Outcome after Neuro-interventional Treatment of Intracranial Aneurysm (as a First Treatment Modality)

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Abstract: Endovascular treatment is widely applied as the first-line treatment for intracranial aneurysms and includes simple coiling (SC), stent-assisted coiling (SAC), flow diversion stent, and flow disruption stent. The present study is a retrospective cohort study performed in Imam Khomeini Hospital, Department of Neurovascular Intervention, between March 2016 and March 2021. A total number of 229 patients with intracranial aneurysms who underwent therapeutic intravascular interventions were enrolled, of which 89 were treated with SC, 111 with SAC, 25 with flow diversion stent, and 4 with flow disruption stent. The mean age of the subjects was 51.8±12.6 years, and 51.1% were male. Modified Raymond-Roy classification (MRRC) was used to define the occlusion outcome. The success rate, considered as Class I and Class II of MRRC at treatment time was 89% (94.4% in SC, and 84.7% in SAC), which was increased to 90.9% (94% in SC, 93% in SAC, 69.6% in flow diversion stenting, 100% in flow disruption) at 6-month follow-up, and 84.6% (80.8% in SC, 87.8% in SAC, 78.3% in flow diversion stenting, and 100% in flow disruption) at 12-month follow-up. The mean

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modified Rankin Scale (mRS) before the procedure was 0.05±0.26 which was increased to 0.22±0.76 after the procedure, 0.22±0.76 at 6 months, and 0.30±0.95 at 12 months (P<0.001). Similar to previous studies, the present study demonstrates that neurovascular intervention can treat ruptured aneurysms as the first therapeutic modality with favourable outcomes. A double-blind, randomized clinical trial is needed to eliminate the confounding factors and better demonstrate the outcome.

Introduction

Intracranial aneurysm is the abnormal bulging of the intracerebral vessels that stands the world's third most common cerebrovascular disease with an incidence of 3.6–6% of the population. Moreover, the intracranial aneurysms are the leading cause of subarachnoid hemorrhage (SAH) and are responsible for 22–25% of mortalities due to cerebrovascular diseases (Wardlaw and White, 2000; Juvela, 2003). The treatment options for a brain aneurysm include surgical treatment, e.g., clipping, wrapping, etc., and endovascular intervention. Endovascular intervention is widely applied as the first-line treatment for brain aneurysms following the International Subarachnoid Aneurysm Trial (ISAT) study (Molyneux et al., 2002, 2005), in which authors compared long-term efficacy of surgical treatment with endovascular intervention. They concluded that the probability of death and dependency is higher in clipping than in endovascular procedures. At the same time, the likelihood of disability-free survival was higher in endovascular procedures than in surgical clipping at ten years. Therefore, in terms of efficacy, these two methods were considered almost equal (Molyneux et al., 2015).

Several methods have been developed for intravascular intervention of intracranial aneurysms. The first method was simple coiling (SC), which is filling aneurysms with the coil. SC has some limitations, such as limitations in treating wide-neck aneurysms and a high risk of aneurysm recurrence (Wiebers et al., 2003; Gallas et al., 2005; Iijima et al., 2005; Li et al., 2006; Pouratian et al., 2006). These limitations resulted in the advent of new endovascular approaches, e.g., balloon-assisted coiling (BAC), stent-assisted coiling (SAC), flow diversion stenting, and flow disruption approach (Pierot and Wakhloo, 2013). These methods have been widely studied in terms of their clinical efficacy and long-term complications (Juvela, 2003; Zhang et al., 2022).

One of the most critical issues in treating intracranial aneurysms is the condition of neurological functions after procedures in treated subjects. Neurologic dysfunctions significantly affect the patient's quality of life and may include a variety of symptoms in different functions, including language, memory, consciousness, and attention (Gao et al., 2022). Therefore, cognitive dysfunction after treating intracranial aneurysms is a matter of concern. The present study investigated the clinical features and neurologic status at discharge, 6, and 12-month follow-ups using the modified Rankin Scale (mRS).

Material and Methods

Subjects

The present study is a retrospective cohort study that evaluates 229 subjects who had undergone endovascular treatment for a brain aneurysm in Imam Khomeini Hospital's Department of Neurovascular Intervention, Tehran, Iran, between March 2016 and March 2021.

Inclusion criteria were as follows: 1) patients with ruptured saccular intracranial aneurysm who were diagnosed with magnetic resonance imaging (MRI) or computed tomography (CT)-angiography; 2) patients aged more than 18 years; 3) patients for whom endovascular treatment included SC, SAC, flow diversion stenting, and flow disruption.

Exclusion criteria were as follows: 1) fusiform or dissecting aneurysm; 2) association with intracranial arteriovenous malformation (AVM), 3) previous coiled or clipped intracranial aneurysm; 4) immunosuppressed patients; 5) active infectious disease (endocarditis, meningitis); 6) follow-up less than a year; 7) absolute contraindication to the contrast agent; 8) platelet lower than 50,000 at admission; 9) known coagulopathy; 10) international normalized ratio (INR) more than three without a history of oral anticoagulant ingestion; 11) advanced atherosclerotic stenosis; 12) advanced vascular tortuosity in intracerebral vasculature; 13) treatment-resistant vasospasm interfered with navigation during the intervention; 14) history of cognitive dysfunction before the onset of the aneurysm.

The hospital file was evaluated, and the required data, including the demographic variables (age, sex, the history of antiplatelet usage, hypertension [HTN], diabetes mellitus [DM], hyperlipidemia [HLP], and smoking history); clinical variables (subarachnoid hemorrhage, rupture of the intracranial aneurysm, modified Rankin Scale at pre-procedure phase, discharge, 6-month, and one-year follow-up); radiologic variables (the location, size, and shape of aneurysm); treatment-related variables (anesthesia type, different endovascular approaches); and the post embolization outcome (Raymond-Roy occlusion classification in pre-procedure phase, 6- and 12-month follow-up), were collected.

Location of the aneurysm

Considering the location, the aneurysms were classified into the following groups: 1) anterior communicating artery (AComA) and anterior cerebral artery (ACA); 2) terminal internal carotid artery (ICA) and posterior communicating artery (PComA); 3) proximal ICA; 4) middle cerebral artery (MCA); 5) basilar artery; 6) vertebral artery and posterior cerebral artery (PCA).

The size of the aneurysm

Considering the size, the aneurysms were classified according to the sac diameter, neck diameter, and dome/neck ratio:

Sac diameter (according to the Unruptured Cerebral Aneurysm Study [UCAS] classification):
- Small: the maximum diameter of an aneurysm less than 5 mm
- Medium: the maximum diameter of an aneurysm between 5 and 10 mm
- Large: the maximum diameter of an aneurysm between 10 and 25 mm
- Giant: The maximum diameter of an aneurysm is more than 25 mm

Neck diameter:
- The maximum neck diameter of less than 4 mm
- The maximum neck diameter of equal to or more than 4 mm

Dome/neck ratio:
- less than 1.5
- equal to or more than 1.5

Evaluation of outcome

The primary angiographic results after treatment were assessed by the Raymond-Roy occlusion classification (RROC) and divided into three categories: Class I: complete obliteration; Class II: residual neck; Class III: residual aneurysm. The treatment was considered successful in the cases with complete occlusion and residual neck (Class I and II). The follow-up (F/U) angiography was performed at six months and 12 months. After reviewing angiographic images, RROC was used to determine the neurologic function of the subjects.

Intraoperative contrast agent extravasation or presence of coil out of aneurysm was in favor of aneurysm rupture. The intra-arterial contrast agent stagnation, intraluminal filling defect, disappearance of the distal vessels, and ischemic signs and symptoms during angiography at primary, 6 months, and 12 months were considered thromboembolic events. In the cases with a functional neurological deficit (FND) or acute headache, the bleeding and rebleeding were evaluated by CT scan and digital subtraction angiography (DSA).

The clinical neurologic status at the pre-procedure phase, discharge, 6-month, and one-year follow-up was evaluated by mRS. mRS is a test evaluating the neuro-cognition disability of the patients and can include a range of 0–5 in which a score of more than two is considered the worst outcome.

Statistical analysis

After collecting the data and required variables, a statistic specialist analysed the data using SPSS 16 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp). The continuous variables were reported as mean ± SD (standard deviation). Categorical variables were reported by number and percentage. Comparison between groups was performed using the chi-square test, Mann-Whitney U test, Kruskal-Wallis test, or ANOVA, based on the type of variables. The Kolmogorov-Smirnov test was used to assess the normality of data. The significant value for this study was considered 0.05.

Ethical considerations

The local institutional ethics committee approved the study, and informed consent was obtained from each participant.

Limitations

The limitations of this study were the short follow-up of the patients, loss of follow-up in some cases, and possible hospital file deficiency.

Results

Two hundred twenty-nine patients were enrolled in the study. The mean age of patients was 51.8 ± 12.6 (12–84 years). One hundred seventeen patients were male (51.1%), and 112 were female (48.9%). Eighty-nine patients were treated by SC, 111 by SAC, 25 by flow diversion stenting, and four by flow disruption. Risk factors of cardiovascular disease, clinical features, radiologic features of aneurysm, follow-up assessments, and technical aspects of procedures were assessed. Table 1 shows the detailed demographic data of patients in four different treatment groups. The distribution of the demographic data was not significantly different between each intervention group.

The most prevalent bleeding type among the subjects was SAH, seen in 184 patients (80.3%). Other bleeding types, intraventricular hemorrhage (IVH) and intraparenchymal hemorrhage (IPH) were seen in 32 (14%) and 13 (5.7%) patients,

Table 1 – Demographic characteristics of the patients in terms of intervention type

		Whole patients	SC (No.=89)	SAC (No.=111)	FD (No.=25)	F Dis. (No.=4)	P-value
Gender	M	117 (51.1)	47 (52.8)	57 (51.4)	12 (48)	1 (25)	0.53
	F	112 (48.9)	42 (47.2)	54 (48.6)	13 (52)	3 (75)	
Age		51.8 ± 12.6 (12–84)	50.5 ± 12.6 (12–84)	52.4 ± 13.1 (18–81)	52.4 ± 10.3 (31–71)	62.3 ± 10.7 (49–75)	0.39
HTN		94 (41.0)	32 (36.0)	50 (45.0)	9 (36)	3 (75)	0.22
HLP		17 (7.4)	4 (4.5)	12 (10.8)	1 (4)	0	0.36
DM		20 (8.7)	7 (7.9)	9 (8.1)	3 (12)	1 (25)	0.48
Smoking		61 (26.6)	23 (25.8)	30 (27.0)	7 (28)	1 (25)	0.85
CVA		8 (3.5)	3 (3.4)	4 (3.6)	1 (4)	0	0.99

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption; HTN – hypertension; HLP – hyperlipidemia; DM – diabetes mellitus; CVA – cerebrovascular accident; F – female; M – male; the data have been presented as No. (%) or mean ± standard deviation

Table 2 – Distribution of different hemorrhage types and Hunt-Hess grading scale among patients with subarachnoid hemorrhage (SAH)

		Whole patients	SC (No.=89)	SAC (No.=111)	FD (No.=25)	F Dis. (No.=4)	P-value
Bleeding type	SAH	184 (80.3)	72 (80.9)	89 (80.2)	20 (80)	3 (75)	0.94
	IVH	32 (14.0)	11 (12.4)	16 (14.4)	4 (16)	1 (25)	
	IPH	13 (5.7)	6 (6.7)	6 (5.4)	1 (4)	0	
Hunt-Hess grading in SAH patients	I	17 (9.2)	10 (13.9)	7 (7.9)	0	0	0.33
	II	136 (73.9)	50 (69.4)	66 (74.2)	18 (90)	2 (66.7)	
	III	31 (16.8)	12 (16.7)	16 (18)	2 (10)	1 (33.3)	

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption; IVH – intraventricular hemorrhage; IPH – intraparenchymal hemorrhage

Table 3 – Distribution of aneurysms locations in all patients and each group separately

Location	Whole patients	SC (No.=89)	SAC (No.=111)	FD (No.=25)	F Dis. (No.=4)	P-value
ACA, AComA	78 (34.1)	46 (59)	30 (38.5)	2 (2.5)	0	0.003
PComA	6 (2.6)	3 (50)	3 (50.0)	0	0	
Terminal ICA	46 (20.1)	6 (13)	28 (60.9)	11 (23.9)	1 (2.2)	
Proximal ICA	26 (11.4)	5 (19.2)	15 (57.7)	6 (23.1)	0	
MCA	38 (16.6)	17 (44.7)	17 (44.7)	4 (10.6)	0	
Basilar A	26 (11.4)	9 (34.6)	13 (50.0)	1 (3.8)	3 (11.5)	
PCA, Vertebral A	9 (3.9)	3 (33.3)	5 (55.6)	1 (11.1)	0	

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption; ACA – anterior cerebral artery; AComA – anterior communicating artery; PComA – posterior communicating artery; ICA – internal carotid artery; MCA – middle cerebral artery; PCA – posterior cerebral artery

respectively. The most common bleeding type in treatment groups was SAH. The distribution of the different bleeding types among different groups did not show statistical differences (P=0.94) (Table 2). Hunt-Hess grading (HHG) scale was assessed in patients with SAH. The most prevalent HHG scale was grade 2 (in all patients and each treatment group). There was no statistical association between the treatment group and HHG (P=0.33) (Table 2).

The distribution of aneurysm locations in each intervention territory is mentioned in Table 3. The most common type of aneurysm location was ACA and AComA

Table 4 – Association between aneurysm features and different treatment groups

		Whole patients	SC (No.=89)	SAC (No.=111)	FD (No.=25)	F Dis. (No.=4)	P-value	Post-hoc test
Height size (mean ± SD)		8.96 ± 4.98	6.93 ± 2.97	10.37 ± 5.65	9.80 ± 5.44	9.75 ± 4.35	<0.001	SC<(SAC= FD=F Dis.)
Width size (mean ± SD)		5.98 ± 3.35	4.49 ± 2.17	6.87 ± 3.70	7.00 ± 3.51	8.00 ± 2.45	<0.001	SC<(SAC= FD=F Dis.)
Neck size (mean ± SD)		4.16 ± 2.21	2.64 ± 0.91	5.05 ± 2.18	5.36 ± 2.71	6.00 ± 0.82	<0.001	SC<(SAC= FD=F Dis.)
Aneurysm size categories	small (<4 mm)	10 (4.4)	7 (70.0)	1 (10.0)	2 (20.0)	0	<0.001	
	intermediate (4–10 mm)	156 (68.1)	70 (44.9)	71 (45.5)	12 (7.7)	3 (1.9)		
	large (>10 mm)	63 (27.5)	12 (19.0)	39 (61.9)	11 (17.5)	1 (1.6)		
Neck size categories	small (<4 mm)	111 (48.5)	79 (71.2)	25 (22.5)	7 (6.3)	0	<0.001	
	wide (≥4 mm)	118 (51.5)	10 (8.5)	86 (72.9)	18 (15.3)	4 (3.4)		
D/N ratio	<1.5	127 (55.5)	20 (15.7)	84 (66.1)	20 (15.7)	3 (2.4)	<0.001	
	≥1.5	102 (44.5)	69 (67.6)	27 (26.5)	5 (4.9)	1 (1.0)		

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption; SD – standard deviation; D/N – dome-to-neck

(34.1%), followed by terminal ICA and PComA (22.7%), MCA (16.6%), proximal ICA and basilar artery (11.4%), PCA and vertebral artery (3.9%), and PComA (2.6%), respectively. Different treatment methods were not accomplished similarly in various anatomical aneurysms (P=0.003). Most patients with ACA-AComA aneurysms were treated with SC, while most patients with terminal ICA and PComA were treated with SAC.

The association between aneurysm features and different treatment groups is demonstrated in Table 4. The mean height, width, and neck size of aneurysms were 8.96 ± 4.98 mm (2–29 mm), 5.98 ± 3.35 mm (2–20 mm), and 4.16 ± 2.21 mm (2–17 mm), respectively. Aneurysms treated with the SC method were smaller than the other three treatment methods (P<0.001). A similar pattern was seen for aneurysm width and aneurysm neck size (i.e., the aneurysms treated with the SC method had smaller width and neck size considering the other three methods) (both P-values < 0.001).

After the categorization of aneurysm size (<4 mm, 4–10 mm, and >10 mm) and aneurysm neck size (<4 mm, and ≥4 mm), we assessed the distribution of different treatment methods in each size category. As we can see in Table 4, this association was statistically significant; in fact, small aneurysms were treated more with SC, while large aneurysms were treated more with SAC. In addition, aneurysms with small necks were treated more with SC, while wide necks were treated more with the SAC method (both P-values < 0.001). On the other hand, aneurysms with a dome-to-neck (D/N) ratio lower than 1.5 were treated more with SAC, while other aneurysms were treated more with the SC method (P-value < 0.001).

The type of all aneurysms was saccular. All neuro-intervention procedures were conducted via femoral puncture, and a bi-plane angiography machine was performed all except one. In 67 patients, the procedure was performed under general anesthesia (29.3%). Table 5 describes the intervention method and treatment sessions conducted for patients. In most patients, the embolization was completed in the first session (144 patients, 62.9%; 57 in SC, 61 in SAC coiling, 22 in flow diversion stenting, and 4 in flow disruption), while for 79 patients, the procedure was completed in the second session (34.5%; 30 in SC, 46 in SAC, and 3 in flow

Table 5 – Association between the number of treatment sessions and different treatment groups

		Whole patients	SC (No.=89)	SAC (No.=111)	FD (No.=25)	F Dis. (No.=4)	P-value
Session time	first	144 (62.9)	57 (64.0)	61 (55.0)	22 (88)	4 (100)	0.04
	second	79 (34.5)	30 (33.7)	46 (41.4)	3 (12)	0	
	third	6 (2.6)	2 (2.2)	4 (3.6)	0	0	

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption diversion stenting). For six patients, a third session was required to complete the procedure (2.6%; 2 in SC and 4 in SAC).

As mentioned, the modified Raymond-Roy classification assessed clinical outcomes of aneurysm occlusion (MRRC). This assessment was performed immediately after the procedure and in 6- and 12-month follow-ups. We compared the data of different treatment methods. In addition, we compared aneurysm filling in each treatment method at successive times (immediately after the procedure and in 6- and 12-month follow-ups).

In the present study, the initial RROC Class I, RROC Class II, and RROC Class III were achieved in 73.5%, 15.5%, and 11% of the patients, respectively. These rates were 77.5%, 16.9%, and 5.6% in the SC group and 70.3%, 14.4%, and 15.3% in the SAC group, respectively. At the 6-month follow-up, the RROC Class I, RROC Class II, and RROC Class III were achieved in 69.4%, 21.5%, and 9.1% of the patients, respectively. These rates were 69.9%, 24.1%, and 6% in the SC group, 68%, 25%, and 7% in the SAC group, 69.6%, 0, and 30.4% in flow diversion stenting, and 100%, 0, and 0 in flow disruption, respectively. At the 12-month follow-up, the RROC Class I, RROC Class II, and RROC Class III were achieved in 69.1%, 15.5%, and 15.5% of the patients, respectively. These rates were 65.1%, 15.7%, and 18.1% in the SC group, 69.4%, 18.4%, and 21.2% in the SAC group, 78.3%, 0, and 21.7% in flow diversion stenting, and 100%, 0, and 0 in flow disruption, respectively. The aneurysm filling was not statistically different between treatment methods in each time session. In addition, the rate of aneurysm recurrence at successive times for each treatment method is not high enough to make statistical significance.

Most aneurysms stayed unchanged with time; however, some recurred in 6 and 12 months. The rate of worsening in aneurysm filling with time was more than the rate of improvement in aneurysm filling (Table 6). Comparison of 12-month follow-up with the after-procedure situation was statistically significant for the SC group but was not significant in the SAC group. This means a higher rate of aneurysm recurrence was observed in the SC group compared to the SAC group. More precisely, the difference in successive time sessions in SC groups showed that the main worsening of aneurysm filling occurred when we compared the data from 6 and 12 months and the comparison of data from after the procedure and 12 months. Data demonstrated that the recurrence of aneurysms accelerated after six months. The comparison of successive time sessions for SAC did not show a significant difference (all P-values greater than 0.31). In addition, a comparison of 6 months and 12 months in the FD (flow diversion stenting) group did not show a significant difference (P-value = 0.16).

Table 7 describes the distribution of adverse events following the intervention. Aneurysm rupture during the procedure occurred in 8 patients (3.5%; 3 in SC and 5 in SAC). Intraprocedural thromboembolism events were seen in 21 patients (9.2%; 7 in SC, 10 in SAC, 3 in flow diversion stenting, and 1 in the flow disruption group). Intraprocedural thromboembolism was more common than the six and

Table 6 – Aneurysm filling after procedure and successive follow-ups based on modified Raymond-Roy classification in all patients and terms of treatment groups

MRRC		Whole patients			SC (No.=89)			SAC (No.=111)			FD (No.=25)	F Dis. (No.=4)	P-value
MRRC class after procedure	I	147 (73.5)			69 (77.5)			78 (70.3)			–	–	0.16
	II	31 (15.5)			15 (16.9)			16 (14.4)			–	–	
	III	22 (11.0)			5 (5.6)			17 (15.3)			–	–	
MRRC class after 6 months	I	145 (69.4)			58 (69.9)			68 (68.0)			16 (69.6)	3 (100)	0.62
	II	45 (21.5)			20 (24.1)			25 (25.0)			0	0	
	III	19 (9.1)			5 (6.0)			7 (7.0)			7 (30.4)	0	
MRRC class after 12 months	I	143 (69.1)			54 (65.1)			68 (69.4)			18 (78.3)	3 (100)	0.50
	II	32 (15.5)			14 (15.7)			18 (18.4)			0	0	
	III	22 (15.5)			15 (18.1)			12 (21.2)			5 (21.7)	0	
P-value (3 F/U sessions)		0.07			0.015			0.92			–	–	
Comparison of 0 and 6-months													
Worse		37	1 to 2	27	18	1 to 2	13	19	1 to 2	14	–	–	
			2 to 3	3		2 to 3	1		2 to 3	2			
			1 to 3	7		1 to 3	4		1 to 3	3			
No change		117	1	108	53	1	49	64	1	59	–	–	
			2	7		2	4		2	3			
			3	2		3	0		3	2			
Improve		29	3 to 2	11	12	3 to 2	3	17	3 to 2	8	–	–	
			2 to 1	15		2 to 1	9		2 to 1	6			
			3 to 1	3		3 to 1	0		3 to 1	3			
P-value		0.21			0.12			0.79			–	–	

MRRC	Whole patients			SC (No.=89)			SAC (No.=111)			FD (No.=25)			F Dis. (No.=4)			P-value
Comparison of 0- and 12-months																
Worse	48	1 to 2	24	26	1 to 2	13	22	1 to 2	11	–			–			
		2 to 3	5		2 to 3	4		2 to 3	1							
		1 to 3	19		1 to 3	9		1 to 3	10							
No change	102	1	98	46	1	44	56	1	54	–			–			
		2	1		2	0		2	1							
		3	3		3	2		3	1							
Improve	31	3 to 2	7	11	3 to 2	1	20	3 to 2	6	–			–			
		2 to 1	19		2 to 1	10		2 to 1	9							
		3 to 1	5		3 to 1	0		3 to 1	5							
P-value	0.008			0.002			0.39			–			–			
Comparison of 6- and 12-months																
Worse	31	1 to 2	12	18	1 to 2	6	13	1 to 2	6	0	1 to 2	0	0	1 to 2	0	
		2 to 3	10		2 to 3	8		2 to 3	2		2 to 3	0		2 to 3	0	
		1 to 3	9		1 to 3	4		1 to 3	5		1 to 3	0		1 to 3	0	
No change	156	1	125	58	1	48	74	1	58	21	1	16	3	1	3	
		2	19		2	7		2	12		2	0		2	0	
		3	12		3	3		3	4		3	5		3	0	
Improve	20	3 to 2	2	7	3 to 2	1	11	3 to 2	1	2	3 to 2	0	0	3 to 2	0	
		2 to 1	14		2 to 1	5		2 to 1	9		2 to 1	0		2 to 1	0	
		3 to 1	4		3 to 1	1		3 to 1	1		3 to 1	2		3 to 1	0	
P-value	0.09			0.028			0.31			0.16			1			

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption; MRRC – modified Raymond-Roy classification; F/U – follow-up

Table 7 – Association between the adverse events and different treatment groups

		Whole patients	SC (No.=89)	SAC (No.=111)	FD (No.=25)	F Dis. (No.=4)	P-value
Rupture during procedure		8 (3.5)	3 (3.4)	5 (4.5)	0	0	0.78
Thromboembolic events	intra-procedure	21 (9.2)	7 (7.9)	10 (9.0)	3 (12)	1 (25)	0.80
	in 6-month	6 (2.6)	2 (2.2)	3 (2.7)	1 (4)	0	0.75
	in 12-month	3 (1.3)	1 (1.1)	2 (1.8)	0	0	0.95
Rebleeding in 1 year		15 (6.6)	5 (5.6)	8 (7.2)	2 (8)	0	0.80
Morbidity	at discharge	18 (7.9)	8 (9.0)	7 (6.3)	3 (12)	0	0.49
	after 6-month	17 (7.4)	6 (6.7)	9 (8.1)	2 (8)	0	0.94
	after 12-month	19 (8.3)	8 (9.0)	9 (8.1)	2 (8)	0	0.96
Mortality	in hospital	16 (7.0)	5 (5.6)	9 (8.1)	1 (4)	1 (25)	0.74
	after 6-month	4 (1.7)	1 (1.1)	2 (1.8)	1 (4)	0	0.58
	after 12-month	2 (0.9)	0	2 (1.8)	0	0	0.61

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption

Table 8 – Association of mRS between different treatment groups

mRS		Whole patients	SC (No.=89)	SAC (No.=111)	FD (No.=25)	F Dis. (No.=4)
before procedure	0	209 (91.3)	81 (91)	102 (91.9)	22 (88)	4 (100)
	1	7 (3.1)	5 (5.6)	1 (0.9)	1 (4)	0
	2	3 (1.3)	0	2 (21.8)	1 (4)	0
	3	8 (3.5)	2 (2.2)	5 (4.5)	1 (4)	0
	4	2 (0.9)	1 (1.1)	1 (0.9)	0	0
	5	0	0	0	0	0
	6	0	0	0	0	0
at discharge	0	191 (83.4)	76 (85.4)	92 (82.9)	20 (80)	3 (75)
	1	7 (3.1)	3 (3.4)	2 (1.8)	2 (8)	0
	2	7 (3.1)	1 (1.1)	5 (4.5)	1 (4)	0
	3	4 (1.7)	4 (4.5)	0	0	0
	4	3 (1.3)	0	2 (1.8)	1 (4)	0
	5	1 (0.4)	0	1 (0.9)	0	0
	6	16 (7.0)	5 (5.6)	9 (8.1)	1 (4)	1 (25)
in 6 months	0	189 (82.5)	77 (86.5)	89 (80.2)	20 (80)	3 (75)
	1	5 (2.2)	2 (2.2)	2 (1.8)	1 (4)	0
	2	6 (2.6)	1 (1.1)	4 (3.8)	1 (4)	0
	3	6 (2.6)	3 (3.4)	2 (1.8)	1 (4)	0
	4	3 (1.3)	0	3 (2.7)	0	0
	5	0	0	0	0	0
	6	4 (1.7)	1 (1.1)	2 (1.8)	1 (4)	0
in 12 months	0	184 (80.3)	75 (84.3)	86 (77.5)	20 (80)	3 (75)
	1	6 (2.6)	2 (2.2)	3 (2.7)	1 (4)	0
	2	9 (3.9)	3 (3.4)	5 (4.5)	1 (4)	0
	3	5 (2.2)	3 (3.4)	1 (0.9)	1 (4)	0
	4	3 (1.3)	0	3 (2.7)	0	0
	5	0	0	0	0	0
	6	2 (0.9)	0	2 (1.8)	0	0

SC – simple coiling; SAC – stent-assisted coiling; FD – flow diversion stenting; F Dis. – flow disruption; mRS – modified Rankin Scale

12 months thromboembolic events. Moreover, the SC group had the highest rate of thromboembolic events.

Similarly, 6-month and 12-month morbidities more commonly occurred at discharge in the SC group. Rebleeding in one year was also commonly observed in the SC group (15 cases). In-hospital, at 6-month, and 12-month mortality was more common in the SC group.

Regarding the clinical neurological situation, we assessed the mRS among the patients (Table 8). Among all patients, the mean mRS before the procedure was 0.05 ± 0.26, which increased to 0.22 ± 0.76 after the procedure, to 0.22 ± 0.76 in

6 months, and to 0.30 ± 0.95 in 12-month follow-up (P<0.001). Pairwise comparisons of mRS between different sessions were statistically significant for all comparisons before the procedure and at discharge, before the procedure and six months, and before the procedure and 12-month follow-up (all P-values < 0.001). This means deterioration of neurological status after the procedure. Comparisons of mRS between discharge and 6-months and 12-months were not statistically significant (P-values = 0.16 and 0.12), and the comparison between 6- and 12-months was borderline (P=0.049).

In the SC group, comparison of mRS before the procedure with mRS at discharge and mRS in 6 months and mRS in 12 months were all significant or borderline (P-values = 0.003, 0.065, and 0.036, respectively) in favour of slight deterioration of clinical situation and function. Comparison of all time pairs after the procedure (for example, comparison of discharge mRS with six months mRS) did not show a statistical difference. A similar scenario occurred in the SAC group. In the SAC group, all comparisons of mRS in pre-procedure time with after-procedure time points (including discharge mRS, six months mRS, and 12 months mRS) showed statistically significant differences; P-values were as follows: <0.001, 0.002, and 0.001, respectively. This favours slight deterioration of the patient's clinical situation and neurological function. Comparisons of mRS in all time points after the procedure did not show any statistically significant difference, meaning no significant clinical change (improvement or deterioration) in the clinical condition and function of the patients after the procedure and with time spent. FD group and F. Dis (flow disruption) did not show statistically significant changes in mRS before and after procedures (all P-values greater than 0.05).

Discussion

Following the publication of the ISAT study in 2002, endovascular treatment became the mainstay of intracranial aneurysm treatment in many centers (Molyneux et al., 2002). Moreover, it is one of the standard treatment modalities for both ruptured and unruptured intracranial aneurysms (Ferns et al., 2009). Another fundamental study with a similar background is the Barrow Ruptured Aneurysm Trial (BRAT) study, which demonstrated that the one-year outcome after treatment of ruptured aneurysms was better with coil embolization than with surgical clipping. The authors followed the patients for ten years and concluded that there was no significant difference in clinical outcome between the two treatment groups. On the other hand, while coiling had a significant advantage for posterior circulation aneurysms at one year, this study did not show the significant difference at longer follow-up. Moreover, the complete occlusion rate was significantly lower (22% vs. 93%), and the rate of cross over to the opposite treatment method was higher (36% vs. 1%) in coil-assigned patients (Spetzler et al., 2019).

Coiling has some limitations; first, as an initial treatment, all the aneurysms are not completely occluded; second, the patients with the ruptured aneurysm are at risk of early rebleeding; and third, there is a risk of reopening the aneurysm even in the case with adequate initial coil packing (Ferns et al., 2009). The factors that may play a role in initial incomplete coil occlusion include the large size of the aneurysm, intraluminal thrombosis, low packing density, initial incomplete occlusion, the duration of follow-up, ruptured aneurysm, aneurysm in the posterior circulation, and the large neck to dome ratio (Ferns et al., 2009).

A study evaluated 35 symptomatic or asymptomatic saccular aneurysms in Egypt, in which, similar to our study, females and males had the same distribution. However, the mean age of the patients was lower than our study (45.7 ± 13 vs. 51.8 ± 12.6). Similar to our findings, hypertension was the most common risk factor for intracerebral aneurysm. 96.8% of the patients were symptomatic. 32.2% of the patients were in grades 1 and 2 of H and H (Hunt and Hess scale) grade, and 67.8 in grades 3 and 4. The complete occlusion rate was 82.9%, the residual neck rate was 11.4%, and the residual sac rate with contrast within the coil mass was 2.9%. Follow-up demonstrated that 23 patients had mRS 0, 1, 2 (good outcome), and eight patients 3, 4, 5, 6 (poor outcome). Two patients died after surgery. The mean duration of follow-up was 33.03 ± 15.96 months. Moreover, at follow-up, the permanent complete occlusion, the residual neck, and the residual aneurysm rates were 79.3%, 10.3%, and 10.3%, respectively. There was no case of delayed ischemia or rebleeding. Two patients had a significant recurrence and needed retreatment. This study's risk factors for poor outcome were a history of myocardial infarction (MI), H and H grade, mRS, fisher grade, vasospasm, and vasospasm-related infarct. The immediate angiographic results showed no risk factor. Multivariate analysis demonstrated that H and H grade, mRS at admission, fisher grade, vasospasm-related infarct, and shunt-needed hydrocephalus were related to poor outcomes (Elewa, 2018).

In a study, Ferns and his co-workers (2009) systematically reviewed the studies with more than 50 patients who underwent coiling and had sufficient follow-up. 65.4% of patients had ruptured aneurysms. The mean duration of follow-up was 14.1 months, and 66.6% of aneurysms were in the anterior circulation. The initial complete occlusion, near-complete, and incomplete occlusion rates were 62.3, 29.5, and 8.2%, respectively. The sufficient initial occlusion rate was 91.2%, and the incomplete occlusion rate was 8.8%. In the follow-up, the complete, near-complete, and incomplete occlusion rates were 61.5, 22.5, and 15.8%, respectively. The sufficient complete rate was 83.4%, and the incomplete occlusion rate was 16.6%. Reopening and retreatment rates were 20.8 and 10.3%, respectively (Ferns et al., 2009).

In a multicenter study, Sophie Gallas and her colleagues (2005) evaluated 705 ruptured intracranial aneurysms treated with Guglielmi Detachable Coils. The initial complete occlusion rate was 72.6%, subtotal occlusion was 25%, and incomplete occlusion was 2.4%. On extended follow-up (mean 36 months), the complete, subtotal, and incomplete occlusion rates were 73.9, 25.9, and 0.17%, respectively. The overall mortality was 11.4%, and the procedure-related mortality was 1.4%. The morbidity was 8.6% (Gallas et al., 2005).

In follow-up, the sufficient occlusion, reopening, and retreatment rates were 92.6, 15.5, and 6.5% in the anterior circulation, and 70.4, 22.5, and 14.5% in the posterior circulation. The reopening and retreatment rates increased with the increased aneurysm size. Although the rupture of an aneurysm was demonstrated as a risk factor for the reopening of the aneurysm in other studies, the ruptured aneurysm had a higher sufficient occlusion rate and lower reopening and retreatment rates (Ferns et al., 2009). These findings are consistent with the results of our study, which showed that coiling of the ruptured aneurysms resulted in adequate occlusion rate.

Raymond et al. (2003) evaluated the decisive factors in angiographic recurrence after endovascular treatment in a study. 501 aneurysms in 466 patients were surveyed. The mean age was 54.20 ± 12 years. 74% of the patients were female. 35.6% of the patients have multiple aneurysms. The recurrence rate was 33.6% in 12.31 months. Minor or stable recurrence was 22.1% in 33.6 month follow-up, and major recurrence was 20.7% in 16 month follow-up. The bleeding rate was 0.8% (3 patients) in 13 months of follow-up, related to angiographic recurrence. The factors related to the recurrence in this study included the treatment in the acute phase of aneurysm rupture, the size of the aneurysm, the width of the neck, the primary suboptimal angiographic results, and the duration of follow-up. The age, sex, and location of the aneurysm had no effect. The major recurrence rate was 25.1% in patients treated after aneurysm rupture and 16.3% in patients without rupture. The larger size of the aneurysm and increased neck width had a solid relation to recurrence. The significant prognostic factors for recurrence or regression were an aneurysm of more than 10 mm, a ruptured aneurysm, residual neck, residual aneurysm, and longer follow-up (Raymond et al., 2003).

Laurent Pierot et al. (2020) evaluated the one-year bleeding and rebleeding rate following intracranial aneurysm coiling. They followed 1,140 patients for 12 months. The bleeding rate was 0.0% and 1.0% in patients with unruptured and ruptured aneurysms. Multivariate analysis demonstrated that incomplete aneurysm occlusion after initial treatment (2.0% in incomplete aneurysm occlusion vs. 0.2% in complete aneurysm occlusion) and dome-to-neck ratio (1.5 ± 0.5 with rebleeding vs. 2.2 ± 0.9 without rebleeding) were associated with the rebleeding occurrence (Pierot et al., 2020). In our study, the 1-year rebleeding rate of the ruptured aneurysms in the SC and SAC groups were 5.6 and 7.2%, respectively. The underlying cause of the higher rebleeding rate in our study might be the smaller sample size and differences in aneurysm size and type between the two communities.

Petra Cimflova et al. (2021) reported the result of their study in 2020. They evaluated clinical and radiologic outcomes in 23 patients with M2 and more distal aneurysms who underwent flow diversion. The complete or near-complete occlusion occurred in 70% of the patients in 30-month follow-up. Moreover, 70% of patients had an mRS score of excellent (0 and 1) within six months of follow-up (Cimflova et al., 2021). However, in our study, the mRS score of zero in the flow-diversion group was observed in 88% of the population before discharge, which was preserved at 80% in the subsequent follow-ups.

Imamura and his co-workers (2020) retrospectively surveyed 5,358 patients. The intraprocedural rupture rate, ischemic complications, and rebleeding rate were 4.1, 4.2, and 1.2%, respectively. The factors related to intraprocedural rupture included female, bifurcation type, a size less than 5 mm, emergency treatment, local anesthesia, and balloon-assisted coiling. The factors which were effective in ischemic complications included poor grade in World Federation of Neurosurgical Societies (WFNS) grading, width neck, and stent-assisted coiling. The affective factors in rebleeding included poor WFNS grading, bifurcation type, width neck, and body filling as the initial result (Imamura et al., 2020).

After endovascular treatment, Laurent Pierot and co-workers (2008) evaluated the immediate clinical outcome for unruptured intracranial aneurysms. Six hundred forty-nine patients were analysed. Coiling, SAC, and BAC were performed in 54.9, 37.3, and 7.8% of the patients. Endovascular treatment was unsuccessful in 4.3% of the patients. The complications were observed in 15.4% of the patients (7.1% thromboembolic events, 2.6% intraprocedural rupture, and 2.9 device-related events). The complications which resulted in a temporary or permanent neurologic deficit occurred in 5.4% of the patients. The one-month morbidity and mortality were 1.7 and 1.4%, respectively (Pierot et al., 2008).

In a study by Chalouhi and colleagues in 2013, compared to coiling, treatment with pipeline embolization device (PED), which is a type of flow diversion, showed a lower need for retreatment of the unruptured aneurysms. The results of our study also showed similar findings. As shown in Table 5, there was a lower need for second and third-session treatments in the F Dis. Group (Chalouhi et al., 2013).

The results of our study also showed that compared to the 6-month (69.9%), RROC in the flow diversion group was improved at 12 months (78.3%). Interestingly, the RROC was reduced at 6 and 12 months in the SC and SAC groups. Therefore, it could be concluded that flow diversion is more effective in RROC at six and 12-month follow-ups. However, according to the nature of this study which is a retrospective study and the small number of patients in the flow diversion group, these data could not be generalized. Therefore, a larger prospective randomized clinical trial is required to compare the efficacy of coiling with flow diversion.

Conclusion

Similar to the other studies, the results of the present study are promising and demonstrate the effectiveness of the neurovascular intervention as a first therapeutic modality for ruptured and unruptured aneurysms. A double-blind, randomized clinical trial that compares the patients who underwent coiling and flow diversion is needed to eliminate the efficacy and confounding factors affecting the outcome of ruptured intracranial aneurysm subjects.

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