 erkek ve 11 kadından oluşmakta idi ve yaş ortalaması 67,27±12,63 idi. Ölçülen hematom hacmi 89,78 ± 54,13 cm<sup>3</sup>, beyin hacmi 1329,91± 2098,35 cm<sup>3</sup> ve yüzde hacim 8,14 ± 4,92 cm<sup>3</sup>. Bilinç durumunda zayıflama olan vakaların beyin hacim değerleri istatistiksel olarak anlamlı bulundu (p <0.05).

**Sonuç:** Kusması olan hastaların kanama hacminin daha fazla olabileceği akılda tutulmalıdır.

**Anahtar Kelimeler:** Kronik Subdural Hematom, Cavalieri's Prensibi, Acil Tıp

## INTRODUCTION

Chronic subdural hematoma is an often seen clinical condition in neurosurgery. It occurs more commonly in elderly patients with a greater life expectancy. This condition is usually seen as a result of rupture (especially traumatic) of the cortical vessels. It can easily develop in patients with cerebral atrophy, alcoholism or anticoagulant use. It is a delayed complication of an insignificant benign trauma and has not been noticed in most patients. The estimated incidence is around 7.4 out of 1000000 (1). The symptoms vary from patient to patient. Unexplained, worsening neurological findings should be considered. Neurological squeals, such as focal neurological symptoms or seizures, can be caused by simple mechanical compression or by chemical irritation of the underlying brain cortex (2,3).

Computerized tomography (CT) is actually a method of imaging 2D images of 3D organs. The evaluation of these tests is subjective and depends on the experience of the individual carrying out the procedure. A series of methods are used in order to calculate the total volumes of organs or structures of their components. If the structures cannot be isolated from the components in their environment, Cavalieri's principle, which is a stereological method, can be used in a reliable manner. Cavalieri's principle is the most frequently used volume calculation method among stereological methods (4). It has been shown that each 3D structure can be calculated in an unbiased and effective manner with this method, and that an evaluation can be made free of errors that can be caused by 2D images (5-10).

Calculation of the volume via Cavalieri method has been studied and successfully applied on various organs in previous studies (11-13). In addition, many investigators have used the Cavalieri method together with CT in vivo to calculate volume (14-16).

The objective of this study was to determine whether cavalier principle, with hematoma volume, brain volume and hematoma volumes in CT of patients diagnosed with CSDH who were referred and hospitalized in emergency department were calculated and correlated with clinical findings of patients.

## MATERIAL AND METHODS

All patients with CSDH admitted to our Emergency Medicine Department, from January 2014 to February 2016, were collected retrospectively. Helsinki Declaration was followed in this study.

Approval for our study was provided from the İzmir Katip Çelebi University Atatürk Training

and Research Hospital Clinical Research Ethics Committee (2016/08-229).

Our inclusion criteria; age  $\geq 18$  years old, diagnosis of CSDH (confirmed via brain non-contrast CT imaging).

Our exclusion criteria; warfarin or other anticoagulant use and bleeding disorders, arteriovenous malformations, patients with missing data, intracranial venous sinus thrombosis, cerebrovascular abnormality, intracranial tumor, other pathologies accompanying CSDH (cranial fracture, subarachnoid hemorrhage, acute subdural and epidural hematoma and other organ injuries, bilateral subdural hemorrhage).

Medical records were evaluated for patient age, gender, time of discharge or death, time of admission, cause of subdural hematoma (spontaneous or traumatic), past medical history (hypertension, heart disease, diabetes mellitus, stroke, and other) and use of antiplatelet therapy. Systolic arterial pressure, diastolic arterial pressure, mean arterial pressure (MAP), APTT (Active partial thromboplastin time), INR (International Normalized Ratio), Glucose, type of treatment (surgical intervention or conservative), length of hospital stay (LHS) and presence of the midline shift were recorded. Neurological function on admission was measured using Glasgow Coma Scale (GCS), which was recorded on the life squad of emergency department records. Measurements of the CSDH's volume were calculated by two clinicians. The clinicians were trained by an experienced radiologist. The clinicians were blind to the study protocol. Non-contrast CT scans of the patients were acquired from the hospital imaging database.

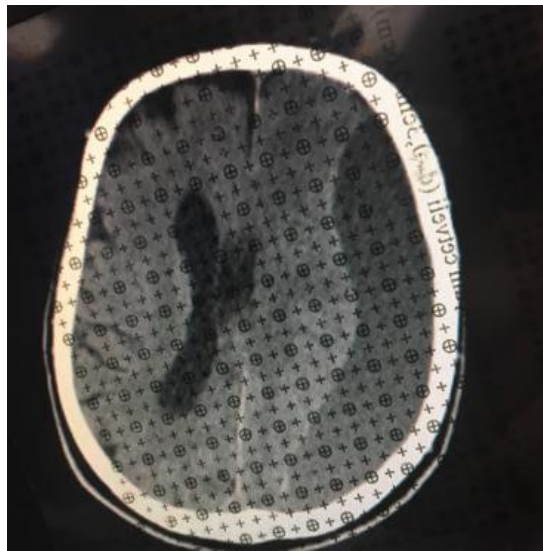
**Stereological Estimations:** All volumes were estimated from Cavalieri's principle. According to this principle, the combined point-counting grid (CPCG) was placed over the section series after which the numbers of coarse points hitting all of the brain area including the hematoma area were counted along with the number of fine points hitting only the hematoma (Figure 1). Owing to the proportion of the fine to coarse points is which was 1/4 in the CPCG, the volume fraction of hematoma within all of the brain was estimated using the following equation:

$$V_V(H, B) = \frac{\sum P_H}{4 \times \sum P_B}$$

$V_V(H, B)$ : the volume fraction of hematoma to brain volume.

$\sum P_H$ : Total number of points that hit the hematoma area.

$\sum P_B$ : The total number of points that hit all brain including hematoma.



**Figure 1.** The common point counting grid (CPCG) superposed over the computed tomography images. Intracranial structure and hematoma areas in the images of each patient were counted.

It must be noted that the 4 in the equation is due to the area fraction of the CPCG that we used. In this principle the number of points hitting the hematoma and the number of points hitting all of intracranial structures including hematoma were the only essential values. This principle is not affected by the reduction/magnification rate of the images (17-19).

**Statistical Analysis:** SPSS 20.0 version (SPSS, Chicago, IL, USA) was used to analyze the data of our study. Mean and standard deviation (SD) for normal distribution data, median and interquartile range (IQR) and percentage of categorical data for non-normally distributed data are summarized as descriptive. The difference between the categorical variables was determined by the  $\chi^2$ -test. Variable distribution was analyzed via Kolmogorov–Smirnow test.  $P < 0.05$  was considered statistically significant.

## RESULTS

The sample consisted of 22 males and 11 females (ratio 2:1), with an age interval of 26–85

years a mean age of  $67,27 \pm 12,63$  years with mean age for women and men being  $62,18 \pm 18,14$  years and  $69,82 \pm 8,12$  years, respectively. There was no statistically significant difference between the ages of male and female individuals included in the study ( $p > 0,05$ ).

There was no statistical significant relationship between the past medical history, cause of hematoma, treatment, and gender and percentage of CSDH volume ( $p > 0.05$ ).

Clinical characteristics of patients have been summarized in Table 1.

In cases with vomiting, hematoma volume and percentage volume values were found to be statistically higher than hematoma volume and percentage volume values of cases without vomiting ( $p < 0.05$ ). There was no statistically significant difference between the groups in terms of other variables ( $p > 0.05$ ).

The brain volume values of patients with unconsciousness as admission complaints were found to be statistically higher compared to the brain volume values of patients with no unconsciousness ( $p < 0.05$ ). There were no statistically significant differences between the groups in terms of other variables (Table 2).

**Table 1.** Distribution of clinical characteristics of patients

		n	%
Past Medical History	DM	8	24,2
	Heart Disease	8	24,2
	HT	17	51,5
	Other	4	12,1
	SVO	3	9,1
Complaint	Headache	16	48,5
	Vomiting	2	6,1
	Seizure	6	18,2
	Unconsciousness	2	6,1
	Syncope	7	21,2
	Other	4	12,1
	Hemiplegia	9	27,3
	Hemiparesis	4	12,1
Bleeding Cause	Traumatic	11	33,3
	Spontaneous	22	66,7
Shift		18	54,5
Treatment	Surgical	22	66,7
	Conservative	11	33,3
		Mean±SD	Min.-Max.
Systolic Blood Pressure		135,64±32,29	60-200
Diastolic Blood Pressure		77±15,68	40-110
Mean Arterial Pressure		97,55±20,27	46,6-133,33
Glasgow Coma Scale		14,39±1,54	8-15
APTT		27,39±3,35	20,9-35,5
INR		1,08±0,09	0,89-1,28
Glucose		141,45±80,68	78-481
Hospitalization duration		7±6,64	1-38
Hematoma volume		89,78±54,13	4,41-220,81
Brain volume		1329,91±2098,35	377,73-12965,38
Percentage		8,14±4,92	0,69-18,91

DM: Diabetes Mellitus, HT: Hypertension, CVA: Cerebrovascular Accident; MAP: Mean Arterial Pressure, APTT: Active Protrombin Time, INR: International; Normalized Ratio, CT: Computerized Tomography

**Table 2.** Relationship between Clinical Characteristics of Patients and Brain, Hematoma and Percentage Volumes

Clinical Features		N	Hematoma volume	p	Brain volume (cm <sup>3</sup> )	p	Percentage volume(cm <sup>3</sup> )	p
			(Mean±SD)		(Mean±SD)		(Mean±SD)	
Gender	Female	11	73,91±61,31	0,181	815,79±192,28	0,001*	8,15±5,98	0,849
	Male	22	97,71±49,78		1586,97±2546,4		8,13±4,46	
Headache	Yes	16	95,82±37,02	0,305	947,15±154,34	0,264	9,28±3,76	0,130
	No	17	84,08±67,12		1690,16±2915,38		7,06±5,71	
Vomiting	Yes	2	215,03±8,17	0,019	1063,25±234,94	0,546	17,07±2,61	<b>0,024*</b>
	No	31	81,7±44,84		1347,12±2165,58		7,56±4,46	
Seizure	Yes	6	113,59±61,28	0,273	2982,58±4891,61	0,401	8,57±6,71	0,963
	No	27	84,48±52,2		962,65±217,46		8,04±4,59	
Unconsciousness	Yes	2	174,63±65,32	0,065	7097,38±8298,61	<b>0,029*</b>	8,1±10,07	0,940
	No	31	84,3±49,73		957,82±201		8,14±4,74	
Syncope	Yes	7	68,2±35,93	0,186	1024,87±317,67	0,218	6,83±3,86	0,481
	No	26	95,59±57,23		1412,04±2361,92		8,49±5,17	
Hemiplegia	Yes	9	114,54±56,03	0,124	1024,57±178,36	0,275	10,07±4,36	0,135
	No	24	80,49±51,53		1444,42±2462,68		7,41±5,01	
Hemiparesis	Yes	4	91,82±90,37	0,825	1038,41±225,26	0,659	7,21±5,89	0,659
	No	29	89,49±49,73		1370,12±2238,94		8,27±4,88	
Bleeding Cause	Spontaneous	11	82,75±50,77	0,717	2050,58±3623,16	0,909	6,67±4,68	0,222
	Traumatic	22	93,29±56,56		969,58±224,28		8,87±4,97	
Shift	Yes	18	75,35±54,5	0,093	1751,56±3106,6	0,885	6,44±5,15	0,051
	No	15	101,8±52,29		978,54±229,54		9,55±4,37	
Treatment	Surgical	22	95,24±39,9	0,147	1486,55±2571	0,593	8,93±4,26	0,169
	Conservative	11	78,85±76,4		1016,64±216,45		6,56±5,93	

DM: Diabetes Mellitus, HT: Hypertension, CVA: Cerebrovascular Event

The GCS values and hospitalization times of cases with surgical treatment were statistically higher than those of the conservative patients ( $p < 0.05$ ). There were no statistically significant differences between the groups in terms of other variables. When the results of the unary regression analysis were examined for variables that were

considered to affect the percentage volumetric values of the cases, the interaction between age and percentage values was found to be statistically significant ( $p < 0.05$ ). The interaction of other variables with percentage values was not statistically significant ( $p > 0.05$ ) (Table 3).

**Table 3.** Unary regression analysis results for variables considered to be effective on percentage volumetric values

	B	t	p	95% CI	
Gender	-0,024	-0,013	0,990	-3,787	3,740
Age (year)	0,145	2,235	<b>0,033*</b>	0,013	0,278
Systolic TA (mmHg)	-0,022	-0,807	0,426	-0,077	0,033
Diastolic TA (mmHg)	-0,042	-0,750	0,459	-0,156	0,072
MAP	-0,048	-1,127	0,269	-0,135	0,039
GCS	0,276	0,483	0,633	-0,890	1,442
Bleeding	2,207	1,225	0,230	-1,469	5,883
Shift	3,106	1,876	0,070	-0,270	6,483
Treatment	-2,371	-1,320	0,196	-6,032	1,291
APTT	0,072	0,275	0,786	-0,465	0,609
INR	7,404	0,756	0,455	-12,567	27,376
Glucose	0,010	0,952	0,348	-0,012	0,032
LHS (Day)	0,409	3,690	<b>0,001*</b>	0,183	0,636

TA: Tension Arterial MAP: Mean Arterial Pressure, GCS: Glasgow Coma Scale APTT: Active Protrombin Time, INR: International Normalized Ratio, LHS: Length of Hospital Stay

## DISCUSSION

CSDH is a common problem in neurosurgery practice and is easily treated with minimal mortality and morbidity (20). CSDH patients may present to the hospital with a wide range of complaints and the onset and progression of symptoms may vary from days to weeks. Elderly patients are often presented with multiple symptoms that can mimic stroke or rapidly progressing dementia (20).

There are some studies investigating the relationship between intracranial hematoma volume and the clinical features of the patients (17,21,22). ABC/2 or computer-assisted volumetric analysis techniques have been used in these studies.

In this study, the relationship between hematoma with brain volume fraction, age, clinical results, GCS and shift amount were investigated using Cavalieri principle rather than evaluating CSDHV by itself. This method has been used for epidural hematoma and CSDH by Kalkan et al. (18) and Saritas et al. (19).

Our series were similar to those of the previous studies in terms of age and gender ratio (23) with a mean age of 68 years and a male predominance (66,7%). Mean age (68 years) was comparable with series of Aspegren et al. (71.8 years), Pieracci et al. (79.4 years) and Miranda et al. (80.6 years) (24-26). Also, the preponderance of male subjects (66.3%) in the current analysis has been regularly reported in CSDH studies (24,26-30).

When examined with regard to comorbid diseases, it was observed similar to the study by Gonzales et.al. that hypertension (51.5%) and diabetes mellitus (24.2%) were the most prevalent in our patients (17).

Patients with CSDH can be presented in a variety of ways, and symptom onset and progression may range from days to weeks. In a study of 1000 patients with CSDH, the most common symptoms at admission were behavioral disorder (28.5%), headache (25.1%) and limb weakness (24.8%). The most common complaints in our study were headache (48.5%) and our rate was higher than in the literature. Limb weakness (39.4%) was detected from other admission symptoms. Although behavioral disorder has been reported to be the dominant clinical feature in elderly patients (17), none of our patients expressed this complaint.

Patients subjected to the analysis presented the whole spectrum of the initial neurological presentation ranging from GCS 15 up to comatose patients (GCS = 8 in one of subjects). Many patients had a slight or moderate decrease in consciousness levels (GCS score 13-15), but older patients with CSDH do not typically present in coma (24,30). Despite our findings, some distribution has been published previously by Gonugunta et al. (here, 11.9% of the patients had a GCS < 8 at admission) (31). This low ratio of

patients should be of a special concern, since the initial neurological condition was the most potent factor impacting the final outcome, both in previous reports (20,31,32). GCS values and length of stay in our study were statistically significant and consistent with this opinion.

When Szczygielski et al. examined patients with CSDH using anticoagulants, the correlation between hematoma size, space-effect shift and neurological outcome, as defined by midline shift, showed no significant correlation between hematoma characteristics and discharge (33).

Van den Brink et al suggested that the volume of the hematoma did not correlate with preoperative neurological conditions (34). In their study, computerized volumetry of off-line digital CT scans were used to determine the relation between hematoma volume with both patient characteristics upon admission as well as a six-month outcome. There was also no statistical significant correlation between GCS upon admission and the percentage of CSDH volume in the study carried out by Saritas et.al. and the results of these two studies were parallel with those of our study (19).

Hematoma volume and percentage values of the patients who complained of vomiting at the referral of emergency were statistically more significant compared to those who did not have vomiting complaints. However, no literature has been found that correlates vomiting and hematoma volume.

The most common cause of SDH is head trauma and the history of trauma was 72% in Borger et al. study (36) and 66.7% in our study.

Studies have reported midline shift in 86% of patients with CSDH and 61% of patients with non-traumatic CSDH (37,38). In 54.5% of our patients, midline shift was detected. Ikeda et al. reported that the degree of midline shift in CSDH was not always correlated with hematoma volume (39). No

statistically significant difference was determined between midline shift and hematoma volume and percentage values in our study.

Schneck et al. and Saritas et al. reported that 63% and 86% of patients with subdural hematoma underwent surgical evacuation (19,38). It was determined in the present study that 66,7% of the patients were treated with surgery.

As stated in our study, van Havenbergh et al. reported that CT findings (hematoma volume, brain volume/hematoma volume, midline shift and residual subdural collections had no influence on the outcome. The only statistically significant factor for the outcome of patients with CSDH was the neurological condition at the time of treatment (40).

#### Limitations

Our study had a few limitations. The first one was the limited number of subjects fulfilling the inclusion criteria. The second one was that it was a single-center study. The final one was its retrospective design. Many multi-center and prospective studies carried out with a greater number of patients are needed in this field.

#### Conclusion

It was concluded in our study that was carried out for determining whether the calculation of the cavalier principle with hematoma volume, brain volume and their ratios during the computed tomography of patients with CSDH who were admitted to emergency department would make a contribution to the clinical examination or not that the data obtained did not provide any additional contribution to the final clinical decision-making process.

Unlike other clinical units that utilize this method, the calculation was not considered a practical application in emergency ward conditions and for emergency ward physicians.

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