



## Efficacy of Treatment Modalities for Management of Third Nerve Palsy Induced by Posterior Communicating Artery Aneurysm: Reports of 12 Cases with Short Literature Review

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### Abstract

Posterior Communicating Artery Aneurysms (PComAAs) may induce third nerve palsy. The aim of our study was to evaluate clinical outcomes of surgical clipping versus endovascular coiling. We retrospectively analyzed seven patients who underwent endovascular coiling and five patients who underwent surgical clipping who had PComAAs associated with Third Nerve Palsy (TNP) at our centre. The following parameters: age of patients, size of aneurysms, Subarachnoid Hemorrhage (SAH), degree of third nerve palsy, symptoms to surgery period, and follow up period were assessed. In this study, it was found that: 58.3% (7/12) patients had been treated by endovascular coiling while 41.7% (5/12) patients received surgical clipping. Complete improvement of third nerve palsy was achieved in all five patients (100%) undergoing surgical clipping while only four (57.1%) patients had a complete recovery and an incomplete improvement was seen in 42.8% patients in patients undergoing endovascular coiling. Moreover, complete recovery of TNP was 44.8% and incomplete recovery was 44.2% for cases undergoing endovascular coiling out of 174 cases whereas complete improvement was seen to be 76% and incomplete improvement was 19.2% in patients out of 182 cases that underwent surgical clipping. It was found that the early management of third nerve palsy, the degree and severity of third nerve palsy at the beginning of insult contributed towards the influence of nerve recovery. We conclude the patients that have undergone different procedures should be followed up and investigated for a longer time before saying which procedure is best and most effective.

**Keywords:** Posterior communicating artery aneurysms; Third nerve palsy; Endovascular coiling; Surgical clipping; Digital subtraction angiography

### Introduction

Posterior Communicating Artery Aneurysms (PComAAs) are the most common intracranial aneurysms and are second most common aneurysm among all (25% of all aneurysms) aneurysms representing 50% of all internal carotid artery aneurysms [1]. The mechanical complication related to pressure to nearby structures can occur with unruptured (by themselves) or ruptured (compression by haemorrhage or hematomas) can occur with PcomAA. Third Nerve Palsy (TNP) is common clinical presentation of both ruptured and un-ruptured (PComAA) [2-4]. To date, the exact pathophysiologic mechanisms underlying aneurismal third nerve palsy remains unknown. There are many theories published about the pathophysiologic mechanism of TNP, which are as follows: direct mechanical compression of third nerve palsy by enlargement of aneurismal sac in suprasellar cistern, nerve injury by arterial pulsation of aneurysm as well as by pressure from arterial bleeding due to rupture of aneurysm, and irritation from subarachnoid hemorrhage [5-8]. The onset and the course of TNP may be acute or slow depending on the rate of progression of aneurysm volume, progression towards aneurismal wall dissection and the terminal events of accompanying subarachnoid hemorrhage. If the aneurysm is dilated, treatment is indicated to prevent impending risk of aneurysm rupture or re-rupture and to hasten nerve recovery. Surgical Clipping (SC), a classic procedure that has been practiced for long is regarded as the standard method of treatment as it allows immediate alleviation of mass compression [9,10]. However, another treatment modality does exist which is called Endovascular Coiling (EVC). EVC is now being widely used as alternative

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**Table 1:** Characteristics of both groups of patients who underwent surgical clipping (SC) and endovascular coiling (EVC).

NO. Of patients	Age, year/Sex	Deficit(TNP)	Treatment methods	Diameter of aneurysm (mm)	Aspect ratio	SAH	Fisher grading	Symptom to treatment period, days	Start to pupil recovery, days	Resolution of TNP	Follow-up period (months)
1	48/F	Complete	Coiling	2.9	2.8	Yes	2	30	6 days	Complete	24
2	59/F	Complete	Coiling	3.8	2.2	No	1	15	3 days	Complete	30
3	55/F	Incomplete	Coiling	7	1.7	Yes	3	9	7 days	Complete	50
4	63/F	Complete	Coiling	4	1.6	Yes	2	25	3 days	Incomplete	9
5	42/F	Incomplete	Coiling	5	2.3	Yes	3	5	5 days	Complete	30
6	71/F	Complete	Coiling	5	3.5	Yes	3	30	3 days	Incomplete	3
7	47/F	Complete	Coiling	6.6	2	Yes	3	25	5 days	Incomplete	3
8	69/F	Complete	Clipping	4	1.7	Yes	3	35	3 days	Complete	36
9	52/F	Incomplete	Clipping	3.4	3.5	Yes	2	7	2 days	Complete	12
10	56/F	Incomplete	Clipping	3	2	Yes	3	3	2 days	Complete	6
11	63/F	Complete	Clipping	5	1.7	Yes	4	20	4 days	Complete	12
12	50/M	Incomplete	Clipping	4.5	1.3	Yes	3	8	5 days	Complete	21

treatment modality for embolization PComAAs where coils are passed through femoral artery route. It is minimally invasive and stands superior regarding the cost, morbidity and hospital stay yet there are concerns regarding the coiling that could contribute to the mass effect and compromise nerve recovery. There have been numerous studies demonstrating the usefulness and superiority of surgical clipping [11], and endovascular coiling [2,9,12,13]. Moreover, other studies have also demonstrated no significance difference in the clinical outcomes between the methods of coiling and clipping [14]. Thus, there seems to be a continuous debate regarding the feasibility of these procedures and no clear cut guidelines or strategies to employ one or the other exists. All of the decisions taken are based clinically and radio logically and we feel that further larger studies between the two procedures are the prerequisites of concluding the efficacy of these procedures.

Here, we describe the findings of cases at our centre with PComAAs with TNP that underwent both of these procedures and try to align ourselves with the findings of previous studies. We also try to base our opinions on the clinical findings at follow up studies and try to devise a clinical strategy for future guidance in patients with PComAAs with TNP, which still is an unmet clinical need at our centre.

## Materials and Methods

The details of patients that underwent these two procedures (SC and EVC) at second affiliated hospital, Anhui Medical University were acquired from the hospital database records. The cases of 84 PComAAs were gathered within the timeframe of January 2009 to December 2014. There were 12(14.3%) patients that presented with features of TNP. Among these twelve patients, seven patients underwent endovascular coiling and five patients underwent frontotemporal craniotomy under microscope and clipping of PComAAs. The confirmatory diagnosis of PComAAs was based on following radiographic images: three dimensional CTA and whole brain digital subtraction angiogram. The demographic data of each case are summarized in (Table 1). The parameters that considered for analysis were: the initial degree of TNP, age of patients, the size of the aneurism (maximal transverse diameter of the aneurysm sac), and the clinical presentation (ptosis, diplopia and, ophthalmoplegia), the presence or absence of subarachnoid hemorrhage, follow up periods.

The clinical outcomes of TNP in the follow up category were divided into 2 groups with early being before 12 months and late being after 12 months for both the procedures.

Similarly, complete TNP was defined as patients presenting with any of the complications of diplopia, ptosis of upper eye lid, ophthalmoplegia (impairment of medial, upward and downward gaze), and pupillary dysfunction. Absences of any of these clinical features were labeled as cases with incomplete TNP. Angiographic follow-up was performed using Digital Subtraction Angiography (DSA) in all patients so as to evaluate the prolapsed of coils and any recanalization of treated PComAAs. Finally, based on the clinical findings, the cases were stratified into 4 different groups with common features, for patients that underwent EVC as well as SC. A “complete recovery” group comprised of cases that had no diplopia in all direction of gazes, complete resolution of ptosis and partial or complete recovery of pupillary function. Similarly, “incomplete recovery” group was composed of patients that had residual ptosis, residual diplopia in medial, upward, downward gaze with or without normal primary gaze, and pupillary dysfunction. The third “stable” group was the ones that received no benefit from coiling or clipping and finally the “worse” group comprised of patients that had deteriorated in terms of clinical outcomes with the two procedures.

## Literature search methodology

PubMed database was searched and all the articles published between 2002 and 2014 (Table 2) were considered. The key words used for the search were-Posterior communicating artery, aneurysm, third nerve palsy, surgical clipping, and endovascular coiling. This data was then designed as descriptive rather than absolute.

## Data analysis

The data were presented as mean  $\pm$  standard deviation and median with inter-quartile range (25<sup>th</sup> and 75<sup>th</sup> percentage) for continuous variables, depending upon normality of distribution. Categorical variables were represented by count and percentages. We did not analyze data statistically to find out significant p- value due to limited number of cases.

## Results

### Surgical series

Five patients aged range 50 to 69 years old (mean age, 58  $\pm$  7.9

**Table 2:** Summary of existing literature of TNP recovery following (a) surgical clipping and (b) endovascular coiling. (a) Reported outcomes for TNP after surgical clipping.

Author, year	Patients	Complete	Incomplete	Stable	Worse
	NO	Recovery	Recovery	NO (%)	NO (%)
		NO (%)	NO (%)		
Yanaka et al. (2003)	16	7(43.8%)	6(37.5%)	2(12%)	1(6.3%)
Chen et al. (2006)	7	6(85.7%)	1(14.3%)	0	0
Ahn et al. (2006)	7	3(42.9%)	4(57.1%)	0	0
Yang et al. (2008)	74	67(90.5%)	7(9.5%)	0	0
Yerramneni et al. (2010)	13	10(76.9%)	3(23.1%)	0	0
Javalkar et al. (2010)	26	15(57.7%)	5(19.2%)	6(23.1%)	0
Park et al. (2011)	13	12(92.3%)	1(7.7%)	0	0
Chang et al. (2013)	10	7(70%)	3(30%)	0	0
Patel K et al. (2014)	9	5(55.6%)	4(44.4%)	0	0
Brigui et al. (2014)	7	6(85.9%)	1(11.1%)	0	0
Total	182	138(76%)	35(19.2%)	8(4.3%)	1(0.5%)

(b) Reported outcomes for TNP palsy after endovascular coiling.

Author, year	Patients	Complete	Incomplete	Stable	Worse
	Number	Recovery NO (%)	Recovery NO (%)	NO (%)	NO (%)
Inamasu et al. (2002)	1	1(100%)	0	0	0
Kim et al. (2003)	3	0	3(100%)	0	0
Stiebel et al. (2003)	11	0	11(100%)	0	0
Chen et al. (2006)	6	2(33.3%)	4(66.7%)	0	0
Ahn et al. (2006)	10	6(60%)	3(30%)	1(10%)	0
Mansour et al. (2007)	7	6(85.7%)	0	1(14.3%)	0
Hanse et al. (2008)	21	8(38%)	11(52.3%)	2(9.7%)	0
Kassis et al. (2009)	21	7(33.3%)	12(57.1%)	1(4.8%)	0
Santillan et al. (2010)	11	7(63.6%)	2(18.2%)	2(18.2%)	0
Ko and Kim (2011)	10	7(70%)	1(10%)	2(20%)	0
Zhang et al. (2011)	13	7(53.8%)	6(46.2%)	0	0
chalouhi et al. (2013)	37	14(37.8%)	19(51.4%)	4(10.8%)	0
Brigui et al. (2014)	14	11(78.8%)	2(14.3%)	NA	NA
Patel k et al. (2014)	9	6(66.7%)	3(33.3%)	0	0
Total	174	78(44.8%)	77(44.2%)	13(7.5%)	0

years) were treated with clipping of aneurysmal neck via pterional approach. Two patients (2/5; 40%) presented with complete TNP and three patients (3/5; 60%) presented with incomplete TNP. Duration of symptoms to surgery ranged from 3 to 35 days (mean, 14.6 ± 13 days). Mean duration of follow-up in surgical group was 17.4 ± 11.7 months ranging from 6-36 months. All patients (5/5, 100%) patients showed complete resolution of TNP.

### Endovascular series

It was found that seven patients with an age range of 42 to 71 (mean age, 55 ± 10.2 years) were treated using endovascular detachable coiling. Five patients had presented with complete TNP (5/7; 71.4%) and two with incomplete TNP (2/7; 28.6%). The duration of symptoms to embolisation ranged from 5 to 30 days (mean, 19.8 ± 10.2 days). The mean duration of follow-up in endovascular group was 21.2 ± 17.3 months (ranging from 3-50 months). Four patients (4/7; 57%) demonstrated complete resolution of TNP and three

patients (3/7; 43%) showed incomplete resolution of TNP (Table 1). Post-operative CT scans did not show any intracranial hemorrhage or ischemia and no any sever complication was found in both treatment modalities as well as angiographic during follow- up period did not show any re-canalization.

### Published Research

Published literature search reported 174 patients of PComAAs associated with third nerve palsy undergoing endovascular coiling and 182 patients undergoing surgical clipping from 2002 to 2014 as shown in Table 2. Endovascular groups showed complete recovery of third nerve palsy in 44.8%, incomplete recovery of TNP in 44.2%. Surgical groups showed complete recovery in 76%, incomplete recovery in 19.2% as shown in Table 2 and Figure 1.

### Discussion

Intracranial aneurysms has been found to be one of the most

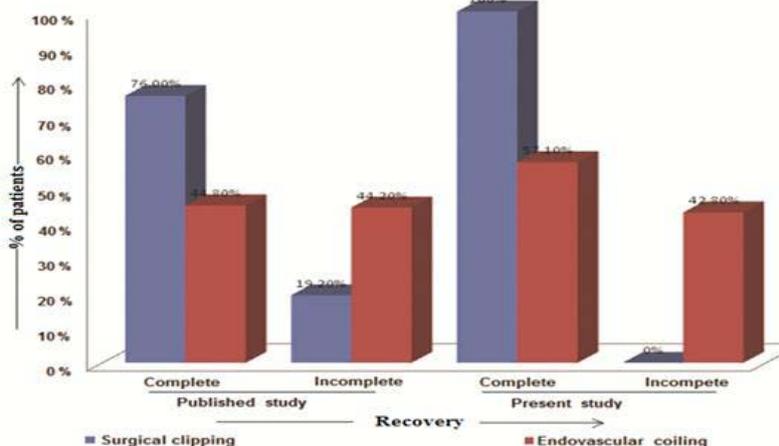


Figure 1: Shows rate of third nerve palsy recovery in patients who underwent surgical and endovascular therapy in published research and present study.

Table 3: Co-relation between variables and complete recovery of TNP after surgical clipping and endovascular coiling.

Variables	Complete recovery of TNP	
	Clipping, NO (%)	Coiling, NO (%)
<b>Age:</b>		
<50 year	1(100%)	2(67%)
>50 year	4(100%)	2(50%)
<b>Symptoms to surgery days:</b>		
<10 days	3(100%)	3(100%)
10-20 days	1(100%)	1(50%)
>20 days	1(100%)	1(33%)
<b>Size of aneurysm (mm):</b>		
<5mm	4(100%)	2(67%)
>5mm	1(100%)	2(50%)
<b>SAH:</b>		
Yes	5(100%)	3(50%)
No	0(0.0%)	1(100%)
<b>TNP:</b>		
Complete	2(100%)	2(40%)
Incomplete	3(100%)	3(100%)
<b>Follow up period ( months):</b>		
<12 months	3(100%)	0(0.0%)
>12 months	2(100%)	4(100%)

common cause of clinical presentation of third nerve palsy [15] and the most common location has been found to be posterior communicating artery [12,16-18]. Due to close anatomical proximity of posterior communicating artery to third cranial nerve, the incidence of third nerve palsy in patients induced by posterior communicating artery aneurysms has been reported to vary from 30% - 40% [19-23]. The best treatment modality for management of PComAAs associated with TNP is still debated although Chen PR et al. [9] and Güresir et al. [10] have considered beneficial results of surgical clipping by decompressing the mass effect of aneurysm and allowing better nerve recovery. The first surgical series that included 55 patients of aneurysmal third nerve palsy was published in 1947 by Jefferson et al. [24]. For many decades, surgical clipping has been the gold standard treatment modality for management of PcomAAs

associated with TNP. However, one of the first endovascular series, which included report of three patients embolized successfully, was published in 1999 [5]. Moreover, larger studies have also been conducted that have also reported improvement of TNP after coiling [25-27]. With these different studies, both of the procedures are seen to be successful on their own and with their own claim for superior modality of treatment of PcomAA. Outcomes of third nerve palsy after endovascular coiling and surgical clipping have been compared in few study groups. Ahn et al. [8] compared ten endovascular coiling patients with seven surgical clipping patients and reported no significant difference in recovery of third nerve palsy in two groups. A recent retrospective single-centre study by Brigui et al. [28] and Patel et al. [29] compared coiling versus clipping and came to the same conclusions. In other retrospective study, Chen PR et al. [9] reported

complete recovery in 6 of 7 patients undergoing surgical clipping versus 2 of 6 patients undergoing endovascular coiling versus and concluded that surgical clipping is superior to endovascular coiling. Güresir et al. [10] reported significantly better resolution of TNP after surgical clipping with complete resolution occurring in 4 of 4 versus only 3 of 7 endovascular groups. Güresir et al. [10] reported complete and incomplete recovery occurred in 32% (17/54) and 43% (23/54) patients respectively undergoing endovascular coiling versus 55% (72/132) and 38% (50/132) patients respectively undergoing surgical clipping in their systemic review of the literature regarding third nerve palsy induced by PComAAs. Our study showed that complete recovery in 57.1% (4/7) patients undergoing endovascular coiling versus 100% (5/5) patients undergoing surgical clipping (Figure 1). When the results of all endovascular and surgical groups including our own small case series were combined, complete and incomplete TNP recovery was found to be 45.3% (82/181) and 44.2% (80/181) versus 76.5% (143/187) and 18.7% (35/187). On the basis of these results, we consider that surgical therapy is highly effective and efficient in promoting third nerve recovery in patients with PcomAAs.

The degree of direct mechanical compression by PcomAAs, nerve irritation by hemorrhagic blood or pulsation of PComAAs aneurysm on the oculomotor nerve are considered to be the main pathophysiological events determining complete or incomplete recovery of TNP. It is believed that surgical clipping relieves both mass effect and pulsatility of aneurysmal sac, but coils embolization relieves only irritation induced by aneurysm pulsatility because itself causes the mass effect. Birchall et al. [5] and Hanse et al. [25] reported that loss or decrease of arterial pulsation by coils embolization may be more important for early resolution of third nerve palsy than decompression of third nerve palsy from aneurysmal sac by clipping [5,25]. In the present study, our study showed that there is one early (<12 month) resolution of third nerve palsy out of five patient in surgical group, but there is no any early (<12month) resolution of third nerve palsy in endovascular group (Table 3). And also, function of parasympathetic fiber running in the dorso-medial aspect of third nerve [30] which reflects the pupillary reaction, usually is first ocular sign to recover [3,17,19,31]. we also found that first ocular sign subsided was pupillary function with mean recovery of 3.2 days in surgical group versus mean recovery of 4.6 days in endovascular group. We also aspirated all the aneurysm after clipping to decompress the third nerve that causes shrinkage and thromboses of aneurysm even if Lanzino et al. [32] reported there is no association between TNP recovery and nerve decompression. This study shows that decompression of third nerve by surgical clipping results earlier recovery from symptoms than endovascular coiling.

Regardless of the treatment modalities, we consider that time interval between onset of palsy and surgery is the most important recovering factor. Botterel et al. [19] and Soni et al. [3] reported complete recovery in third nerve palsy only when treatments were performed within 10 days from onset of third nerve palsy. Even cases are limited; our study found the best results in patients undergoing treatment within 10 days than undergoing treatment after 20 days in both treatment modalities. So, we agree with their conclusion. It is believed that the third nerve initially suffers minor damage such as neurapraxia with reversible conduction block [25]. Treatments during this stage provide excellent results with rapid recovery. But, probability for complete recovery are minimal when third nerve palsy has already existed for few weeks or months, because third nerve probably has undergone sever axonal degeneration.

In the literature, various factors have been found to influence TNP recovery including the degree of TNP [9,10,17,25,33,34], interval between symptoms to surgery [5,6,9,17,20,31,35] subarachnoid hemorrhage [34,36,37], patients age and cardiovascular risk factors [8]. In the present study, we found that incomplete TNP at presentation results complete recovery in 100% (3/3) patients and 100% (2/2) patients undergoing endovascular coiling versus surgical clipping. So, our results are consistent with results of Zhang et al. [34], who reported a rate of complete recovery as high as 100% in patients presenting with incomplete TNP versus only 25% in those patients presenting with complete TNP. Likewise, Chang et al. [11] also reported that TNP recovered completely in 6 of 8 patients with incomplete TNP vs.1/2 with complete TNP.

Patient's age, size of aneurysms were found to have no influence on recovery of third nerve palsy [14,24]. Chen PR et al. [9] and watanabe A et al. [38] reported that there was no influence of SAH in recovery of third nerve palsy in their clipping series. But, positive influence of SAH in recovery of TNP was reported by Mansour et al. [37] and Kassis et al. [36] in both of their clipping series and Fujiwara et al. [12] did not find any relation between presence or absence of SAH and recovery of TNP after surgery. Hen et al. [9] and Watanabe et al. [38] have also same results with Fujiwara et al. [12]. In the present study, we found both complete recovery in 50% (3/6) and 100% (4/4) patients with SAH who underwent endovascular and surgical therapy respectively. We believe that blood clots irritate the nerve and induce third nerve injury rather than direct mass effects by PComAAs [36]. We think that earlier re-absorption of blood clot in patients with SAH may provide more probability of complete recovery of minor injured third nerve. The length of follow –period that was found to influence better recovery rates with both endovascular and surgical therapy. Even though it was not significant statistically, we found that complete recovery in 100% (4/4) patients undergoing endovascular therapy versus 100% (3/3) patients undergoing surgical therapy where follow-up time was longer (>12 month). It is believed that sever degenerated third nerve by PComAAs takes longer time to recover regardless of treatment modalities. Our results is controversial with those of Chen PR et al. [9] and Hanse et al. [25], who reported that TNP recovery occurs invariably within 6 and 12 month following treatment respectively. And also, Kassis et al. [36] also reported one patient completely recovered in 20 months after treatment. We consider that exact role of recovery time and mechanism of healing of degenerated nerve need to be investigated further.

## Conclusion

Our findings demonstrate that both procedures of EVC and SC, demonstrates improvement of third nerve palsy induced by PComAA without any sever complication. Similarly, complete recovery of TNP is more likely associated with incomplete third nerve palsy compared to complete third nerve palsy initially. Similarly, early therapeutic management (<10 days) institution, results in complete recovery of third nerve palsy. It was also found that longer follow-up period (>12 months) was also shown to have positive influence, this however has not been well documented in any previous studies and needs further validation of our findings. The decrease of mass effect by surgical clipping may affect early recovery from sign/symptoms of third nerve palsy than endovascular coiling. Large prospective randomized studies with long follow-up are required to conclude the role of endovascular and surgical therapy for management of third nerve palsy induced by posterior communicating artery aneurysm.

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