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Comparative Analysis of the Risk Factors Influencing Recovery of Function from Oculomotor Nerve Palsy in Unruptured and Ruptured Posterior Communicating Artery Aneurysms

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ABSTRACT

AIM: To assess the risk factors and simultaneously compared the benefits of procedures (clipping vs. coiling) in the recovery of function from oculomotor nerve palsy (OMNP) between cases with unruptured and ruptured posterior communicating artery (PCOM) aneurysms.

MATERIAL and METHODS: Among the 225 cases of aneurysm treated in our department between July 2018 and February 2020, 25 patients with PCOM aneurysm with OMNP (unruptured: n=13; ruptured: n=12) were retrospectively analysed.

RESULTS: The average duration from onset of symptoms to treatment in unruptured PCOM aneurysm cases was 13.33 ± 3.76 days compared with 7.41 ± 2.42 days in ruptured aneurysm cases. Moreover, an 80% improvement was observed when OMNP was treated within 17 days with the earliest improvement noticed in 33.05 ± 18.75 days in unruptured aneurysm cases compared with 39.66 ± 31.75 days in ruptured PCOM aneurysm cases. Stepwise logistic regression analysis revealed that the type of aneurysm (better recovery in unruptured aneurysm cases) was a significant risk factor (p=0.0126), but not the procedure (clipping vs. coiling) performed, for function recovery from OMNP.

CONCLUSION: Patients with unruptured PCOM aneurysms with OMNP have a better recovery rate than those with ruptured PCOM aneurysms. No procedural (clipping vs. coiling) advantages were observed on the recovery of function from OMNP. Transmitted pulsation reduction significantly affects the recovery of function from OMNP.

KEYWORDS: Unruptured and ruptured, PCOM aneurysms, Risk factors, Clipping vs. coiling

ABBREVIATIONS: PCOM: Posterior communicating artery aneurysm, **OMNP:** Oculomotor nerve palsy, **CT:** Computed tomography, **DSA:** Digital subtraction angiography, **MRS:** Modified Rankin Scale, **ROC:** Curve-Reciever operating characteristics curve, **AUC:** Area under curve

INTRODUCTION

The reported incidence of oculomotor nerve palsy (OMNP) in patients with posterior communicating artery (PCOM) aneurysm is 11%–56%. Several studies have evaluated the effects of the type of procedure (clipping vs. coiling) for treating PCOM aneurysms on the recovery of OMNP (5,11,15,17). However, the findings of these studies are mixed as few have suggested that clipping results in better recovery, whereas some favor coiling over clipping. Besides the type of procedure, other associated risk factors, such as age, size of the aneurysm, duration from onset of symptoms to treatment, preoperative severity of OMNP, and

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subarachnoid hemorrhage (SAH), influence the recovery of function from OMNP. Few studies have shown the risk factors affecting the recovery of function from OMNP in patients with unruptured PCOM aneurysm, and fewer studies have reported the difference in outcome between patients with unruptured and ruptured PCOM aneurysms in terms of OMNP as they need separate considerations (9,12,20). Various mechanisms had been proposed to explain the cause of OMNP including transmitted pulsation, irritating effect of the blood on the oculomotor nerve, and compressive effect of blood clots causing neuropraxic effect over the nerve. This study compares the risk factors affecting postoperative recovery of function from OMNP between patients with unruptured and ruptured PCOM aneurysms, simultaneously evaluates the comparative benefits of procedures (clipping vs. coiling) in postoperative recovery of function from OMNP, and determines the major mechanisms behind the occurrence of OMNP in these cases.

MATERIAL and METHODS

Our institution's ethical committee approved this study (IEC no. 2020/705; consent from the patients or their relatives for publication has been obtained). In this study, we retrospectively analyzed 225 cases of aneurysms treated at our center between July 2018 and March 2020. Among these 225 cases, 75 had PCOM aneurysm and 25 presented with OMNP. Data on the patients' demographic characteristics, clinical features, risk factors under consideration, extent of OMNP, procedure performed, postoperative recovery, Fischer grade on head computed tomography (CT), Hunt and Hess grade, preoperative and postoperative Modified Rankin Scale (MRS) score, postoperative response on subsequent follow-up in the improvement of OMNP were obtained from the patients' medical record sheets. Twenty-five cases who met the inclusion criteria—PCOM aneurysm with preoperative OMNP and documented evidence of aneurysm on CT angiography and 3D rotational digital subtraction angiography without a history of diabetes—were included in the study.

The degree of OMNP was classified into complete or partial depending upon the presence or absence of the functions of the oculomotor nerve. Complete OMNP was defined as the presence of diplopia, ptosis, ophthalmoplegia, and pupillary dysfunction. Partial OMNP was defined as the presence of partial impairment of extraocular movement with pupillary sparing or involvement.

The patients were divided into two groups—unruptured PCOM aneurysm and ruptured PCOM aneurysm with OMNP groups. Various risk factors influencing the recovery of function from OMNP in both groups were evaluated separately. In addition, we analyzed the influence of the type of procedure (microsurgical clipping vs. endovascular coiling) on the recovery of function from OMNP.

The patients and their relatives were explained the microsurgical clipping and endovascular coiling, and decision to perform which procedure was taken according to their consent. Intraoperative events were recorded in the operative notes. Clinical outcomes were categorized into response and no response. Complete symptomatic recovery and partial relief were included in the response (improvement) group, and unchanged symptoms or deterioration from incomplete to complete palsy were included in the no response (no improvement) group. Complete resolution of diplopia and ptosis, full range of extraocular movement, and recovery of pupillary reaction were the criteria for complete recovery.

Statistical Package for the Social Sciences (version 24; IBM Corp., Armonk, NY, USA) was used for all data analyses. The risk factors that had positive correlation coefficients were considered for further statistical analysis. Fisher's exact test and the chi-square test were used to compare the differences in parameters and clinical outcomes between the groups for categorical variables. The Mann–Whitney U test was used to compare the means if data were skewed to the right. P values of less than 0.05 were used to denote statistical significance. Finally, to test the power of the significance of the risk factors that have P values of <0.05 on linear univariate regression analysis, stepwise logistic regression analysis was conducted.

RESULTS

The mean age at presentation was 53.92 ± 5.66 years and 46.19 ± 9.19 years in the unruptured and ruptured PCOM aneurysm groups, respectively. The male–female ratio was almost similar in both groups (Tables I, II).

In the unruptured PCOM aneurysm group, 16.52% of the cases had aneurysm sizes of less than 5 mm and 61.52% cases had aneurysm sizes between 5 mm and 10 mm (Table I), whereas in the ruptured group, 42% cases had aneurysm sizes of less than 5mm and 50% had aneurysm sizes between 5 mm and 10 mm. The size of the aneurysm was not a factor significantly affecting the postoperative recovery of function from OMNP in this study. We observed large-sized horseshoe-shaped unruptured aneurysms without OMNP in patients who underwent coiling (Figures 1-3) and 6-mm-size ruptured aneurysms causing complete OMNP in patients who underwent clipping. The average duration from the onset of symptoms to treatment was 13.33 ± 3.76 days and 7.41 ± 2.42 days in the unruptured and ruptured PCOM aneurysm groups, respectively. In both the unruptured and ruptured PCOM aneurysm groups, a shorter duration from the onset to treatment was significantly associated with earlier recovery of function from OMNP. The patients treated within 14 days in both groups had shown a faster recovery of function from OMNP than those treated more than 14 days. The average duration from treatment to the appearance of the first sign of improvement was 33.05 ± 18.75 days and 39.66 ± 31.75 days in the unruptured and ruptured PCOM aneurysm groups, respectively; however, the difference in the overall recovery time between the groups was insignificant (Figure 4).

Among all patients, 58% underwent clipping and 42% underwent coiling in the ruptured PCOM aneurysm group, whereas 52% cases underwent clipping and 48% underwent coiling in the unruptured PCOM aneurysm group. No significant difference in the postoperative recovery of function from OMNP following either procedure was observed (p=0.67) (Table III).

Table I: Demography of Unruptured PCOM Aneurysm Presenting with OMNP

Patients characteristics	**Clipping group**		**Coiling group**	
	n	**%**	**n**	**%**
Sex, 1. Male	3/13	23	3/13	23
2. Female	3/13	23	4/13	31
Age in years (mean ± SD)]	49.7 ± 8.42 (SD)		51.17 ± 10.46 (SD)	
Preop duration of Ptosis in days	13.33 ± 3.76 (SD)		15.58 ± 6.72 (SD)	
Size of the aneurysm	**n**	**%**	**n**	**%**
< 5 mm	1/13	7.69	1/13	7.69
> 5 mm and < 10 mm	4/13	30.76	4/13	30.76
> 10 mm	1/13	7.69	2/13	15.38
Oculomotor Nerve palsy, 1. Incomplete	2/13	15.38	4/13	30.76
2. Complete	5/13	38.46	2/13	15.38
Modified Rankin Scale				
Score 0	2/13	15.38	1/13	7.69
Score 1	4/13	30.76	4/13	30.76
Score 2	0		2/13	15.3

Table II: Demography of Ruptured PCOM Aneurysm with OMNP

Patients characteristics	**Clipping group**		**Coiling group**	
	n	**%**	**n**	**%**
Sex, 1. Male	3/12	25	2/12	16.6
2. Female	4/12	33.3	3/12	25
Age per years [range (mean ± SD)]	47.6 ± 6.36 SD		52.18±9.34SD	
Preop duration of ptosis in days	8.47±2.63SD		5.488±1.92 SD	
Size of the aneurysm	**n**	**%**	**n**	**%**
< 5 mm	3/12	25	2/12	16.6
> 5 mm and < 10 mm	4/12	33.3	2/12	16.6
> 10 mm	0/12	0	1/12	8.33
Hunt and Hess scale				
Grade 1–2	4/12	33.3	3/12	25
Grade 3	3/12	25	2/12	16.6
Grade 4	0/12	0	0	0
Oculomotor nervepalsy, 1. Incomplete	4/12	33.3	3/12	25
2. Complete	3/12	25	2/12	16.6
Modified Rankin Scale				
Score 0	2/12	16.6	1/12	8.33
Score 1	4/12	33.3	3/12	25
Score 2	1/12		1/12	
Fisher grading on CT Head				
Grades 1–2	6/12	50	2/12	16.6
Grades 3–4	1/12	8.33	3/12	25

Table III: Procedural Comparision for Postoperative Improvement in Cases of PCOM Aneurysm with OMNP

	Procedure		
Postoperative OMNP	**Microsurgical clipping**	**Endovascular coiling**	
Complete recovery	10	6	16 (64.0%)
Incomplete recovery	3	4	7 (28.0%)
No recovery	1	1	2 (8.0%)
	14 (56.0%)	11 (44.0%)	25
	Chi-squared	0.794	
	DF	2	
	Significance level	P=0.6722	
	Contingency coefficient	0.175	

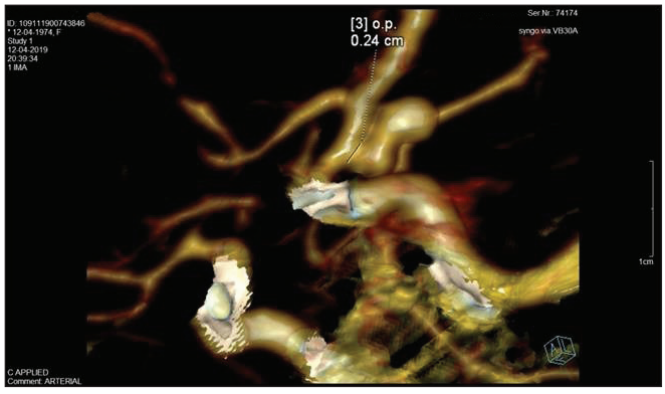

Figure 1: 3D computed tomography angiography (CTA) reveals a large-size 1.5-cm multilobulated posterior communicating artery (PCOM) aneurysm compressing the oculomotor nerve.

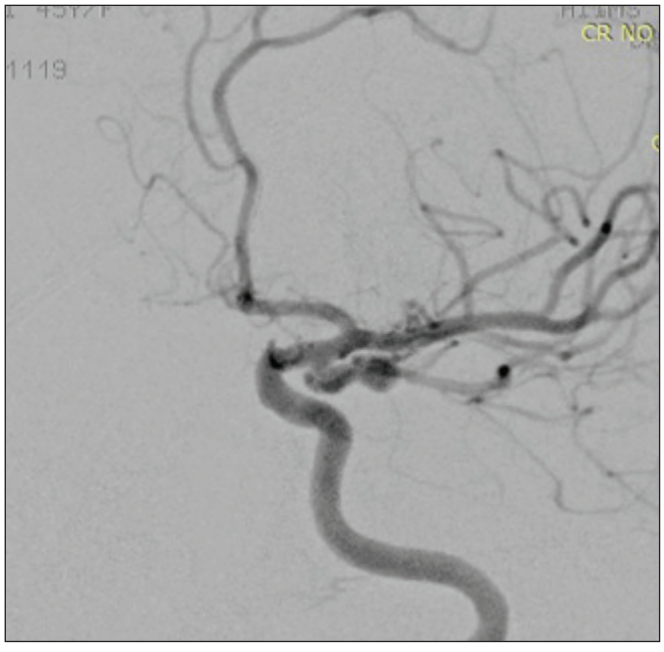

Figure 2: Digital subtraction angiography (DSA) of the same patient shows a horseshoe-shaped multilobulated projection toward the oculomotor nerve.

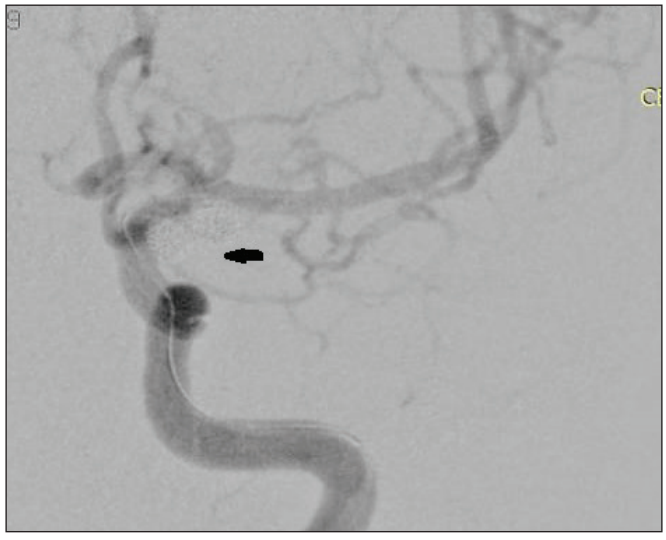

Figure 3: A posterior communicating artery aneurysm obliterated using balloon-assisted coil embolization with no post-coiling oculomotor nerve palsy.

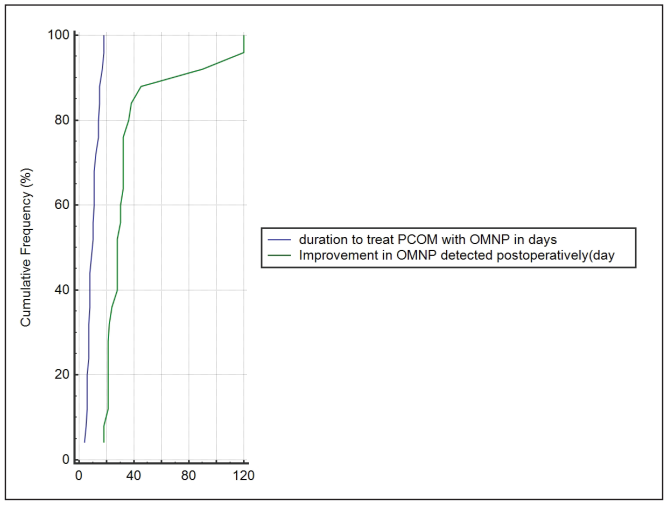

Figure 4: A cumulative graph showing the time of onset of oculomotor nerve palsy in patients with posterior communicating artery aneurysm and postoperative recovery.

Vasospasm was noted in two patients with unruptured PCOM aneurysm and three patients with ruptured PCOM aneurysm, which improved subsequently after Nimodipine infusion. Shunt-dependent hydrocephalus was noted in one patient with ruptured PCOM aneurysm.

Following stepwise logistic regression analysis of the factors found to be significant on univariate regression analysis, namely, size of the aneurysm, type of the aneurysm, preoperative severity of OMNP, treatment time, and treatment procedure, only type of the aneurysm retained the power of significance with a p value of 0.0182 (Table IV). On comparative analysis of the risk factors affecting the recovery of function from OMNP on receiver operating characteristic (ROC) curve, we found that the type of the aneurysm has an area under the curve (AUC) value of 0.88 and positive predictive value of 88%, which was the highest among other risk factors (Figure 5).

In the unruptured PCOM aneurysm group, 84.62% of the cases had complete recovery, 7.69% had incomplete recovery, and 7.69% had shown no recovery until the last follow-up. In the ruptured PCOM aneurysm group, 75% of the patients had shown complete recovery, 8.33% had incomplete recovery, and 16.66% did not recover at all. Stepwise logistic regression analysis revealed that recovery of function from OMNP was significantly affected by the presence of an unruptured PCOM aneurysm (p=0.0182). In the unruptured PCOM aneurysm group, all six patients with incomplete OMNP had full recovery, whereas only five of the seven cases with complete OMNP had achieved full recovery. Meanwhile, in the ruptured PCOM aneurysm group, six of the seven patients with incomplete OMNP had full recovery, whereas three of the five cases with complete OMNP had full recovery (Table V).

Follow-up duration was 12.76 ± 4.28 months and 10.66 ± 4.84 months in the unruptured and ruptured PCOM aneurysm groups, respectively (Table V). Several studies have performed comparative analysis of the recovery of function from OMNP showing better recovery of function from OMNP in cases with unruptured and ruptured PCOM aneurysm treated with coiling than those treated with clipping (Table VI).

DISCUSSION

OMNP is a morbidity associated with PCOM aneurysm, usually detected in the postoperative period. Prolonged recovery of function from OMNP impacts the physical quality of life of patients. Few studies in the literature have compared the influence of risk factors on the recovery of function from OMNP between patients with ruptured and unruptured PCOM aneurysms (9,12,19.20). Such studies are needed as associated risk factors may have varying impacts on the recovery of function from OMNP given the different pathophysiological conditions in ruptured and unruptured PCOM aneurysms.

Table IV: Stepwise Logistic Regression Analysis of Risk Factors Affecting Improvement of OMNP with P Value <0.3 in Univariate Regression Analysis

	Factors	Regression coefficient	Standard error	Odds ratio	95% confidence interval	p
1	Size of the aneurysm	0.497	0.234	0.672	0.309-1.205	0.117
2	Type of the aneurysm	3.175	0.989	1.192	0.218-4.945	**0.018**
3	Preoperative severity of OMNP	-4.336	3.438	3.034	0.259-3.734	0.134
4	Treatment time	-0.143	0.059	0.958	0.605-1.214	0.334
5	Treatment procedure	-2.188	0.741	0.041	0.007-0.161	0.284

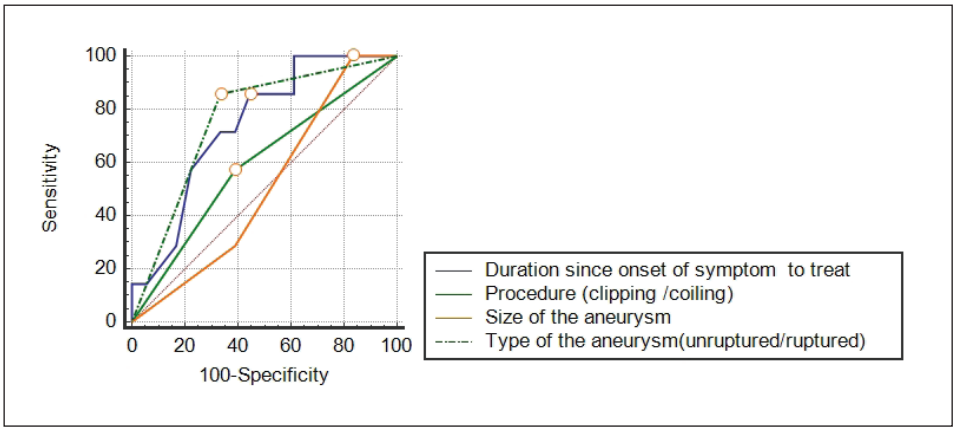

Figure 5: Comparative receiver operating characteristics curve showing area under the curve (AUC) of the risk factors affecting the recovery of function from oculomotor nerve palsy in patients with posterior communicating artery aneurysm.

Table V: Improvement in OMNP in Cases with PCOM Aneurysms on Follow up

	Preoperative OMNP in PCOM aneurysm	**Postoperative Recovery in OMNP in PCOM aneurysm**			**Improvement noted first(average duration indays)**	**Follow up (months)**
Unruptured PCOM Aneurysms		complete	incomplete	No improvement		
Full OMNP	7	5	1	1	33.05 ± 18.75 (SD)	12.76 ± 4.28 (SD)
Partial OMNP	6	6	0	0		
Recovery in unruptured aneurysm	13	11 (84.62%)	1 (7.69%)	1 (7.69%)		
Unruptured PCOM Aneurysms						
Full OMNP	5	3	0	2	39.66 ± 31.75 (SD)	10.66 ± 4.84 (SD)
Partial OMNP	7	6	1	0		
Recovery in ruptured aneurysm	12	9 (75%)	1 (8.33%)	2 (16.66%)		

Table VI: Comparative Results of Improvement in OMNP from Literature in PCOM Aneurysm Cases

Sl.no	**Studies and authors**	**Type of the aneurysm with OMNP without SAH**		**Type of the aneurysm with OMNP with SAH**		**Complete OMNP**		**Incomplete OMNP**	
		CR	**PR**	**CR**	**PR**	**CR**	**PR**	**CR**	**PR**
1	Ahn et al. 2006 (1)								
	clipping	3	4			3	3	1	0
	coiling	6	4			2	5	3	0
2	Brigui et al. 2014 (4)								
	clipping	5	1	1	0	3	1	2	0
	coiling	5	2	3	1	4	1	4	1
3	Nam et al. 2010 (14)								
	clipping	5	2			3	2	2	0
	coiling	5	0			4	0	1	0
4	Patel et al. 2014 (15)								
	clipping	0	2	6	1	3	3	3	0
	coiling	1	0	4	1	4	4	2	0
5	Khan et al. 2018 (12)	5		6					
	clipping	5	0	5	0	6	0	5	0
	coiling	4	2	4	1	7	5	3	1
6	**Present study**								
	clipping	6	1	5	2	5	2	3	2
	coiling	6	0	4	1	6	0	6	1

CR: *Complete recovery,* ***PR:*** *Partial recovery.*

The incidence of OMNP in this study was 25%. Moreover, the incidence of OMNP was 16.83% and 8.87% in the unruptured and ruptured PCOM aneurysm groups, respectively. Yerramneni et al. have reported a 13% incidence of OMNP in their study, and Chalouhi et al. have observed an 11.9% incidence of OMNP in their study (5,17). In a study by Zhong et al., among 102 cases with OMNP, 53.9% (n=55) had unruptured aneurysms and 46% (n=47) had ruptured aneurysms, which is similar to the findings of this study (52% and 48%, respectively) (20).

The average age at presentation in the unruptured and ruptured PCOM aneurysm groups was 53.92 years, which conforms to that in the studies by Patel et al., Ahn et al., and Brigui et al. (1,4,15). In this study and other studies, age was not found to influence the recovery of function from OMNP.

The average duration from the onset of symptoms to treatment was longer in the unruptured PCOM aneurysm group than that in the ruptured PCOM aneurysm group as the decision to operate was delayed in the unruptured PCOM aneurysm group. In this study, the duration from the onset of symptoms to treatment had positively influenced the recovery of function from OMNP, showing that a shorter duration from the onset of symptoms to treatment results in better recovery. Javalkar et al. have reported an 81% recovery when such cases were operated within 3 days and 75% recovery when they were treated after 3 days (10). Our findings were similar to the study by Zhong et al. who have reported a mean interval between OMNP onset and treatment of 17.7 days (range, 1–180 days), and in their meta-analysis, they have revealed that the duration from OMNP onset to treatment in such cases reach even up to 3 weeks (20). The prolonged neuropraxic effect of transmitted pulsation, hematoma, and vasculopathy caused by bleeding in the surrounding cisterns leads to poor recovery of function from OMNP in cases with delayed treatment.

On univariate analysis, the severity of OMNP seemed to have a significant effect on the recovery of function from OMNP in both the unruptured and ruptured PCOM aneurysm groups in this study, although it did not reach statistical significance on stepwise logistic regression analysis. Similar findings were noted in the studies by Engelhardt et al., Tan et al., Zhong et al., and Guresir et al. Moreover, they have suggested that preoperative severity of OMNP has a profound effect on postoperative recovery in both the unruptured and ruptured PCOM aneurysm groups (6,8,16,20).

No significant difference in the improvement of OMNP was observed between clipping and coiling. Zheng et al. and Guresir et al. in their studies and Khan et al. in their meta-analysis found a better outcome in patients with ruptured PCOM aneurysm with OMNP who underwent clipping than those who underwent coiling (8,12,19). Similar to our findings, studies by Nam et al., Ahn et al., and Zhong et al. did not observe any procedural advantages (coiling vs. clipping) in both unruptured and ruptured PCOM aneurysm cases (1,14,20).

We found significantly better recovery of function from OMNP in patients with unruptured PCOM aneurysm than those with ruptured PCOM aneurysm, which may be because the compression effect of transmitted pulsation is a major contributory factor for OMNP compared with SAH with a harmful effect in terms of the irritant effect and external compression and consequent neuropraxic effect of blood clots (3). Kassis et al. have found that patients who presented with SAH had a higher likelihood of recovery than those with unruptured aneurysms (p=0.007) (11). Based on their findings, it can be hypothesized that the mechanism of OMNP in patients with SAH may include inflammatory and microvascular effects secondary to the blood in the cisterns and that this effect may have a more favorable natural history and may be responsive to corticosteroids. Zheng et al. in a meta-analysis involving patients with SAH have reported a significant difference in the complete recovery of function from OMNP between the clipping and coiling groups, favoring the clipping group, which conforms to the most recent meta-analysis on this topic conducted by Gaberel et al. (7,19). In terms of total efficiency, defined as any kind of improvement on OMNP in patients with SAH, no significant difference was found between clipping and coiling as reported in the studies by Zhong et al., Ahn et al., and Nam et al. (1,14,20). The findings of this study failed to demonstrate an advantageous effect of one treatment modalities over the other. This suggests that the transmitted pulsation effect, not the irritant and compressive effect of cisternal blood, is the main culprit in causing OMNP. Our findings and justification conform to the studies by Birchall et al., Ko and Kim, and Zhang et al. (2,13,18).

In this study, full recovery was observed in 80% of the patients, partial recovery in 8%, and no improvement in 12% cases. Full recovery from complete OMNP was observed in 58% and partial improvement in 19% of cases in a study by Javalkar et al. (10). In a study by Zhong et al., 57 (55.9%) patients completely recovered and 43 (42.2%) patients showed partial recovery, whereas two (1.9%) patients showed no sign of recovery of oculomotor nerve function at the last follow-up (20). In a study by Kasis et al. (11), complete recovery was observed in 35% of the patients studied, partial recovery in 65%, and no recovery in 5%. Variations in recovery are mainly due to the variability in defining the initial severity and recovery parameters in different studies (7,8,12,20).

CONCLUSION

Patients with unruptured PCOM aneurysm have better recovery of function from OMNP than those with ruptured PCOM aneurysm. No procedure (clipping vs. coiling) has demonstrated an advantage over the other in terms of recovery of function from OMNP in patients with unruptured and ruptured PCOM aneurysms, thus suggesting that the reduction of transmitted pulsation is a major deciding factor in the recovery of function from OMNP.

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