RESEARCH ARTICLE

Endovascular coil embolization of ruptured and unruptured intracranial aneurysms: review of a 15-year single center experience in Pakistan

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Abstract

Objective: To assess the outcome of endovascular treatment of intracranial aneurysm over 15 years.

Methods: The retrospective study was conducted at the at Radiology Department of Aga Khan University Hospital, Karachi, and comprised medical records from April 2003 to April 2018 of patients who received endovascular treatment for intracranial aneurysm. Multiple variables reviewed included demographics, clinical presentation, aneurysm morphology, technique used, technique outcome and clinical outcome. Data was analysed using SPSS 22.

Results: Of the 242 patients, 111(45.8%) were males and 131(54.1%) were female. The overall mean age was 46.3+/-13.543 years (range: 9-78years). Aneurysm size was <5mm in 95(40.4%) patients, 5-10mm in 98(41.7%) and >10mm in 42(17.9%) patients. Aneurysms were located in the anterior communicating artery in 93(38.4%) patients, internal carotid artery 48(19.8%) patients and posterior communicating artery 26(10.7%) patients. Patients with higher initial Hess and Hunt grade were more likely to have higher modified Rankin scale score after treatment (p=0.001). Overall, 222(91.7%) patients were treated successfully. Complications were noted in 37(15.2%) patients and 10(4.0%) patients died.

Conclusions: No correlation was found between Hess and Hunt grades and aneurysm severity based on aneurysm size, neck and ruptured/unruptured cases.

Keywords: Intracranial aneurysm, Ruptured aneurysms, Endovascular procedures, Therapeutic embolisations.

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Introduction

In the past 20 years, the treatment and management of intracerebral aneurysm have seen dramatic advancement. Non-invasive high-quality neuro-imaging techniques like computed tomography (CT) angiography and magnetic resonance (MR) angiography have made it easier to diagnose patients with unruptured and ruptured intracranial aneurysms (IA).[1] It has been shown that even small unruptured aneurysms may enlarge and bleed unpredictably. Asymptomatic patients with unruptured aneurysm have risk of subarachnoid haemorrhage (SAH). Hence, physicians need to thoroughly assess each patient's risk factors and should have adequate knowledge of the disease course and treatment modalities that can be offered.[2] Even with advance diagnostic and therapeutic techniques, the mortality rate for SAH is high and approximated to be 50%. It is reported that less than 60% of the patients that survive after SAH treatment would return to normal, functioning, independent life.[3] Patients with SAH have risk of re-bleeding that is approximately 2-28% in the first 72 hours.[4] Therefore, timely assessment and management of IAs are the most effective treatment to prevent further aggravation and recurrence.

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Many factors are considered before deciding the correct treatment modality for each individual patient. Management of aneurysm depends on the patient's age, aneurysm site and size, co-morbid conditions along with technical skills, resources and complication risk after repair.[5] Aneurysms can be managed surgically by placing a clip across the neck of the aneurysm. This is an effective and safe procedure and is dependent on microsurgical techniques and skills of an experienced surgeon.[6] In a study, surgical clipping resulted in 0.8% mortality rate and 3.4% permanent morbidity. It was reported that untreated unruptured intracranial aneurysms had 10-year cumulative risk of aneurysmal bleeding leading to mortality and morbidity of no less than 7.5%. It was suggested that based on natural course of disease, surgical clipping showed a superior outcome.[7]

The other treatment option includes endovascular technique. After the results of International Subarachnoid Aneurysm Trial (ISAT) in 2002, this was the preferred modality for the management of ruptured aneurysms.[8] Two major complications seen with endovascular embolisation technique are thromboembolism and intraoperative aneurysm rupture. In relation to this, ISAT did a comparison between endovascular coiling versus neurosurgical clipping in aneurysm SAH. After 1 year of follow-up, there were fewer deaths or dependency in the endovascular group than the neurosurgical group, with

absolute risk reduction of 6.9%.[9] Regarding endovascular treatment, a large multicentre study, called the Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms (CLARITY), showed that the rate of thromboembolic complications in patients treated for ruptured aneurysm was not influenced by the location of the aneurysm, but was affected by aneurysm size and neck size. It was further mentioned that the rate of intraoperative rupture is linked to aneurysm location, but not aneurysm size.[10]

There are limited hospitals and technically-skilled doctors in Pakistan using endovascular treatment for IAs. The current study was planned to assess the outcome of endovascular treatment of IAs over 15 years at the first centre that started endovascular management of aneurysms in Karachi, Pakistan.

Materials and Methods

The retrospective 15-year audit was conducted at the Radiology Department, Aga Khan University Hospital (AKUH), Karachi, Pakistan, and comprise medical records from April 2003 to April 2018. After approval from the institutional ethics review committee, hospital computer records were searched to gather a list of all the patients diagnosed with IAs. Based on the inclusion criteria, all asymptomatic and symptomatic as well as emergency and elective patients who were diagnosed with ruptured intracranial saccular aneurysms of size >2mm and unruptured intracranial saccular aneurysm of size >3mm, and received endovascular management were included. Those excluded were records related to patients with fusiform aneurysms, severe vascular spasm, more than 80% neck-to-body ratio in acute ruptured aneurysm, and having difficult anatomy like very tortuous internal carotid artery (ICA).

Each patient's medical record was thoroughly assessed by an expert radiologist specialising in neuro-imaging. Multiple variables were reviewed, like patients' demographics, initial clinical presentation using Hess and Hunt (H&H) grading, angiographic characteristics, like rupture/unruptured aneurysms, location of aneurysm, size of aneurysm, wide/narrow neck of aneurysm, endovascular technique used and outcome, post-procedure success rate and complications, post-procedure modified Rankin Score (mRS), and mortality. Based on initial clinical presentation, each patient was graded using H&H.[21] Initial HnH scores were compared to assess initial severity with post-treatment mRS.

Wide neck was defined as neck >50% neck-to-body ratio or >4mm. All the measured aneurysm sizes were categorized in ≤5mm, 5-10mm and ≥10mm groups. Successful outcomes were reported in patients who had better clinical and imaging outcome after endovascular procedure and did not develop any complications. Patients with deteriorating clinical and imaging outcome or those who developed complications were categorised as unsuccessful outcome.

Data was entered in Excel and analysed using SPSS 22. Chi square analysis was conducted. P<0.05 was considered significant. To the best of our knowledge, there has not been any research regarding this topic in Pakistan.

Results

Of the 260 records reviewed, 242(93%) were included; 111(45.9%) males and 131(54.1%) females. The overall mean age was 46.3±13.543 years (range: 9-78 years). Mean aneurysm size was 7.5±5.3mm (range: 2-50mm). Aneurysm size was <5mm in 95(40.4%) patients, 5-10mm in 98(41.7%) and >10mm in 42(17.9%).Of the total, 175(84.5%) emergency patients with ruptured aneurysms were treated immediately on arrival, while 32(15.5%)with unruptured aneurysms had planned elective treatment. There were 126(55.3%) wide and 102(44.7%) narrow neck aneurysms.

Table-1: Ruptured and unruptured aneurysms categoriaed in 3 groups based on size.

Aneurysm sizes/ mm	Total number of patients with aneurysm sizes	Total of ruptured and unruptured aneurysm	Ruptured Aneurysm	Unruptured Aneurysm
≤ 5	95	85	76	9
5 to 10	98	88	77	11
≥ 10	42	34	22	12
Total	235	207	175	32
Missing data	7	35		
Grand Total	242	242		
Chi-Square Tests	Value	Df	Asymp. Sig. (2-sided)	
Pearson Chi-Square	13.682a	2	0.001	
Likelihood Ratio	11.45	2	0.003	
N of Valid Cases	207			

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 5.06.

Table-2: Location of aneurysms with ruptured and unruptured aneurysms.

Location of aneurysms	Total Number	Total of ruptured and unruptured aneurysm	Patients with Ruptured Aneurysm	Patients with Unruptured Aneurysm
A Comm artery	93	82	73	9
ICA	48	38	30	8
P Comm artery	26	20	15	5
Basilar artery	18	16	13	3
MCA	16	15	15	0
A1	12	9	9	0
Vertebral artery	10	9	5	4
DACA	7	6	6	0
PCA	6	6	4	2
PICA	4	4	3	1
ICA/MCA/Basilar	1	1	1	0
Trigeminal artery	1	1	1	0
Total	242	207	175	32
Missing data	-	35		
Chi-Square Tests	Value	df	Asymp. Sig. (2-sided)	
Pearson Chi-Square	17.079a	11	0.106	
Likelihood Ratio	19.967	11	0.046	
N of Valid Cases	207			

a. 13 cells (54.2%) have expected count less than 5. The minimum expected count is .15.

A Comm: Anterior communicating. ICA: Internal cerebral artery. P Comm: Posterior communicating. MCA: Middle cerebral artery. A1: Anterior cerebral artery. DACA: Deep anterior cerebral artery. PCA: Posterior cerebral artery. PICA: Posterior inferior cerebral artery. DACA: Distal anterior cerebral artery.

Table-3: Initial Hess and Hunt grading with aneurysm sizes, neck type and post-treatment outcome.

Before Endovascular procedure	Aneurysm measurements/ mm				Aneurysm Neck		
Hess and Hunt (H&H) Grading	≤ 5	5 to 10	≥ 10	Total Hess and Hunt grade	Narrow	Wide	Total neck
1	18	18	18	54	19	36	55
2	26	22	11	59	27	28	55
3	32	32	8	72	31	38	69
4	17	23	4	44	23	20	43
5	2	3	1	6	2	4	6
Total	95	98	42	235	102	126	228
Outcome							
Successful	82	91	40	213	96	111	207
Unsuccessful	13	7	2	22	6	15	21
Total	95	98	42	235	102	126	228
Chi-Square Tests	Value	df	Asymp. Sig.	Chi-Square Tests	Value	Df	Asymp. Sig.
H&H Grade * Size			(2-sided)	H&H Grade * Neck			(2-sided)
Pearson Chi-Square	14.840a	8	0.062	Pearson Chi-Square	4.381a	4	0.357
Likelihood Ratio	14.084	8	0.08	Likelihood Ratio	4.429	4	0.351
Linear-by-Linear Association	4.036	1	0.045	-	-	-	-
N of Valid Cases	235			N of Valid Cases	228		

a. 3 cells (20.0%) have expected count less than 5. The minimum expected count is 1.07.

a. 2 cells (20.0%) have expected count less than 5. The minimum expected count is 2.68.

Chi-Square Tests	Value	Df	Asymp. Sig.	Chi-Square Tests	Value	df	Asymp. Sig.
Success * Size			(2-sided)	Success * Neck			(2-sided)
Pearson Chi-Square	7.102a	6	0.312	Pearson Chi-Square	6.778a	3	0.079
Likelihood Ratio	8.425	6	0.209	Likelihood Ratio	9.796	3	0.02
N of Valid Cases	235			N of Valid Cases	228		

a. 7 cells (58.3%) have expected count less than 5. The minimum expected count is .53.

a. 4 cells (50.0%) have expected count less than 5. The minimum expected count is 1.35.

Table-4: Initial Hess and Hunt grade and Post treatment modified Rankin scores.

Hess and Hunt Grading	Modified Rankin Scale 0	1	2	3	4	5	6	Total	Missing data	Total known Hess and Hunt grade
1	48	5	1	0	0	0	0	54	0	54
2	22	35	1	1	0	0	0	59	0	59
3	22	20	10	6	7	2	2	69	3	72
4	14	11	4	4	3	3	5	44	0	44
5	0	0	0	0	1	1	3	5	1	6
Total	106	71	16	11	11	6	10	231	4	235
Chi-Square Tests			Value			df		Asymp. Sig. (2-sided)		
Pearson Chi-Square			144.678a			24		0.001		
Likelihood Ratio			127.151			24		0		
Linear-by-Linear Association			65.649			1		0		
N of Valid Cases			231							

a. 27 cells (77.1%) have expected count less than 5. The minimum expected count is .13.

Table-5: Endovascular technique applied at different location with their outcomes.

Locations	Coiling only	Balloon Remodeling	Flow Diverter	Stent Assisted	Successful	Unsuccessful	Total Number
A Comm artery	77	3	0	2	82	11	93
A1	10	2	0	0	12	0	12
Basilar	16	1	0	0	17	1	18
DACA	7	0	0	0	7	0	7
ICA	22	2	4	15	43	5	48
ICA/MCA/Basilar	1	0	0	0	1	0	1
MCA	14	2	0	0	16	0	16
P Comm artery	24	0	0	0	24	2	26
PCA	5	0	0	1	6	0	6
PICA	2	0	0	1	3	1	4
Trigeminal artery	0	1	0	0	1	0	1
Vertebral artery	7	1	1	1	10	0	10
Total	183	12	5	20	222	20	242

A Comm: Anterior communicating. ICA: Internal cerebral artery. P Comm: Posterior communicating. MCA: Middle cerebral artery. A1: Anterior cerebral artery. DACA: Deep anterior cerebral artery. PCA: Posterior cerebral artery. PICA: Posterior inferior cerebral artery. DACA: Distal anterior cerebral artery.

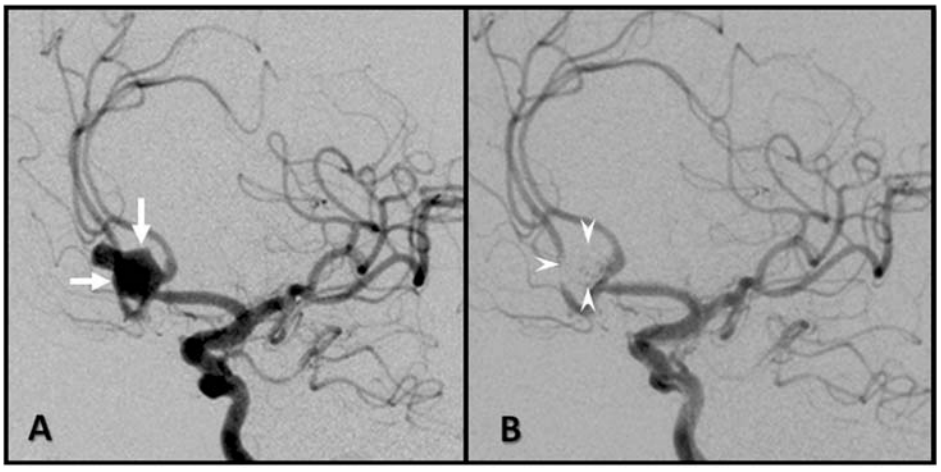

Figure-1: Digital subtraction angiography (DSA) of right internal cerebral artery (ICA) in oblique projections, before (A) and after (B) conventional coil embolisation: a large narrow-neck bilobed aneurysm of the anterior communicating artery (arrows) is seen, which was successfully coiled (arrowheads) using the conventional technique.

There were 7(2.9%) patients with missing information about aneurysm size, and 35(14.4%) patients had missing rupture/ unruptured data, 14(5.8%) had unknown neck orientation, 7(2.9%) had unknown H&H score, and 11(4.5%) had unknown mRS).

Further, 193(82.1%) patients presented with aneurysm size <10mm. Patients with aneurysms <10mm had greater proportion of ruptured aneurysms compared to patients with aneurysms >10mm (Table-1).

Aneurysms were located in the anterior communicating artery (A

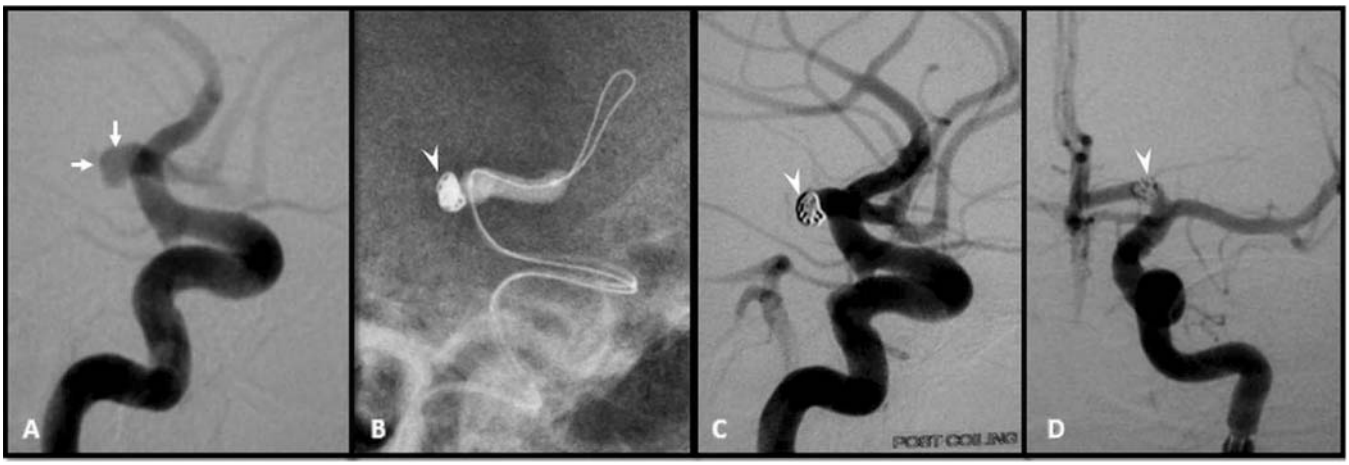

Figure-2: Digital subtraction angiography (DSA) of left internal cerebral artery (ICA) in oblique projections (A-C) and antero-posterior projection (D): demonstrating a small wide-neck saccular aneurysm (arrows) of A1 segment of left anterior cerebral artery (A). It was coiled (arrowheads) using balloon assistance (B). Post-coiling runs (C and D) show successful coiling using the balloon-assisted technique.

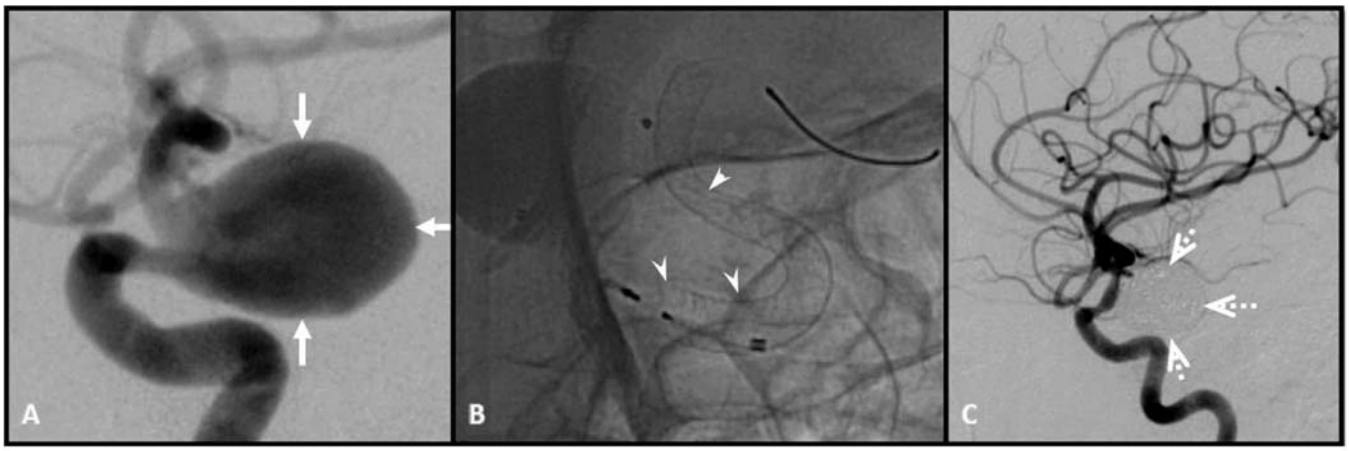

Figure-3: Digital subtraction angiography (DSA) of left internal cerebral artery (ICA) in oblique (A and B) and lateral projections (C): demonstrating a large wide-neck aneurysm (arrows) of supraclinoid part of left ICA (A). A flow-diverter (arrowheads) was successfully deployed across the aneurysm in ICA (B). Post-coiling run (C) shows successful embolisation of the aneurysm (dotted arrowheads) using the flow-diverter-assisted technique.

Comm) in 93 (38.4%) patients, ICA 48(19.8%) patients and posterior communicating artery (P Comm) 26(10.7%) patients (Table-2).

Initial H&H grading with aneurysm sizes, neck type and post-treatment outcome were noted (Table-3).

Findings suggested that patients with higher initial H&H grade were more likely to have higher mRS post-treatment (p=0.001) (Table-4).

Endovascular technique applied at different locations and their outcomes were recorded separately (Table-5). Overall, 20(8.2%) patients had unsuccessful results due to anatomical and technical difficulties. Post procedure complications were seen in 37(15.2%) patients. Of them, 21(8.6%) patients had major complications that included disabling stroke in 9(3.7%), coil migration in 4(1.7%), rupture in 6(2.4%) and spasm with poor outcome in 2(0.8%) patients. There were 10(4.1%) patients who died during follow-up: 4(1.6%) were procedure-related to, 1(0.4%) had infarction noted post-embolisation with an occluded clot in the left pericallosal main trunk, 1(0.4%) died of severe spasm in distal ICA and left anterior cerebral artery (ACA), and 2(0.8%) died due to rupture from basilar artery aneurysms.

Digital subtraction angiography (DSA) in different patients was carried out using the conventional technique Figure-1), the balloon-assisted technique (Figure-2), and the flow-diverter-assisted technique (Figure-3).

Discussion

To the best of our knowledge, the current study is the first on this topic conducted in Pakistan. Since the 1990s, treatment for intracranial aneurysm has seen drastic changes. New advancements are seen in both surgical and endovascular treatment modalities.[11] In the developed countries, like the United States, different modalities like flow diverter and balloon-assisted techniques have been compared with traditional endovascular coiling techniques.[12-14] As a developing country, the real challenges and limitations in Pakistan are with respect to the availability of required endovascular equipment, microsurgical techniques and surgical skills. This is the reason behind having few cases that involve use of stenting, balloon remodelling and flow diverters. Only 183(75.6%) patients were treated with coiling in the current study. Hence, it is not possible to compare different assisted modalities with traditional coiling endovascular technique.

However, compared to other studies, the study showed a large number of successful outcomes (91.7%) after therapeutic endovascular treatment, with low mortality (4.1%). This is comparable to a multi-centre study that had 96.9% and 94%, successful results of aneurysm coiling in ruptured and unruptured aneurysms, respectively, and mortality of 8.6% in ruptured aneurysms and 7.7% in unruptured aneurysms.[15,16] The current study saw greatest number of aneurysms arising from A Comm (93 cases) followed by ICA (48 cases). Similar findings were reported by other studies.[17,18]

IAs are mostly silent, but can rupture unpredictably, leading to grave consequences and even immediate death. Even in developed countries, like the United Kingdom, deaths are reported in 10-15% patients with ruptured aneurysm before they reach hospital.[19] Similarly, many patients die before reaching hospitals in Pakistan. In 2009, a 5-year retrospective review was done at the AKUG on the success, safety and outcome of coiling, reporting only 43 aneurysm cases.[20] The current 15-year audit had a much larger study population of 242 patients, indicating an increase in the number of reported cases of ruptured and unruptured aneurysm since 2009. In the current study, patients with aneurysm size >10mm had lesser proportion of ruptured aneurysm compared to patients with aneurysm size <10mm. This could be one of the reasons explaining why no significant increase was seen in the number of ruptured aneurysms as the aneurysm size increased from ≤5mm to 5-10mm and more.

Several scales have been designed based on patient's initial clinical presentation at the time of admission to predict patient's future functional outcome. Multiple clinical assessors are involved in a research and the inter-rater variability should be considered when interpreting the results. A study on inter-observer variability in grading scale of SHAs included grading scales, like the World Federation of Neurological Surgeons (WFNS) scale, the H&H scale and the Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage (PAASH) scale, and showed H&H scale to have the lowest inter-observer agreement.[21] In the current study, no large number of patients were seen with aneurysm size 5-10mm or ≥10mm. Likewise, wider necks having higher H&H grades were not seen. This could be due to the involvement of multiple clinical assessors for grading and inter-observer variability.

Studies based on Nationwide Inpatient Sample (NIS) (n=148,958) to analyse NIS SAH Severity Score (NIS-SSS) and NIS-SAH Outcome Measure (NIS-SOM) concluded that NIS-SSS and NIS-SOM significantly correlated with H&H grade and mRS respectively. Compared to other grading systems, the study found NIS-SSS and NIS-SOM to be better and provided valid measure of severity and outcome respectively.[22] In relation to this, the results of the current study further prove that patients with lower initial H&H score were more likely to have better clinical outcome with lower mRS scores, while patients with higher initial H&H grade were more likely to have higher mRS after receiving endovascular treatment.

The Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have approved pipeline embolisation device (PED) for the treatment of large or giant, wide-neck intracranial aneurysms of ICA from the petrous to the superior hypophyseal segments. However, the flow divertor does not have the approval to be used for posterior circulation, treatment of aneurysmal SAH, or in the anterior circulation beyond the ICA superior hypophyseal segment. This device is only approved for use in the United States. Additionally, in Europe, PED, silk flow diverter, flow-redirection endoluminal device (FRED), p64 (phenox), surpass streamline and derivo are the available therapies. Due to lack of enough studies, it is not possible to comment on long-term outcomes of these new devices.[23] A recent study concluded that since there has been rapid development of endovascular therapy treatment for IAs, the challenge for the physicians is to adapt accordingly.[24]

In future, further research can be done exploring the type of aneurysm in greater detail, comparing pre-existing risk factors in South-Asian population in ruptured aneurysms, and having greater number of patients treated with assisted modalities, like endovascular balloons, stents, flow diverters and glue-assisted treatments.

One of the limitations of the current study, however, is missing data. All possible efforts were made to extract the relevant required data, but considering this is a 15-year retrospective data review, it was expected that some degree

of missing data records will be encountered. As the current study was an audit of the Interventional Radiology (IR) department, hence it focussed on morphology of aneurysm that appeared on imaging at the time of presentation and the outcomes after therapeutic endovascular treatment. Other secondary demographic details that were not relevant to the study's objectives were not recorded. Moreover, there were only a few patients with aneurysm >10mm (42/235; 17.9%) and mostly coiling was practised (75.6%), which accounts for the similarities seen in success rates among different aneurysm sizes.

Conclusion

Large number of patients with intracranial aneurysms showed successful outcome after treatment with endovascular coiling alone. No correlation was seen between H&H grades and aneurysm severity based on aneurysm size, neck orientation and ruptured/unruptured nature. Patients with higher initial H&H scores were more likely to have higher post-treatment mRS.

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