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Surgical Clipping of Ruptured Intracranial Aneurysm: Experience of a Tertiary Centre in Western India

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Abstract

Background Surgical clipping has been a gold standard procedure for management of intracranial aneurysms. Outcome studies of surgical clipping at institutional level are important to identify modifiable factors and further improve the results. These are even more important in areas where resources are limited, and patient presents late due to ignorance and lack of education. This study is a review of our institutional experience in microsurgical clipping of ruptured intracranial aneurysms.

Methods A retrospective study of patients who underwent surgical clipping for ruptured intracranial aneurysms from January 2014 to February 2020. The medical records of patients were reviewed for demographic data, clinical presentation, radiological investigations, surgery performed and neurological outcome. Outcome at discharge and outcome at follow-up were measured by modified Rankin scale (mRS).

Results In this study of 289 patients, 194 patients (67.13%) had good outcome at discharge (mRS0–2), while 95 patients (32.87%) had poor outcome at discharge (mRS 3–6) and 50 patients (17.30%) expired during hospital stay. Out of 289 patients, 208 patients (71.97%) were admitted after more than 3 days of ictus. Significant factors affecting outcome were neurological status determined by Glasgow coma scale (GCS) score, World Federation of Neurosurgical Societies (WFNS) grade or Hunt and Hess Grade, time interval from onset of subarachnoid hemorrhage to admission, and time interval from admission to surgery.

Conclusion The present study identifies factors for improving outcome in patients of ruptured aneurysm at institutional and community level. Time from ictus to admission and admission to surgery are important modifiable factors in our study.

Keywords
- ruptured intracranial aneurysm
- surgical clipping
- modified Rankin scale
- WFNS Grade

Introduction

Ruptured intracranial aneurysm is a life-threatening disease with significant mortality and morbidity rates.[1,2] Patient commonly presents with sudden onset severe headache, which the patient describes as worst headache of life, often with depressed level of consciousness. Early treatment aimed at occlusion of aneurysm is recommended. Surgical clipping had been a standard procedure for management of intracranial aneurysms. At

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present, microsurgical clipping and endovascular coiling of aneurysm both are accepted as standard treatment modalities. There is wide variability across the regions of world and neurosurgical centers regarding choice of treatment between microsurgical and endovascular treatment.[3] Surgical clipping continues to play a major role in India and other developing countries.[3,4] In a survey regarding practice patterns of cerebral aneurysm treatment in India, Ambekar et al[4] identified significant variations in management of intracranial aneurysm in India. Ikawa et al[5] in their study of outcome of aneurysmal subarachnoid hemorrhage (SAH) in Japan mentioned that outcomes of aneurysmal SAH may not be the same worldwide. Liao et al[2] in their single center study from Taiwan suggested that the therapeutic outcomes may vary with respect to the available methods, and evaluation of clinical results should be individualized in each medical institute. The purpose of the present study is to retrospectively analyze the baseline characteristics of the patients who have undergone surgical clipping and identify factors affecting outcome, outcome assessment and comparison with results of other such studies.

Methods

This study was retrospective analysis of patients who were treated by surgical clipping for ruptured cerebral aneurysm from time period of January 2014 to February 2020 at this Centre. We evaluated the patients with following inclusion criteria: patients with aneurysmal SAH diagnosed on computed tomography angiography (CTA), magnetic resonance angiography (MRA) or digital subtraction angiography (DSA) and treated with surgical clipping. Exclusion criteria included patient receiving endovascular treatment or with previously coiled aneurysm or patient with World Federation of Neurosurgical Societies (WFNS) grade 5 and or could not be taken for clipping for any other reasons.

Patient details including complete demographic profile, clinical status, investigation results, operative findings, and postoperative course were documented from patient medical records. Outcome were documented by reviewing the clinical status of patient as mentioned on the discharge ticket, by telephonic interview and (or) assessment in outpatient department (OPD) during follow-up at 6 month periods as per modified Rankin scale (mRS).

Statistical Analysis and Results

Statistical analyses were done using computer software (SPSS Trial version 23 and primer). The qualitative data were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations (SD). The difference in proportion was analyzed, by using Chi-square test, and the difference in means were analyzed by using Student's *t*-Test. Logistic regression was used to identify independent risk factors for poor outcome among the cases. Level of significance was set at 95% ($p < 0.05$). Total number of patients who underwent surgery for intracranial aneurysm was 289. In all patients, clipping was applied. The age range in our study was 7–80 years with majority of patients presenting in age group of 31 to 70 years (257 patients, 88.88%). Peak incidence was seen in the 4th decade. There was female preponderance (M:F 1:1.2). Headache was the most common presenting symptom, seen in 271 patients (93.77%). Seizure was presenting complaint in 13 patients (4.49%) (►**Table 1**).

Preoperative hydrocephalus was present in 64 patients (22.14%) and five patients had external ventricular drain (EVD) placement before surgical clipping. During postoperative hospital stay, 12 patients required treatment for hydrocephalus. EVD was performed in eight patients and ventriculoperitoneal (VP) shunt in four patients. Intraoperative rupture of aneurysm occurred in 13 patients (4.49%). Reexploration for removal of intracranial hematoma was performed in eight patients (2.77%). Endovascular therapy was attempted in three patients (1.03%), but coil could not be placed, and surgical clipping was subsequently performed in these patients. During the postoperative hospital stay, 51 patients (17.64%) had tracheostomy. The average hospital stay in clipping patients was 15 days. Intervals from onset of subarachnoid hemorrhage (SAH) to admission, onset of SAH to surgery, admission to surgery, and discharge or death is shown in ►**Table 2**. WFNS grade at admission and outcome at discharge is shown in ►**Table 3**.

Follow-up was conducted at 6 months period. Out of the 239 patients who were discharged, follow-up was available for a total of 203 patients. Among the 165 follow-up patients who were discharged in mRS 0 to 2, 160 patients remained in mRS 0 to 2 group, while two patients deteriorated to mRS 5 and there were three deaths. Among the 38 follow-up patients who were discharged in mRS 3 to 5, there were seven deaths. Twenty-one patients improved to mRS 0 to 2. Ten patients remained in poor outcome group mRS 3 to 5.

Discussion

The present study is a retrospective analysis of patients presenting with ruptured intracranial aneurysm and treated with surgical clipping in a single institute. The institute is a tertiary level, referral and teaching center. The institute receives patients mainly from state of Rajasthan and neighboring states of India. Besides, surgical clipping endovascular coiling is also performed at the center. The appropriate treatment strategy in a particular patient was decided by the team of neurosurgeons, neurointerventionists, and the patient's attendants who were thoroughly counseled about pros and cons of each treatment modality. The primary variable measured in the present study is the outcome at discharge of patients with surgical clipping. In our study, 289 patients had surgery, out of which 194 patients (67.13%) had good outcome at discharge as defined by mRS score of 0 to 2, while 95 patients (32.87%) had poor outcome at discharge as defined by mRS 3 to 6 with 17.30% mortality (►**Table 4**).

Table 1 Age, gender, presenting symptoms, history, and radiological investigations and findings

	No. of patients	% ($n = 269$ 100%)
Age (in years)		
1–10	1	0.34%
11–20	6	2.07%
21–30	20	6.92%
31–40	57	19.7%
41–50	81	28.02%
51–60	71	24.56%
61–70	48	16.6%
> 70	5	1.73%
Gender		
Male	131	45.33%
Female	158	54.67%
Presenting symptoms		
Headache	271	93.77%
Vomiting	153	52.94%
Loss of consciousness	90	31.14%
Altered consciousness level at admission	64	22.14%
Neurological deficit	27	9.34%
Seizure	13	4.49%
History		
Hypertension	99	34.56%
Smoking	85	29.41%
Radiological investigation		
NCCT	256	88.58%
MRI	37	12.80%
CT Angiogram	281	97.23%
MR Angiogram	14	4.84%
DSA	45	15.57%
Radiological findings		
SAH	280	96.88%
Hydrocephalus	64	22.14%
IVH	63	21.79%
Number of aneurysms		
Single	265	91.70%
Double	24	8.30%
Aneurysm location for single aneurysm ($n = 265$, 100 %)		**% ($n = 265$, 100 %)**
ACoA.	128	47.71%
MCA	79	30.15%
ICA.	25	9.41%
DACA.	19	7.25%
PCoA	14	5.34%

Abbreviations: ACoA, anterior communicating artery; DACA, distal anterior cerebral artery; ICA, internal carotid artery; IVH, intraventricular hemorrhage; MCA, middle cerebral artery; PCoA, posterior communicating artery; SAH, subarachnoid hemorrhage.

Table 2 Intervals between onset of SAH, admission, surgery, and discharge/death

	Onset of SAH to admission	Onset of SAH to surgery	Admission to surgery	Admission to discharge/ death
03 days or less	81	4	60	0
4–14 days	178	213	218	138
15 or more days	30	72	11	151

Abbreviations: n, number of patients; SAH, subarachnoid hemorrhage.

The outcome of surgical clipping in our institute, based on mRS score, is similar to as reported in literature, although in our study, mortality rates were higher than reported in other studies[5–10] Out of the 289 patients operated, a total of 50 patients had inhospital mortality. Among these 50 patients, 16 patients (32%; 16/50) had WFNS grade 4 at admission. As poor grade SAH is an independent and strong predictor of poor outcome, factors associated with inhospital mortality were analyzed in good grade SAH (WFNS grade 1, 2 and 3) only. Excluding WFNS grade 4 patients, there were 34 patients who had inhospital mortality. Procedure-related (surgery) mortality could be attributed to three patients (6%); one had intraoperative rupture of aneurysm and the other two patients required second surgery for evacuation of intracranial hemorrhage. Postoperative hydrocephalus requiring external ventricular drain developed in eight patients. Among the 50 patients who expired, 13 patients were aged more than 60 years (26%) and six patients had more than one aneurysm (12%). Cerebral infarcts were seen in seven patients (14%). In our institute, the facility of transcranial Doppler was not available, and CTA was performed in cases with declining neurological status. The poor outcome in the remaining 35 patients (70%) was attributed to clinical vasospasm. Intraoperative rupture of aneurysm occurred in 18 patients (6.22%) out of 289 cases. Twelve patients who had intraoperative rupture of aneurysm were discharged with good outcome (66.6%). Six out of these 18 patients expired during the hospital stay (33.3%). Among the six patients who died, three developed clinical vasospasm, and one patient developed postoperative hydrocephalus which required external ventricular drain. Two patients had mortality directly attributable to intraoperative ruptured aneurysm.

In our study, the major factors associated with inhospital mortality were presence of clinical vasospasm, poor grade SAH at admission, and age > 60 years. Other factors included postoperative hydrocephalus, cerebral infarcts, presence of multiple aneurysms, and procedure-related hemorrhage. Patients with symptomatic vasospasm were treated with hypervolemia, hypertension and hemodilution (HHH) therapy along with nimodipine(oral/IV). Endovascular intervention for treatment of vasospasm is not performed in our institute at present.

Table 3 WFNS grade at admission and outcome at discharge

WFNS grade at admission	$n = 289$(%)	Good outcome mRS 0–2	Poor outcome mRS 3–6	Inhospital mortality mRS 6
WFNS grade 1	181 (62.63%)	134 (74.03%)	47 (25.96%)	24 (13.26%)
WFNS grade 2	51 (17.65%)	38 (74.50%)	13 (25.49%)	4 (7.84%)
WFNS grade 3	31 (10.73%)	20 (64.51%)	11 (36.66%)	6 (19.34%)
WFNS grade 4	26 (8.99%)	2 (7.69%)	24 (92.30%)	16 (61.53%)
Total	289 (100%)	194 (67.13%)	95 (32.87%)	50 (17.30%)

Abbreviations: *n*, total no. of patients; mRS, modified Rankin scale; WFNS, World Federation of Neurosurgical Societies.

Table 4 Comparative outcome of surgery

	Present study (outcome at discharge)	Ikawa et al[5] (outcome at discharge)	ISAT (at 2 months F/U)	BRAT (at 1 year F/U)	Wadd et al[8] (outcome at 1 year F/U)	Sodhi et al9 (outcome at discharge)	Sodhi et al[9] (at 3 months F/U)
	Single institute study from India	Multicentric study from Japan	Multicen-tric study from UK, Europe, US, Australia and Canada	Single institute study from North America	Single institute study from Pakistan	Single institute study from India	Single institute study from India
mRS 0–2	194 (67.13%)	1786 (67.00%)	671 (63.1%)	162 (66.1%)	48 (68.6%)	–	–
mRS 3–6	95 (32.82%)	880 (33.00%)	392 (36.9%)	83 (33.9%)	22 (31.4%)	–	–
mRS 6	50 (17.30%)	225 (8.43%)	84 (7.9%)	–	3 (4.3%)	65 (21.2%)	85 (27.7%)
Total	289(100%)	2666 (100%)	1063 (100%)	245 (100%)	70 (100%)	307 (100%)	307 (100%)

Abbreviations: BRAT, Barrow Ruptured Aneurysm Trial; ISAT, International Subarachnoid Aneurysm Trial F/U, follow-up; MRS, modified Rankin scale
Note: Figures indicate number of patients.

Out of 239 patients discharged, follow-up could be performed in 203 patients. The study being retrospective, these patients were evaluated at 6 months duration after discharge. On follow-up of 165 patient who had mRS 0 to 2 at the time of discharge, majority of patients remained in good outcome group (160/165). There were three deaths (1.8%) and two patients deteriorated to mRS 3 to 5. On follow-up of 38 patients discharged in mRS 3 to 5 status, 21 patients improved to mRS 0 to 2, while there were seven deaths (18.42%). Ten patients remained in mRS 3 to 5 group. Analysis of our follow-up results show that majority of patients discharged in good outcome group continued without any adverse event. On the other hand, poor outcome group represents a more dynamic cohort of patients. Although a proportion of patients from poor outcome group improved, the poor outcome group also has higher incidence of mortality in our study (18.42% in poor outcome group compared with 1.8% in good outcome group). In our study, statistically significant factors for differentiating good and poor outcome group were neurological status as determined by GCS, WFNS or Hunt and Hess grade, time interval of ictus to admission, and time interval of admission to surgery (p-value <0.05; ►**Table 5**).

The mean age was more in poor outcome patient than good outcome (49.92 vs. 48.15 years). Advancing age was associated with poor outcome in our study.

The International Cooperative Study on the Timing of Aneurysm Surgery demonstrated that SAH patients who underwent surgery on posthemorrhagic days 4 to 10 had worse outcome than patients treated on days 0 to 3 and days 11 to 14.[4] Analyzing the data presented by Ikawa et al from Japan, among the 2666 patients who had surgical clipping, at least 1590 patients (59.63%) were clipped within 3 days of onset of SAH. Mean duration from hemorrhage to surgery in International Subarachnoid Aneurysm Trial (ISAT) was 1.8 days. In our study of 289 operated patients, only four patients (1.38%) were operated within 3 days of onset of SAH, while 213 patients (73.70%) were operated between 4 to 14 days after onset of SAH. One of the major reasons for the difference in timing of surgery after SAH is delay in arrival to the referral center. In the present study, 178 patients (61.59%) were admitted later than 3 days of onset of SAH. Mean time of interval from onset of SAH to surgery is 12.47 days in our study (►**Table 5**). The time interval from onset of SAH to surgery in present study did not attain statistical significance for differentiating good and poor outcome group. This is attributed to very low number of patients (four) operated within 3 days of onset of SAH and majority of patient being operated in the 4 to 14 days duration. Time from SAH onset to surgery is one of the strong modifiable factors affecting outcome. In our opinion, the delayed

Table 5 Distribution of factors in good outcome and poor outcome group

Group		Age (years)	GCS score	Hunt and Hess grade	WFNS grade	Outcome at discharge (mRS)	Interval from ictus to admission (in days)	Interval ictus to surgery (in days)	Interval admission to surgery (in days)	Interval (admission to discharge/death; in days)
Good outcome	*N*	194	194	194	194	194	194	194	194	194
	Mean	48.15	14.62	2.11	1.43	0.75	7.04	12.21	5.65	15.41
	SD	13.49	0.97	0.82	0.72	0.67	9.02	10.11	2.90	5.61
	Median	50.00	15.00	2.00	1.00	1.00	4.00	9.00	5.00	14.50
	Min	7	8	1	1	0	1	3	1	7
	Max	80	15	4	4	2	60	71	18	41
Poor outcome	*N*	95	95	95	95	95	95	95	95	95
	Mean	49.92	13.42	2.87	2.06	5.22	5.13	13.00	8.58	17.95
	SD	11.80	2.37	1.12	1.24	0.99	5.53	10.54	9.16	10.51
	Median	50.00	15.00	3.00	1.00	6.00	4.00	10.00	7.00	16.00
	Min	19	7	1	1	3	1	3	1	6
	Max	78	15	5	4	6	30	67	66	79
Total	*N*	289	289	289	289	289	289	289	289	289
	Mean	48.73	14.23	2.36	1.66	2.22	6.41	12.47	6.61	16.24
	SD	12.97	1.66	0.997	0.99	2.25	8.08	10.24	5.91	7.67
	Median	50.00	15.00	2.00	1.00	1.00	4.00	10.00	6.00	15.00
	Min	7	7	1	1	0	1	3	1	6
	Max	80	15	5	4	6	60	71	66	79
		0.28	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.06	0.53	< 0.0001	0.007

Abbreviations: GCS, Glasgow Coma Scale; mRS, modified Rankin scale; *n*, number of patients; SD, standard deviation; WFNS, World Federation of Neurosurgical Societies.

presentation to referral center and the resulting delay in surgery may have affected our results.

Time from admission to surgery show that patients operated earlier have better outcome. Mean time interval from admission to surgery was 5.65 days in good outcome group compared with 8.58 days in poor outcome group. Mean time interval from onset of SAH to admission was 7.04 days in good outcome group, while it was 5.13 days in poor outcome group. The findings that the patients who were admitted earlier had poor outcome while patients who were admitted later had better outcome was unexpected. On analysis of our data, it was found that none of the WFNS grade 1 was admitted within 3 days of onset of SAH. Of the entire WFNS grade 2, 3 and 4 patients, more than half were admitted within 3 days of onset of SAH. We concluded that patients who were unconscious, had neurological deficit or higher WFNS/Hunt and Hess grade presented to us earlier than those in WFNS grade 1.

Gender, history of smoking, hypertension, loss of consciousness and seizure, intraoperative rupture of aneurysm, aneurysm size, EVD, VP shunt, and reexploration for hematoma, on analysis, did not reach level of statistical significance (p-value < 0.05) for differentiating outcome at discharge as good or poor. The incidence of adverse events requiring intervention is high in poor outcome group in comparison to good outcome group. It did not come out to be statistical significant in our study, possibly because of the small numbers. We recommend multicenter studies to more accurately clarify the incidence of adverse events during hospital stay and their role in affecting outcome. Poor grade SAH (WFNS grade 4 and 5) is usually associated with unfavorable outcomes.

In the present study, 26 cases were operated in WFNS grade 4. Out of 26 operated cases, 24 (92.30%) had poor outcome, while only 2 (7.69%) had good outcome. During the postoperative hospital stay, 16 (61.53%) patients expired. No patients in WFNS grade 5 were operated, as their general condition was found to be very poor. These patients were managed expectantly till patients improved to good clinical grades. In a study by Ambekar et al, 41% of respondents preferred to wait for a week before attempting repair in a patient with poor grade, while 20.9% recommended surgery within 24 hours and 38.1% within a week.[4] Although Kranthi et al in a single center study from India demonstrated favorable outcome in 53.8% of their operated cases and recommended early surgery for WFNS grades 4 and 5.[11] Poor grade SAH patients have high morbidity and mortality and recommendations include waiting for clinical improvement before intervention or early intervention. In our study, CTA was the most common modality to detect and define aneurysm characteristic after a diagnosis of SAH is made. In a survey from India, 57% of respondents preferred DSA, 41% preferred CTA, while only 2% preferred MRA.[4] In our opinion, good quality CTA with 3D reconstruction is usually sufficient for surgical planning. Although DSA is the gold standard for evaluation, it is not essential to have a DSA in every patient. DSA may be required when CTA fails to provide adequate information.

Conclusion

The present study identifies factors for improving outcome in aneurysmal SAH at institutional level. In our study, time from onset of SAH to admission and time from onset of SAH to surgery are the important modifiable factors affecting outcome after surgery. In present study, the good outcome is comparable to other studies, but the mortality rates are high. The reason may be delay in referral to our institute. In authors' opinion, the outcome can be further improved by enhancing the knowledge of referring physician regarding the importance of early surgery in patients with aneurysmal SAH and the need for prompt referral.

Limitations

This is a single center study and may not reflect the practice patterns of other institutes. This is a retrospective study with lack of randomization and control group. There is a possibility of selection bias. Data collected may not be as accurate as in a prospective research. Also, follow-up could not be done in all patients.

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Conflict of Interest
None declared.

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