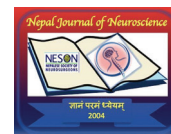


A Study to Detect Risk Factors for Recurrence of Chronic Subdural Hematoma

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Abstract

Introduction: Chronic subdural hematoma (CSDH) is a common type of intracranial hemorrhage in elderly patients. The risk factors for recurrence of chronic subdural hematoma (CSDH) after surgical evacuation has not been completely understood until now, but several risk factors for recurrence have been reported. Meanwhile, the definitive risk factors have not been defined until now. The aim of this study was to study the potential risk factors, including preoperative, operative and post-operative ones for CSDH recurrence

Materials and Methods: The study population comprised of all > 18 year age group patients who were operated for chronic subdural hematoma in Neurosurgery Department of tertiary care center. It was prospective cohort study. Patients who met inclusion criteria, postoperative outcomes were assessed at discharge, then at one month and three months afterwards in the neurosurgery OPD. Both the treatment options i.e. BHC Burr hole craniotomy and minicraniotomy as required as per CT scan or MRI findings.

Results: 7 patients (10.7%) had recurrence, of CSDH. All the recurrences occurred in burr hole operated patients. There was no recurrence in mini craniotomy operated group.

Conclusions: Many risk factors for recurrence of CSDH have been found, including old age, cerebral atrophy, large hematoma, bilateral hematomas, hematoma density, inflammation markers, alcohol ingestion, bleeding tendency, and some technical aspects of surgery such as irrigation with small amount of fluid, not excising thick membrane preventing brain expansion

Key words: risk factor, recurrent CSDH

Introduction

Chronic subdural hematoma (CSDH) is a frequent neurosurgical condition with a rising frequency. In Chronic subdural haematoma the bleeding is venous in origin. Fibrin is deposited as a result of an inflammatory response brought on by blood, and neomembranes are

then organised and created as a result. Plasma effusions or rebleeding from the geomembranes into a subdural collection are caused by increased fibrinolytic activity, which is enhanced by increased plasminogen levels in the outer membrane. After surgical evacuation, the documented recurrence incidence ranged from 5% - 33%¹. Old age, atrophy in brain, bilateral CSDH, clot density, seizures, diabetes mellitus, bleeding propensity, alcohol usage, and postoperative position are some of the risk factors for recurrence of CSDH that have been identified². However, the precise risk variables have not yet been identified. Few studies address the surgical or postoperative aspects; the majority concentrate on preoperative factors. The goal of the study was to evaluate the potential risk factors for CSDH recurrence, with a focus on preoperative, surgical, and postoperative ones.

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Materials and Methods

The study population comprised all > 18-year age group patients who were operated on for chronic subdural hematoma in the Neurosurgery Department of tertiary care center. It was a prospective cohort study. For patients who met inclusion criteria, postoperative outcomes were assessed at discharge, then at one month and three months afterward in the neurosurgery OPD. Both surgical options

i.e. BHC Burr hole craniotomy and minicraniotomy as required as per CT scan or MRI findings.

A thorough history was taken, including any trauma that occurred during the last three months or earlier, the use of anticoagulants or antiplatelet medications within the previous week, drinking, hypertension and diabetes. The patients had a thorough clinical examination as well as a neurological evaluation that included the Markwalder Grading Scale (MGS) and Glasgow Coma Scale (GCS). We acquired routine blood tests and coagulation profiles. Any coagulopathy correction and the requirement for transfusions of blood or blood products were documented. The maximal blood clot thickness, density, midline displacement, and septation in the hematoma are all factors that may be seen in CT details. When there was a question about the septation on the CT brain, an MRI was performed.

Operative Technique

All patients underwent surgical evacuation under General Anaesthesia OR Monitored Anaesthesia Care (MAC). In GA, induction was done with propofol, fentanyl, and cisatracurium and maintenance were done with inhalational agents sevoflurane, desflurane, and propofol infusion. MAC was accomplished with dexmedetomidine, fentanyl with scalp block, and maintenance was done with dexmedetomidine. Patients in the BHC group underwent double BHC (approximately 14 mm diameter) about 8 cm apart over the maximum width of the hematoma under GA or MAC.

by determining the location of clots in reference to the external auditory meatus.

For subjects receiving aspirin, we can administer 8 units of random donor platelet concentrates during skin incision, and we withhold medication from two days to 14 days postoperatively based on the indication. For patients taking Acitrom and Warfarin, we gave injection vitamin K and FFP (fresh frozen plasma) reversal preoperatively, and we deferred medication because of deranged INR. Patients were then put on LMWH (low molecular weight heparin) after 24-48 hours, or removal of drain if a drain was put. In GA, minicraniotomies (about 5-7 cm in size) are performed on all subjects. When planning a craniotomy, particularly a small craniotomy, the coronal view of the CT scan is helpful. The anterior and posterior boundaries can be defined by determining the location of clots in reference to the external auditory meatus.

Linear incision in the coronal plane is made over the largest extent of the hematoma. There were one or two burr holes formed towards the craniotomy's edge. Before utilising the craniotome, the dura was separated from the bone using Penfield Dissector No. 3. A cruciate or horseshoe pattern was used to open the dura, and the

outer and inner membranes were gently irrigated while clots were extracted. There was no aggressive traction or resection. Bipolar cautery was used to coagulate all of the visible membrane (outer layer). Then, hemostasis was complete. After the dura was closed, titanium screws and plates were used to repair the bone flap. The post-operative CT head was performed on all patients in a single day. In every case, an anticonvulsant was administered until the haemorrhage subsided. Depending on the postoperative results, patients were discharged from the hospital around the third to seventh day following surgery when they were no longer in need of it.

Outcomes Assessment

The clinical outcome of the patient was assessed using the Glasgow Coma Scale (GCS) and motor power. Additionally, a postoperative CT scan was performed within 1 day of the surgery to look for any residual hematoma. Literature demonstrates a variety of recurrence-influencing elements. The following recurrence risk variables are examined in our study:

1. Risk factors prior to surgery:
 - i. patient's age
 - ii. Comorbid conditions including high blood pressure, type 2 diabetes, and liver disease.
 - iii. tests like the PT and Hb level.
 - iv. Radiological preoperative parameters:
 - a) The thickness of the haemorrhage might be 10 mm, 10 mm to 20 mm, or >20 mm.
 - b) CSDH architecture like homogenous, trabecular, laminar, separated
2. Operational risk elements
 - i. Number of burr holes: single or double.
 - ii. Drain placement: subgaleal drain or subdural drain.
3. postoperative signs:
 - i. Time of drain: <3 days, 3-5 days ;
 - ii. postoperative fluid collection;
 - iii. postoperative MLS shift;

Data entry and statistical analysis:

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analyzed and statistically evaluated using SPSS-PC-20 version.

Quantitative data were expressed in mean±standard deviation or median with interquartile range and depends on normality distribution difference between two comparable groups were tested by Mann Whitney 'U' test while qualitative data were expressed in percentage. Statistical difference between the proportions was tested by chi-square test or Fisher's exact test. 'P' value less than 0.05 was considered statistically significant

Result

7 patients (10.7%) had a recurrence, of which One patient had coagulopathy with an initial INR of >5 which was corrected and operated but he had persistent coagulopathy and he was alcoholic as well. All the reoccurrences occurred in burr hole operated patients. There was no recurrence in mini craniotomy operated group.

Association of different parameters with recurrence of CSDH

In our study, we found mean age group in the recurrence group of patients was 68.86±15.86 and in no recurrence group of patients was 66.53±12.69. No statistically significant correlation was found between mean age and recurrence of CSDH (p value = 0.52). (Table -1)

Out of 7 patients of recurrence, 6 patients were male, 4 patients were hypertensive, 4 patients were diabetic. Out of 7 patients of recurrence, 5 had unilateral CSDH group and 2 had bilateral CSDH group. 4 patients had history of trivial trauma and 3 patients were alcoholic who had recurrence. One each patient was using anti platelet agent and anticoagulant who had recurrence.

In our study, we found no statistically significant correlation between gender and recurrence of CSDH (p value = 0.99). Also no statistically significant correlation was found between diabetes and recurrence of CSDH (p

value = 0.41), hypertension and recurrence of CSDH (p value = 0.69). Also we found no statistically significant correlation between CAD and recurrence of CSDH (p value = 0.99), anticoagulant agents and recurrence of CSDH (p value = 0.44), antiplatelet agents and recurrence of CSDH (p value = 0.24), alcohol and recurrence of CSDH (p value = 0.67), laterality and recurrence of CSDH (p value = 0.99), placement of drain and recurrence of CSDH (p value = 0.99) But in our study, we found statistically significant correlation between COPD and recurrence of CSDH (p value = 0.02). (Table -2). Multivariate analysis was not done because of small sample size.

Association of pre-op and postop MLS with recurrence in CSDH

No statistically significant correlation was found between pre-op MLS and recurrence of CSDH (p value = 0.18). But in our study, we found statistically significant correlation between postop MLS and recurrence of CSDH (p value < 0.01). (Table- 3,4)

Association of pre-op thickness and postop fluid collection with recurrence in CSDH

In our study, we found no statistically significant correlation between pre-op largest thickness CSDH and recurrence of CSDH (p value = 0.41).

However, in our study we found statistically significant correlation between postop fluid collection and recurrence of CSDH (p value < 0.001). (Table-5)

Table 1: Association of age with CSDH recurrence

	Recurrence (n=7)	No recurrence (n=58)	p value ¹
Mean age	68.86±15.86	66.53±12.69	0.52

¹Man Whitney U test was used

Table 2: Association of different parameters with recurrence in CSDH

	Recurrence (n=7)		No recurrence (n=58)		p value ¹
	No.	%	No.	%	
Gender					
Male	6	10.5	51	89.5	0.99
Female	1	12.5	7	87.5	
CO MORBIDITIES					
Diabetes	4	16.0	21	84.0	0.41
Hypertension	4	13.3	26	86.7	0.69
COPD	2	66.7	1	33.3	0.02*
CAD	1	12.5	7	87.5	0.99
Risk factors					
Anticoagulant Agent	1	20.0	4	80.0	0.44
Anti platelet Agent	1	4.2	23	95.8	0.24
Alcohol	3	14.3	18	85.7	0.67

Side					
Bilateral	2	11.1	16	88.9	0.99
Unilateral	5	10.6	42	89.4	
Drain					
No	2	9.1	20	90.9	0.99
Yes	5	11.6	38	88.4	

¹Chi square or fisher exact test was used * Significant

Table 3: Association of pre-op and postop MLS with recurrence in CSDH

	Recurrence (n=7)	No recurrence (n=58)	p value ¹
Pre-op MLS	9.71±4.64	8.45±3.34	0.57
Postop MLS	8.71±1.60	0.67±1.7	<0.01*

¹Man Whitney U test was used * significant

Table 4: Association of pre-op and postop MLS with recurrence in CSDH

	Recurrence (n=7)		No recurrence (n=58)		p value ¹
	No.	%	No.	%	
Pre- op MLS					
0-5 mm	1	7.7	12	92.3	0.18
6-10 mm	4	11.1	32	88.9	
>10 mm	2	12.5	14	87.5	
Postop MLS					
0-5 mm	0	0.0	56	100.0	<0.01*
6-10 mm	6	75.0	2	25.0	
>10 mm	1	100.0	0	0.0	

¹Chi square test was used * significant

Table 5: Association of pre-op thickness and postop fluid collection with recurrence in CSDH

	Recurrence (n=7)		No recurrence (n=58)		p value ¹
	No.	%	No.	%	
Pre- op largest thickness CSDH					
5-10 mm	1	100.0	0	0.0	0.41
10-20 mm	3	7.5	37	92.5	
21-30 mm	3	14.3	18	85.7	
>30 mm	0	0.0	3	100.0	
Postop fluid collection					
5-10 mm	0	0.0	55	100.0	<0.001*
10-20 mm	3	50.0	3	50.0	
21-30 mm	4	100.0	0	0.0	

¹ Chi square test was used * significant

Discussion

Recurrence is reported in the literature between 5 to 33% after surgery^{1,4}. In our study, 7 patients (10.7%) had developed recurrence. Mondorf *et al*⁵ reported a recurrence rate of 27.8% in the craniotomy patients group and a lower rate of 14.3% in the burr-hole patients

group, stating that BHC should be the preferred surgical evacuation method in the treatment of the CSDH. Mori *et al.*,⁶ reported a lower recurrence rate of 9.8% in burr-hole craniotomy with a closed system. Ernestus *et al.*,⁷ who reported a higher recurrence rate of 18.5% in the burr-hole patient group compared to 12.5% in the craniotomy patient group. Weigel *et al*⁸ reported similar recurrence

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rates in craniotomy and burr-hole trepanation groups. In our study, 7 patients shows reoccurrence, and all of them were from the burr hole group. All recurrences were reoperated within 1 month. In 3 patients, we had done reevacuation through the previous burr hole, In 2 patients were converted to minicraniotomy, and In 2 patients we did tapping of the subdural collection. However, in our study, we had done both burr hole and mini craniotomy after individualizing surgical procedures and better case selection based on imaging study characteristics.

Drain was placed depending on haematoma thickness, history of antiplatelet medication or anticoagulant usage and if there was poor expansion of brain at the time of surgery as per operating surgeon's judgement. In the majority of the published series, there is a sizable body of data that supports the use of external drainage following initial CSDH evacuation.^{9,10,11,12,13,14,}

Studies	Recurrence with drain	Recurrence without drain
Santarius <i>et al.</i> , ¹²	9.3%,	24%,
Ramachandran <i>et al.</i> , ¹⁵	4%,	30%,
Wakai <i>et al.</i> , ¹⁶	5%,	33%,
Tsutsumi <i>et al.</i> , ¹⁷	3.1%,	17%,
Gurelik <i>et al.</i> , ¹⁸	10.5%,	19%,
Sarnvivad <i>et al.</i> , ¹⁹	16%	26%,

With a shorter post-operative hospital stay and lower recurrence, continuous drainage treatment for CSDH is better to the one-time drainage technique.^{9,10} According to Santarius *et al.*¹², the mortality rate at 6 months was lower in the drain group (8.6% vs. 18.1%). However, in other trials, there was no discernible difference between the groups with and without drains in terms of postoperative recurrence and complication rates. However, proponents of the no drain camp contend that installing a drain might result in consequences such brain damage, haemorrhage from neo membranes, and infection without lowering recurrence^{20,21}. According to William *et al*²² where 16% of patients with burr hole without drain deteriorated post operatively and 11% required re-evacuation compared to 7% with a drain in situ who deteriorated post-operatively and required re-evacuation.

There is still controversy about the influence of concomitant diseases on the recurrence rate of the chronic subdural hematoma. The role of diabetes mellitus in the development and the recurrence of chronic subdural hematoma have been debatable. Torihashi *et al.*,²³ and Chon *et al.*,²⁴ have shown DM as an independent factor related with higher but not significant recurrence rates in their studies while Yamamoto *et al.*,²⁵ described a higher recurrence rate in patients without DM. This discrepancy in the studies may be explained by the fact that on one hand

DM often goes along with capillary vasculopathy which then leads to exudation from macro capillaries in the outer CSDH membrane and is therefore, considered to support the development of chronic subdural hematoma. On the other hand, patients with DM suffer from hyperglycaemia which leads to hyperviscosity, a high osmotic pressure and increased platelet aggregation and may therefore be seen as an explanation for decreased rebleeding rates in patients with diabetes mellitus.^{23,24,26} In our study, we found that out of 7 patients of recurrences, 4 had diabetes, we found no statistically significant correlation between diabetes and recurrence (p value-0.41).

Chon *et al.*,²⁴ were able to identify, seizure as independent risk factors for the recurrence of CSDH. Torihashi *et al*²³ reported no significant correlation between hypertension, and the rate of recurrence in their sample of patients. In our study, we found no statistically significant correlation between hypertension and recurrence (p value 0.69) In our study, out of 7 patients of recurrence none had seizure as the presenting complaint. In our study, we also found significant correlation between COPD and recurrence (p value 0.02).

24 patients in our study were on anti platelets and only 1 patient had recurrence. All of these patients were operated on under adequate platelet cover. This may explain low recurrence in this group of over patients. In our study, 5 patients were using anticoagulant drugs and only 1 patient had recurrence, in all of these patients we had given injection vitamin K and fresh frozen plasma for deranged INR. We found no significant correlation between anticoagulant drugs and recurrence (p value 0.44). These findings correlate with the previously published study of Stanisic *et al.*,²⁷ who found no significant influence of concomitant diseases or preoperative anticoagulation on the recurrence rate. There have been a variety of findings about the influence of anticoagulants and anti-platelet medicines on the emergence of CSDH recurrences. Preoperative aspirin use was significantly correlated with recurrent surgeries, according to Forster *et al*²⁸. 's research. However, Lindvall and Koskinen²⁹ found no correlation between the preoperative anticoagulant therapy and the likelihood of CSDH recurrence. Gonugunta and Buxton^{30,31} did not discover a rise in the rate of CSDH recurrence with warfarin usage.. Mori *et al.*,³² for example, identified anticoagulant drugs to have a higher but not significant recurrence rate in their sample of treated CSDH via burr hole craniotomy. However Lee *et al.*,³³ who showed a statistically significant correlation between coagulopathy and the recurrence rate.

According to Gelabert-González *et al.*,³⁴ a correlation is seen between increasing brain atrophy in elderly patients and the decreasing ability of the brain to expand after evacuation and recurrence is seen. In our study we found mean age group in the recurrence group of patients

was 68.86 ± 15.86 and in no recurrence group of patients was 66.53 ± 12.69 . No statistically significant correlation was found between mean age and recurrence of CSDH (p value = 0.52). This is also supported by other authors, who stated that age does not have a significant correlation with the recurrence of chronic subdural haematoma.^{24,27,32,33}

In our study, out of 7 patients with recurrence, 5 had unilateral and 2 had bilateral CSDH, we found no statistical significant correlation between laterality and recurrence (p value 0.99). According to theory, individuals with bilateral Chronic subdural hematoma frequently have prior brain atrophy, which impairs brain re-expansion. However, the bilateral subdural hematoma does not necessarily result in equal CSDH growth. The premorbid brain condition or head tilting might be the cause of this hemispheric pressure discrepancy. Bilateral lesions become unilateral lesions when the CSDH on one side is expanded, eradicating the opposite lesion.³⁵ Matsumoto *et al.*,³⁶ identified that thickness as a recurrence factor, while others²³ reported that bilaterality as a recurrence factor. Old age, cerebral atrophy, large bleed, bilateral bleed, bleed density, inflammation markers, alcohol consumption, a propensity for bleeding, and some technicalities of surgery, such as irrigation with a small amount of fluid rather than excising a thick membrane preventing brain expansion, are among the many risk factors for the recurrence of CSDH that have been reported.^{32,34,37,38}

Greater bleed thickness has been linked in several studies to an increased likelihood of recurrence.^{23,38} According to Yamamoto *et al.*,²⁵ bigger clots have a higher propensity to recur because the subdural area left after surgical evacuation is larger in larger clots. However, we did not find pre-op CSDH thickness to be statistically significantly correlated with higher recurrence rates. (p value 0.41). In our study, we found statistically significant correlation between post op fluid thickness (>10 mm) and recurrence (p value <0.001)

It is disputed if preoperative midline displacement predicts recurrence since investigations have produced contradictory findings. While Ecosa Bae M *et al.*,⁴¹ and Yoon Gyo Jung *et al.*,⁴² came to the conclusion that preoperative midline displacement was not associated significantly with recurrence, Jung Min Lee *et al.*,³⁹ and Dae Hyo Song *et al.*,⁴⁰ found preoperative midline displacement to be an important factor of CSDH recurrence. In our study, we did not find a statistically significant correlation between preoperative midline shift and recurrence of CSDH (p value 0.18). We found statistically significant correlation between post operative midline shift (> 5 mm) and recurrence (p value < 0.01)

Our results contribute to a better understanding of some risk variables and prognostic factors related to CSDH recurrence. To validate our findings and learn more about the potential interactions between different

variables and recurrence, randomised multicentric data with significantly better research power are necessary.

In our study, there were no recurrences after 1 month, and after 3 months' follow-up, both arms had recovered to 96.9% of their pre-treatment levels. Even though one of our patients was asymptomatic, he experienced delayed remission of CSDH at 5 months. In their prospective, randomised, controlled clinical investigation, Gökmen *et al.*⁴³ also argued that there is no need for follow-up after 3 months because there was a 100% cure rate at that point.

Conclusions

Risk factors involved in postoperative recurrence of CSDH in our study as Hypertension, DM, prolonged PT INR, antiplatelet, anticoagulant drug, the thickness of hematoma more than 20 mm in pre-operative CT, post operative MLS and postoperative residual hematoma. But there was no correlation between age of patient, number of burr hole, position of drain and amount of drainage and recurrence of CSDH. This information will help in identifying patients with high incidence of recurrence in order to set close follow ups and acts to reduce the recurrence. Use of drains should be preserved to those patients who propensity to recur, those who are on antiplatelets, anticoagulants and with large CSDHs.

Limitation of the Study and Recommendation

Limitation of our study was the small sample size, so further studies should be conducted over large number of patient to confirm the risk factors of CSDH recurrence and multivariate analysis to be done.

Conflicts of Interest ---The author declares no conflicts of interest regarding the publication of this paper.

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