ORIGINAL ARTICLE

Third Nerve Palsy Due to Intracranial Aneurysms and Recovery after Endovascular Coiling

Michelle Kameda-Smith, Akshat Pai, Youngkyung Jung, Dure Khan, Ashley A. Adile, Katrina Hui, Amanda Martyniuk, Ramiro Larrazabal, Almunder Algird, Paula Klurfan, Thorsteinn Gunnarsson, Forough Farrokhyar, Brian van Adel

ABSTRACT: ***Introduction:*** The modality of treatment of third nerve palsy (TNP) associated with intracranial aneurysms remains controversial. While treatment varies with the location of the aneurysm, microsurgical clipping of PComm aneurysms has generally been the traditional choice, with endovascular coiling emerging as a reasonable alternative. ***Methods:*** Patients with TNP due to an intracranial aneurysm who subsequently underwent treatment at a mid-sized Canadian neurosurgical center over a 15-year period (2003–2018) were examined. ***Results:*** A total of 616 intracranial aneurysms in 538 patients were treated; the majority underwent endovascular coiling with only 24 patients treated with surgical clipping. Only 37 patients (6.9%) presented with either a partial or complete TNP and underwent endovascular embolization; of these, 17 presented with a SAH secondary to intracranial aneurysm rupture. Aneurysms associated with TNP included PComm (64.9%), terminal ICA (29.7%), proximal MCA (2.7%), and basilar tip (2.7%) aneurysms. In general, smaller aneurysms and earlier treatment were provided for patients for ruptured aneurysms with a shorter mean interval to TNP recovery. In the endovascularly treated cohort initially presenting with TNP, seven presented with a complete TNP and the remaining were partial TNPs. TNP resolved completely in 20 patients (55.1%) and partially in 10 patients (27.0%). Neither time to coiling nor SAH at presentation were significantly associated with the recovery status of TNP. ***Conclusion:*** Endovascular coil embolization is a viable treatment modality for patients presenting with an associated cranial nerve palsy.

RÉSUMÉ : Paralysie du troisième nerf en raison d'un anévrisme intracrânien et rétablissement après la pose d'une bobine endovasculaire. ***Introduction*** : Les modalités de traitement de la paralysie du troisième nerf (PTN) associée aux anévrismes intracrâniens demeurent controversées. Bien que les traitements varient selon l'emplacement de l'anévrisme, le clippage (ou *clipping*) microchirurgical des anévrismes affectant les artères communicantes postérieures (ACP) est généralement apparu comme le choix le plus courant, la pose d'une bobine endovasculaire (*endovascular coiling*) ayant aussi émergé comme une option raisonnable. ***Méthodes*** : Nous nous sommes penchés sur les cas de patients atteints de PTN en raison d'un anévrisme intracrânien qui ont ensuite bénéficié d'un traitement dans un centre neurochirurgical canadien de taille moyenne, et ce, sur une période de 15 ans (2003 à 2018). ***Résultats*** : Au total, 616 anévrismes intracrâniens ayant affecté 538 patients ont été traités. La majorité d'entre eux ont bénéficié de la pose d'une bobine endovasculaire alors que seulement 24 patients ont été traités par clippage microchirurgical. Fait à noter, seuls 37 patients (6,9 %) ont donné à voir une PTN partielle ou totale et ont bénéficié d'une embolisation endovasculaire. De ce nombre, 17 ont donné à voir une hémorragie sous-arachnoïdienne (HSA) consécutive à une rupture d'anévrisme intracrânien. Les anévrismes associés à la PTN ont inclus les ACP (64,9 %), l'artère carotide interne terminale (29,7%), l'artère cérébrale moyenne proximale (2,7 %) et la pointe (*tip*) de l'artère basilaire (2,7 %). En général, un traitement plus précoce a été proposé aux patients victimes de plus petites ruptures d'anévrisme associées à des délais moyens de rétablissement plus courts à la suite d'une PTN. Dans la cohorte de patients ayant donné à voir des signes de PTN et ayant bénéficié d'un traitement endovasculaire, 7 d'entre eux étaient atteints d'une PTN complète alors que les autres étaient atteints d'une PTN partielle. Les signes de PTN ont fini par disparaître complètement chez 20 patients (55,1 %) et partiellement chez 10 autres (27,0 %). Ni les délais dans la pose d'une bobine endovasculaire ni des signes de HSA au moment de consulter n'ont été notablement associés au processus de rétablissement à la suite d'une PTN. ***Conclusion*** : En somme, il ressort que l'embolisation endovasculaire au moyen de bobines est une modalité de traitement viable pour les patients présentant une paralysie des nerfs crâniens.

Keywords: Third nerve palsy, Oculomotor palsy, Intracranial aneurysms, Endovascular coiling

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From the Department of Surgery, McMaster University, Hamilton, ON, Canada (MK-S, AP, YJ, DK, AAA, KH, AM, RL, AA, FF, BvA); Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada (MK-S, AM, RL, AA, FF, BvA); Department of Neurosurgery, Sahlgrenska University Hospital, Gothenburg, Sweden (DK, PK); Department of Neurosurgery, Linkoping University Hospital, Linkoping, Sweden (AAA, TG); and Biochemistry, McMaster University, Hamilton, ON, Canada (FF)

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Correspondence to: Michelle Kameda-Smith, Neurosurgery Resident Physician, Department of Surgery, Division of Neurosurgery, Hamilton, General Hospital, 237 Barton Street East, Hamilton, Ontario L8L 2X2, Canada. Email: michellekamedasmith@gmail.com

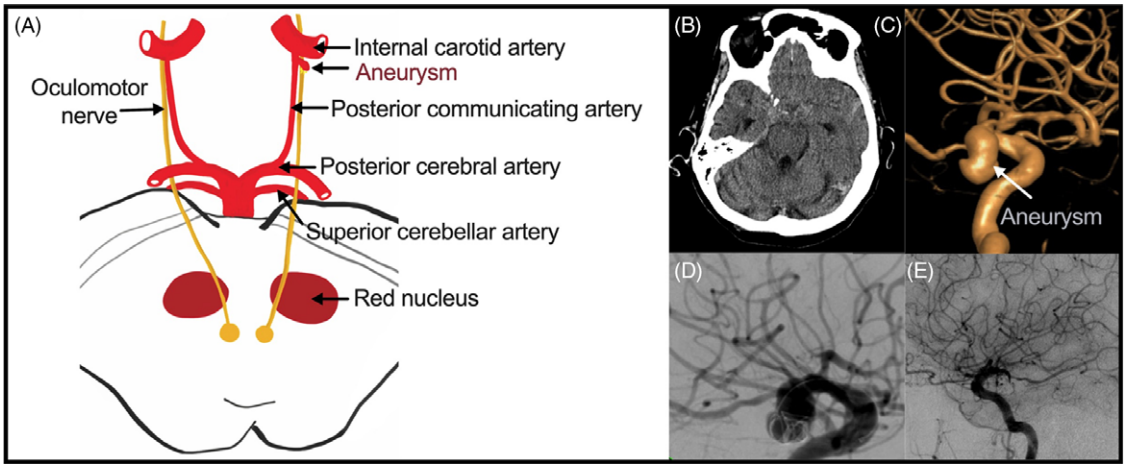

Figure 1: *Intracranial aneurysms causing TNP. (A) Anatomical relationship between the oculomotor nerve and the circle of Willis and its branches. (B) Right-sided PComm aneurysm (C) Volume-rendered image of a PComm aneurysm. (D) DSA image demonstrating a coiling of PComm aneurysm. (E) Post-coiling contrast run demonstrating obliteration of a PComm aneurysm with coil embolization.*

Introduction

Third nerve palsies (TNP), characterized by diplopia, ptosis, ophthalmoplegia, and pupillary dysfunction, is reported to be the most common clinical presentation of posterior communicating artery aneurysms. The risk of TNP in PComm aneurysms is as high as 34–56%[1] The pathophysiology of this phenomenon includes (1) the compressive effect of the aneurysmal outgrowth on the oculomotor nerve and (2) the constant disruptive effect of aneurysmal pulsatility on adjacent cranial nerves. Generally, intracranial saccular aneurysms, if left untreated, can progress over time and may acutely rupture, compromising the quality of life for approximately 35% of patients.[2] Management of either ruptured or unruptured saccular intracranial aneurysms includes open surgical clipping or endovascular repair (i.e. endosaccular and/or endoluminal approaches). Surgical clipping is believed to alleviate the direct mass effect of aneurysms by obliterating the vascular defect with the added capability of reducing the mass effect on adjacent structures by decompressing the aneurysmal mass. Endovascular approaches such as coiling promote progressive thrombosis of the aneurysm sac, thereby achieving decompression by preventing pulsatile movement within the fundus. While open surgical clipping exposes the patient to the risks associated with craniotomy, coiling has been associated with its own inherent risks, namely the potential to worsen the compressive effects of the aneurysm. Furthermore, arterial pulsatility, primarily at the aneurysmal neck, may result in failure of aneurysm exclusion from the circulation and could potentially lead to coil compaction, aneurysm regrowth, and re-rupture.[3]

The vast majority of patients presenting with a TNP are more likely to have a PComm aneurysm, however, saccular aneurysms involving the basilar apex, SCA, and supraclinoid ICA have also been described in patients presenting with a TNP.[4–8] Furthermore, other aneurysm-associated cranial neuropathies have been reported included compression of the optic nerve and trochlear nerve.[6,9] The etiology and pathophysiology underlying TNP secondary to PComm aneurysms has not been clearly elucidated, contributing to the uncertainty in favoring one treatment modality over another. The PComm accompanies the oculomotor nerve through its cisternal course; as such, it is thought posterolateral PComm aneurysms cause TNP secondary to a mass effect (Figure 1).[10] In fact, the angioarchitecture of the aneurysm has been observed to dictate the increased chance of a complete TNP, especially in aneurysms greater than 7mm in size.[11] However, along its course, the oculomotor nerve passes through and between the posterior cerebral artery (PCA) and the superior cerebellar artery (SCA). Recent reports of successful TNP resolution with endovascular coiling of saccular aneurysms lend support to the pathophysiology of TNP secondary to the transmission of arterial pulsatility, or nerve irritation with edema, rather than an isolated mass effect.[11–13]

In this retrospective, single-center study, we analyzed all intracranial aneurysms associated with partial or complete TNP in order to assess the relationship between treatment modality, TNP resolution, and associated predictive factors and compare our findings to the available literature.

Methods

A retrospective cohort study was conducted at a mid-sized Canadian neurosurgical center over a 15-year period (2003–2018). The study was approved by the local university ethics committee. Data were extracted from electronic medical records (Meditech and Sovera) and the Picture Archives and Communication Systems (PACS). To maximize our sample size, all consecutive patients were admitted to the hospital with a Computed Tomography Angiogram (CTA), Magnetic Resonance Angiogram (MRA) or Digitally Subtracted Angiogram (DSA) confirmed intracranial aneurysm who underwent a neurointerventional/neurosurgical procedure by the senior authors were included in the study. Both elective and emergent (i.e. SAH) cases were included for analysis. Complete TNP was defined prior to data extraction as complete ptosis, extraocular muscle palsy, and mydriasis. Partial TNP was any spectrum of deficits that were attributable to the oculomotor nerve that did not comprise the triad of complete TNP. Data were collected using clinical notes from electronic health records at our institution that included copies of all paper charts.

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Table 1: Characteristics of aneurysms associated with TNP undergoing endovascular embolization ($n = 37$)

	N (%)
Age	**Mean 60.1 (SD 11.9)**
Gender	
Male	3 (8.1)
Female	34 (89.4)
Presence of SAH	
Yes	17 (45.9)
No	20 (52.6)
Size of aneurysm	**Mean 9.48 (SD 7.2)**
Location of aneurysm	
Basilar apex	1 (2.7)
ICA	11 (29.7)
MCA	1 (2.7)
PComm	24 (64.9)
Side of aneurysm	
Left	11 (29.7)
Right	25 (67.6)
Midline	1 (2.7)
Pre-intervention TNP status	
Partial TNP	30 (78.9)
Complete TNP	7 (18.9)
Surgical intervention	
Coiling	37 (97.4)

Statistical Analysis

Categorical variables were reported using counts and proportions and compared using the χ^2 or Fisher's test. Continuous variables were reported as mean (SD) and was compared using the independent samples *t*-test or Mann–Whitney U test as appropriate. For pre and post-intervention analysis, McNemar's test was employed for paired data. The level of significance was set at 0.05. SPSS software (www.IBM.com) was used for the analysis.

Results

A total of 538 adult patients underwent treatment for at least one intracranial aneurysm at the Hamilton General Hospital between 2003 and 2018. Table 1 summarizes the TNP cohort showing the 538 patients undergoing 574 treatments with only 37 (6.9%) presenting with clinical signs of a partial or complete TNP. The mean age at presentation of intracranial aneurysm-associated TNP-treated endovascularly was 60.1 (SD 11.9) years, the majority were female (91.8%) with half presenting after a subarachnoid hemorrhage (45.9%). The mean size of aneurysm was 9.48 (SD 7.2, range 2.8–31.8) mm. Over half of the cohort harbored a PComm aneurysm-associated TNP (64.9%) but other locations included ICA (29.7%), MCA (2.7%), and basilar apex (2.7%), with 67.6% of TNP-associated aneurysms located on the right side. The number of patients diagnosed with partial TNP was nearly threefold higher than those presenting with a complete TNP.

Almost the entire cohort of TNP patients was treated with endovascular coiling, with only one patient treated with surgical clipping. Table 2 details the proportion of TNP involvement and surgical intervention received. All 30 patients presenting with a partial TNP underwent endovascular embolization. By contrast, of the eight patients presenting with a complete TNP, one patient underwent surgical clipping while the remaining 7 (87.5%) were treated with coiling (Figure 2). Dichotomizing the SAH and unruptured aneurysm cohorts, the average size of aneurysm (7.07mm *vs.* 12.7mm), time to presentation (2.5 days *vs.* 44 days), and time to improvement (65 *vs.* 198 days) were all higher in the unruptured group. As only one patient with a TNP was surgically clipped with complete recovery of the cranial nerve function, no clinical correlation of TNP recovery and aneurysm procedure was feasible. Given the small cohort, a correlational analysis of time to presentation and recovery was not possible but a trend toward lower likelihood of recovery of TNP with a prolonged time to presentation and time to operative procedure was observed. Table 3 summarizes the trend of the clinical course of the TNP after the intervention. Furthermore, in keeping with previous observations, patients presenting with SAH were less likely to experience TNP recovery after coiling when compared to those presenting with an unruptured aneurysm. In our endovascularly treated cohort, 5/7 (71.4%), 4/10 (40%), and 8/20 (42.9%) of patients with no, partial, and complete TNP recovery, respectively, presented with SAH.

With respect to the location of aneurysm and TNP recovery, a similar proportion of TNP secondary to ICA or PComm recovered either partially or completely (Table 3). However, a higher proportion of TNP that did not experience any recovery was secondary to PComm (24% *vs.* 9.1%). Location of aneurysm was not significantly correlated with TNP recovery (p=0.499). Despite the concerns of mass effect of very large aneurysms, no significant correlation was observed between aneurysm size (i.e. aneurysms ≤10mm, 10–19.9mm, ≥20mm) and TNP recovery ($p = 0.175$, Fisher's exact) despite imaging findings (Table 4).

Discussion

Oculomotor palsy associated with an intracranial aneurysm was first surgically treated by Walter E Dandy in 1937 with complete resolution of the patient's "pea-sized" mesially projected ICA aneurysm-associated cranial nerve palsy after 7 months.[14] While surgical clipping was historically the mainstay of intracranial aneurysm management, there have been remarkable advances in endovascular approaches since the publication of the International Subarachnoid Aneurysm Trial (ISAT), resulting in a significant reduction in the frequency of surgical clipping. While the exact pathomechanism of aneurysm-associated TNP has not been fully elucidated, our single-center experience suggests a role for the pulsatility theory, as we observed a trend toward resolution of TNP of both PComm and non-PComm aneurysms after endovascular aneurysm coiling, especially for cases without accompanying SAH (Table 2). As there was only one patient presenting with a TNP with subsequent clipping of the associated aneurysm, we were unfortunately unable to compare the two modalities for the efficacy of TNP recovery after treatment (i.e. coiling *vs.* clipping). Despite current limitations in published data describing the safety and

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Table 2: Intracranial aneurysm and TNP status

TNP-associated aneurysm location n(%)				
Location of aneurysm	**No TNP ($n = 578$)**	**Partial TNP ($n = 30$)**	**Complete TNP ($n = 8$)**	**Total TNP N (%)**
ACA	16 (100.0)	–	–	–
AComm	181 (100.0)	–	–	–
AICA	1 (100.0)	–	–	–
Basilar apex	81 (96.4)	3 (3.6)	–	3 (2.6)
ICA	94 (91.3)	9 (8.7)	–	9 (23.7)
MCA	60 (98.4)	1 (1.6)	–	1 (2.6)
PComm	109 (81.3)	25 (18.6)	8 (6.0)	25 (65.7)
PCA	3 (100.0)	–	–	–
PICA	26 (100.0)	–	–	–
SCA	7 (100.0)	–	–	–
p-value	<0.001			

TNP dichotomized to SAH presentation		
	SAH	**No SAH**
Mean age	59.5 years (36–83 years)	60.1 years (37–80 years)
Mean size of aneurysm	7.1 mm (2.8–18 mm)	12.7 mm (2.8–31.8 mm)
Mean pre-symptomatic interval	2.5 days (0–3 days)	44 days (0–59 days)
Mean time to improvement	65 days (1–415 days)	198 days (2–602 days)
Mean total FU time	649.7 days (10–1789 days)	1082.2 days (33–3080 days)
% Alive	94.4%	100%

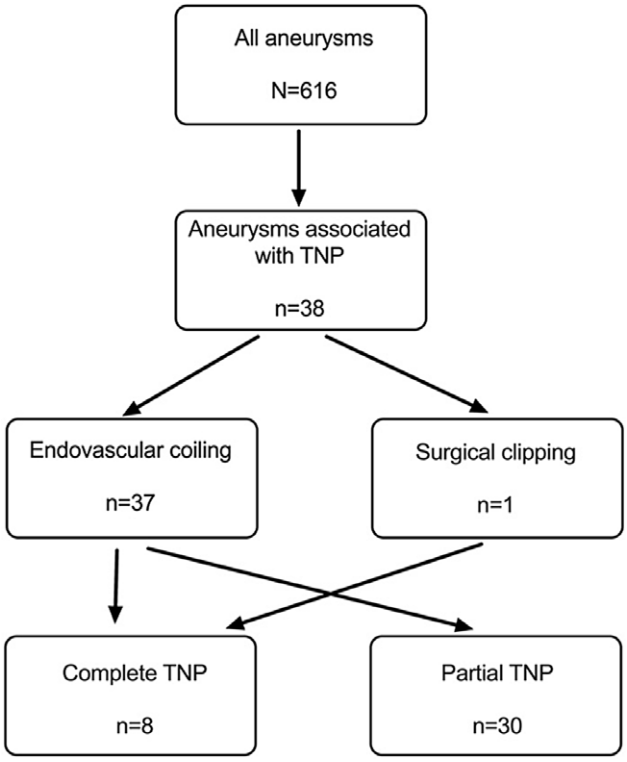

Figure 2: *Flow chart of patients with TNP from a single-center cohort.*

efficacy of endovascular coiling of an aneurysm causing a cranial nerve palsy, there seems to be a general trend toward resolution suggesting the coil mass does not cause a permanent mass effect on the oculomotor nerve[6,8,9,11–13,15–22] (Table 3). Further technological advances have broadened endovascular treatment options with endoluminal and endosaccular devices for treating intracranial aneurysms with complex angioarchitecture, thus the trend toward endovascular management will continue to evolve, and in many centers, it has surpassed open surgical treatment.

The historical evidence for clipping an intracranial aneurysm with associated cranial nerve palsy has almost exclusively been small, retrospective single-center studies, spanning over several years with varying clinician skills and availability of treatment adjuncts (Table 3). Gaberel *et al*. (2016) demonstrated no significant difference in a meta-analysis of 297 patients (RR = 1.48, 95% confidence interval 0.95–2.29, $p = 0.08$), however, these results are limited by the inconsistent follow-up times across the included studies.[23] In a subsequent meta-analysis by Zheng *et al.* that included two additional studies, there was a significant advantage of clipping in achieving full TNP recovery (OR = 4.44, CI interval 1.66–11.84, $p = 0.0003$).[10] The authors in this meta-analysis concluded clipping is associated with a greater rate of total recovery within a subgroup analysis of ruptured aneurysms – the advantage was attributed to the additional mass effect placed on the oculomotor nerve by the hematoma which was decompressed at the time of surgical clipping.[10,23,24] While there are concerns that potential nerve traction could worsen TNP

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Table 3: Intracranial aneurysm and TNP status and clinical outcome after endovascular embolization

TNP-associated aneurysm recovery after treatment n (%)			
Location of aneurysm	**None ($n = 7$)**	**Partial ($n = 10$)**	**Complete ($n = 20$)**
Basilar tip	–	1 (100.0)	–
ICA	1 (9.1)	4 (36.4)	6 (54.5)
MCA	–	–	1 (100.0)
PComm	6 (24.0)	5 (20.0)	13 (54.2)
p-value	0.499	–	–

TNP-associated aneurysm and recovery according to the intervention received		
TNP cohort details	**n (%)**	**Intervention**
TNP involvement		**Coiling ($n = 37$)**
None	578 (93.8)	555 (96.0)
Partial	30 (4.9)	30 (100.0)
Complete	8 (1.3)	7 (87.5)
p-value	0.246	
TNP resolution		**Coiling ($n = 37$)**
None	7 (18.4)	7 (100.0)
Partial	10 (26.3)	10 (100.0)
Complete	21 (55.3)	20 (95.2)
p-value	0.660	
Time to operation (days)	47.05 (127.1)	24.5 (58.1)
Mean time to improvement (days)	164.85 (292.1)	245.2 (488.3)
Mean clinical FU	1054.12 (1000.0)	889.4 (823.8)

TNP-associated aneurysm and pre-symptomatic and preoperative interval and outcome				
	n	**Median duration**	**Minimum**	**Maximum**
Pre-symptomatic interval				
No resolution	7	0	0	30
Partial resolution	10	0	0	30
Complete resolution	20	0	0	59
Preoperative interval				
No resolution	7	1.0	0	4
Partial resolution	10	2.0	0	26
Complete resolution	20	2.0	0	252

during surgical clipping, the physical decompression of the aneurysmal sac has the added benefit of reducing both pulsatility and mass effect.[13] During surgery, nerve adhesions can also be lysed to potentially further improve TNP outcomes.

To further support our hypothesis of aneurysmal pulsatility-associated TNP, there are limited large-scale comparative studies analyzing differences in outcome between surgical the intervention (i.e. clipping *vs.* coiling) with no definitive conclusions drawn due to a small number of cases (Table 4). Overall, these studies suggest greater rates of TNP recovery with clipping compared to coiling.[12,17,18,24,25] However, in the absence of randomized trials, surgical clipping was and continues to be broadly regarded as a reliable approach to aneurysm-induced TNP with single-center rates of complete resolution ranging from 58.0% to 92.3%.[10,26] Predictably, patients selected for endovascular treatment tended to be poorer surgical candidates, as they were older and presented with more comorbidities (e.g. diabetes, hypertension, hyperlipidemia).[11] While our study cannot offer direct comparisons of these modalities, 20 of the 37 (54.1%) patients treated with endovascular coiling experienced complete TNP recovery. The rate of TNP recovery (81.6%) after coiling in our patients was similar to other published single-centered cases[6,8,11,15,17–22] and significantly greater than the 42.5% reported in the meta-analysis data.[10] The significance of timing in endovascular therapy also remains ambiguous, with suggestions that treatment within a week may improve recovery rates.[27] The duration of preoperative TNP is thought to be an important prognostic factor; in its initial stages, TNP secondary to vessel

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Table 4: Studies reviewing TNP recovery after intracranial aneurysm treatment

Author, Year (recruitment timeline)	Study design	N, Age, % male	Pre-op TNP status	TNP recovery	Clip	Coil	*p*-value	Aneurysm location	Complications		Time to treatment			Follow-up period		% unruptured		
									Clip	Coil	Clip	Coil	*p*-value	Clip	Coil	Clip	Coil	*p*-value
Ahn *et al.*, 2006[15] (2000-2004)	Single-centre, retrospective	17 52.6 0.0%	Any	Complete	3/7 (42.9%)	6/10 (60.0%)	0.69	PComm (17/17) (100%)	No response		3.1 ± 2.8 days		–	17.6 ± 10.9 months		17/17 (100%)		–
			Any	All	7/7 (100.0%)	9/10 (90.0%)	–		0/10 (0.0%)	1/10 (10.0%)								
Brigui *et al.*, 2014[16] (2004-2012)	Single-center, retrospective	21 53.1 23.1	All	Complete	6/7 (85.7%)***	8/14 (57.1%)***		PComm 21/21 (100.0%)	No response		6.8 days	8.0 ± 9.9 days	–	2.8 ± 2.8 years	3.8 ± 3.2 years	1/7 (14.3%)	4/14 (28.6%)	–
			Partial	Complete	2/2 (100%)	4/6 (66.7%)			0/7 (0.0%)	3/14 (21.4%)								
			Complete	Complete	3/4 (75.0%)	4/7 (57.1%)												
Chen *et al.*, 2006[17] (1999-2004)	Single-centre, retrospective	13 55.4 7.7%	All	Complete	6/7 (85.7%)	2/6 (33.3%)	–	PComm (13/13) (!00%)	–	–	17.9 days	6 days	–	41 months	14 months	4/7 (57.1%)	5/6 (83.3%)	0.3
			Partial	Complete	3/3 (100%)	2/3 (66.7%)												
			Complete	Complete	3/4 (75.0%)	0/3 (0%)												
Engelhardt *et al.*, 2015[9] (2000-2013)	Single-centre, retrospective	23 47.8 20.8%	All	Complete	7/9 (77.8%)	4/14 (28.6%)	0.03	Carotid siphon 1/23 (4.3%) Ophthalmic artery 1/23 (4.3%) AChoA 2/23 (8.7%) PComm 19/23 (82.6%)	No response		11 ± 9.4 days	25 ± 82.6 days	0.64	33.2 ± 36.9 months	58.8 ± 42.6 months	5/9 (55.6%)	12/14 (85.7%)	0.16
			All	All	9/9 (100.0%)	11/14 (78.6%)	0.25		0/9 (0.0%)	3/14 (21.4%);								
Güresir *et al.*, 2011[13] (1999-2008)	Single-centre, retrospective	11 - -	All	Complete	4/4 (100%)	3/7 (42.9%)	–	PComm (11/11) (100%)	–	–	–	–	–	–	–	1/4 (25.0%)	5/7 (71.4%)	–
			Partial	Complete	2/2 (100%)	–	–											
			Complete	Complete	2/2 (100.0%)	–	–											
Khan *et al.*, 2013[18] (2000-2013)	Single-centre, retrospective	11 52.2 5.9%	All	Complete	7/8 (87.5%)	4/9 (44.4%)	0.13	PComm (17/17) (!00%)	–	–	4 days	4 days	0.42	at least 6 months		5/8 (62.5%)	6/9 (66.7%)	0.97
Kwon *et al.*, 2009[25] (1999-2009)	Single-centre retrospective	63 - -	All	Complete	42/55 (76.4%)	3/8 (37.5%)	0.037	PComm (63/63) (100%)	–	–	–	–	–	–		–	–	–
Mino *et al.*, 2015[6] (2003-2014)	Single-centre, retrospective	17 64.8 5.9%	All	Complete	7/9 (77.8%)	5/8 (62.5%)	0.62	ICA-Ach (1/17) (5.8%) ICA-PComm (16/17) (94.1%)	–	–	18.2 ±17.6	3.5 ± 2.7	0.034	33 months		8/9 (88.9%)	6/8 (75.0%)	0.58
			All	All	9/9 (100%)	8/8 (100%)	–											
Nam *et al.*, 2010[19] (2004-2008)	Single-centre, retrospective	19 53.9 21.1%	Partial	Complete	3/3 (100%)	1/2 (50.0%)	–	PComm (14/19) (73.6%) Other (5/19) (26.3%)	No response		6.1 days	10.1 days	–	22 months		19/19 (100%)		–
			Complete	Complete	3/6 (50.0%)	5/8 (62.5%)	–		1/9 (11.1%)	3/10 (30.0%)								
			All	All	7/10 (70.0%)	8/10 (80.0%)	0.58											

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Table 4. *Continued*

Author, Year (recruitment timeline)	Study design	N, Age, % male	Pre-op TNP status	TNP recovery	Clip	Coil	*p*-value	Aneurysm location	Complications		Time to treatment			Follow-up period		% unruptured		
									Clip	Coil	Clip	Coil	*p*-value	Clip	Coil	Clip	Coil	*p*-value
Patel *et al.*, 2014[20] (2005-2009)	Single-centre, retrospective	18 60.0 16.7%	All	Complete	6/9 (66.7%)	5/9 (55.6%)	–	PComm 18/18 (100%)	–	–	2.22 ± 1.30	5.7 ± 6.0	–	–	–	2/9 (22.2%)	1/9 (11.1%)	–
			Partial	Complete	3/3 (100%)	2/2 (100 %)	–											
			Complete	Complete	3/6 (50.0%)	3/7 (42.9%)	–											
Schuss *et al.*, 2011[8] (1999-2009)	Single-centre, retrospective	20 49.8 25.0%	All	Complete	4/12 (33.3%)	3/8 (37.5%)	–	ACommA 5/20 (25.0%) ICA 15/20 (75.0%)	No response		5.3 ± 6.6 months	5.6 ± 7.8 months	–	25.7 ± 30.1	19.6 ± 34.4	20/20 (100.0%)		–
			All	All	9/12 (75.0%)	3/8 (37.5%)	0.20		3/11 (27.3%)	5/8 (62.5%)								
Signorelli *et al.*, 2020[12] (2006-2013)	Multi-centre, retrospective	55 53.7 40%	All	All	21/24 (87.5%)	19/31 (61.3%)	–	PComm 55/55 (100%)	No response		11 days		–	5 years	4 years	55/55 (100%)		–
									3/24 (12.5 %)	12/31 (38.7%)								
Su *et al.*, 2019[21] (2001-2013)	Single-centre, retrospective	39 49.0 38.5%	Partial	Complete	–	15/20 (75.0%)	–	PComm (39/39; 100%)	No response		22.5 ± 57.8 days		–	19.8 ± 9.0 months		39/39 (100%)		–
			Complete	Complete	–	3/19 (15.8%)	–		–	7/32 (21.95%)								
			All	Complete	–	18/39 (46.2%)	–											
			All	All	–	32/39 (82.1%)	–											
Tan *et al.*, 2015[22] (2008-2013)	Single-centre, retrospective	176 52.5 45.45%	All	Complete	123/132 (93.2%)	14/44 (31/8%)	–	PComm 176/176 (100.0%)	Vasospasm		11.18 ± 9.73	10.20 ± 8.51	0.55	at least 12 months		23/44 (52.3%)	64/132 (48.5%)	.66
			All	All	130/132 (98.5%)	30/44 (68.2%)	<0.001		6/132 (4.5%)	2/44 (4.5%)								
									Hydrocephalus									
									16/132 (12.1%)	9/44 (20.5%)								
									No response									
									2/132 (1.5%)	14/44 (31.8%)								
Yanaka *et al.*, 2003[7] (1985-2001)	Single-centre, retrospective	15 60.0 14.3%	All	Complete	7/14 (50.0%)	0/1 (0.0%)	–	Basilar (1/15) (6.7%) AChorA (2/15) (1.3%) PComm (12/15) (80.0%)	1/14 (7.1%)	0/1 (0.0%)	17.3 ± 16.8 days		–	25.7 ± 21.2 months		15/15 (100%)		–
Zhong *et al.*, 2019[11] (2012-2017)	Single-centre, retrospective	102 59.8 16.7%	All	Partial	20/39 (51.3%)	23/63 (36.5%)	0.31	PComm 102/102 (100.0%)	No response		17.10 ± 15.60	18.06 ± 34.07	0.87	35 months		27/39 (69.2%)	28/63 (44.4%)	0.024
			All	Complete	19/39 (48.7%)	38/63 (60.3%)	0.31		0/39 (0.0%)	2/63 (3.2%)								
									Hydrocephalus									
									0/39 (0.0%)	8/63 (12.7%)								

*Unreported for 11 patient.

**For ruptured aneurysms, no difference w/unruptured aneurysms.

***Pre-operative TNP status for 1 patient unknown.

conflict is likely a result of neuropraxia, while axonal degeneration and ischemia follow within months.[28] Furthermore, recovery is more likely with incomplete preoperative TNP ($p = 0.03$, OR = 4.2),[13] which may reflect the degree and subsequently reversibility of nerve damage. Of note, recovery rates with endovascular coiling in single-arm studies reported lower rates of TNP recovery when compared to surgical clipping (range 35.0–61.8%),[10,11,21] despite greater rates reported for shorter time to treatment, smaller aneurysm size, and stent use. This emphasizes the concept that recovery of TNP after aneurysm treatment is multifaceted and multiple factors including and not limited to the duration of TNP, size of aneurysm, past medical history, SAH presentation have to be taken into account when determining the safest and effective management modality. Our results are unexpected, given the longer mean time to treatment (47.1 days *vs.* 10.5 days) and larger mean aneurysm size (8.62 mm and 7.40 mm), with comparable age and follow-up period in the endovascularly treated group.

A significant limitation to meta-analyses of TNP recovery and intracranial aneurysm treatment, in general, is the definition of a complete and partial TNP. For example, one study considered complete TNP was the presence of concurrent ophthalmoplegia, ptosis, and diplopia,[9] while another study required ptosis, extraocular muscle palsy, and mydriasis for the same diagnosis.[13] Furthermore, individual studies were found to be highly variable in their time to treatment, and follow-up duration. Despite lower rates of TNP recovery in the literature, recovery nonetheless was observed in endovascularly coiled patients suggesting the pulsatility theory of neurapraxia may be the predominant pathomechanism by which the TNP develops as opposed to the compressive mass effect of the aneurysm on the oculomotor nerve. Specific to our study, the intrinsic selection bias inherent to all retrospective studies, there are several limitations to our findings (e.g. small number of clipped patients not facilitating a comparative analysis of TNP recovery, limited objective documentation of definition of TNP, and poor granularity of data regarding assessment of recovery).

Conclusion

In our intracranial aneurysm-associated TNP cohort, the vast majority of the patients in this study experienced either partial or complete TNP resolution (31/38; 81.6%), establishing the feasibility of the endovascular approach for TNP secondary to PComm aneurysms. With the fast pace of endovascular technological advances in aneurysm treatment and expanded use of flow diverters in addition to a consistent diagnostic definition of TNP is required to resolve the question of the efficacy of TNP resolution after endovascular coil embolization of TNP-associated intracranial aneurysms. Our findings support the role of pulsatility-induced neurapraxia of the oculomotor nerve causing aneurysm-induced TNP and provide evidence for the utility of endovascular repair of this entity.

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Disclosures

The authors have no conflicts of interest to declare.

Statement of Authorship

MKS, BvA, TG, PK, FF, RL, AA conceptualized the research question. MKS, AP, KH, AAA, YJ extracted that data from the databases. AM provided administrative support. MKS, BvA, AP, AAA, DK, FF analyzed and interpreted the data. MKS wrote the manuscript with significant revisions contributed by BvA, AP, YJ, and FF. BvA, TG, PK, and FF supervised the study. All authors reviewed the results and commented on the manuscript.

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