Turk Neurosurg 32(1):52-57, 2022

Original Investigation

DOI: 10.5137/1019-5149.JTN.32533-20.3

Received: 25.09.2020
Accepted: 05.01.2021

Published Online: 28.06.2021

Risk Factor Assessment and Outcomes of Intra Procedural Rupture of Intracranial Aneurysm During Endovascular Treatment: A Race Against Time

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ABSTRACT

AIM: To identify the risk factors for aneurysmal intra-procedural rupture (IPR) of intracranial aneurysms suring endovascular treatment, and to discuss its management and outcomes.

MATERIAL and METHODS: A total of 106 patients with cerebral aneurysm who have undergone endovascular treatment (EVT) were included in this study, with a mean follow-up period of 17.2 months. Risk factors for IPR, such as the aneurysm's location, size and morphology, etc. were evaluated, and the chi-squared test was used for statistical analysis. Clinical outcomes were assessed using the modified Rankin scale (mRS) at 15 months.

RESULTS: Among all 106 patients who have undergone EVT, five (4.7%) had aneurysmal IPR as well as ruptured aneurysms with subarachnoid haemorrhage (SAH). Among those five patients, primary coiling was performed in three cases and balloon/stent-assisted coiling was performed in two cases, with complete occlusion of the aneurysmal sac achieved in four (4/5) patients. Clinical follow-up with the mRS scores of the patients revealed mortality in one patient (20%), favourable outcomes in three patients (60%) and unfavourable outcomes in one patient (20%).

CONCLUSION: Aneurysmal IPR is considered a rare but important complication of endovascular coiling that is associated with poor clinical outcomes. Several risk factors are significantly associated with IPR, such as small-sized aneurysm (<3.5 mm), presence of bleb and parent vessel tortuosity. Acom location, irregular shape and past episode of SAH also increase the risk of IPR, but such association was found to be statistically insignificant in our study. Although IPR is considered a devastating complication, good clinical outcomes can be achieved with early detection and proper management using rapid aneurysmal coil packing and occlusion.

KEYWORDS: Aneurysm, Endovascular, Intraprocedural, Rupture, Risk factors

ABBREVIATIONS: IPR: Intra procedural rupture, **EVT:** Endovascular treatment, **SAH:** Subarachnoid haemorrhage, **HHS:** Hunt and Hess scale, **mRS:** modified Rankin scale, **DSA:** Digital subtraction angiography, **MRA:** Magnetic resonance angiography, **ICA:** Internal carotid artery, **Acom:** Anterior communicating artery, **Pcom:** Posterior communicating artery

INTRODUCTION

Intra-procedural rupture (IPR) of cerebral aneurysms is a serious complication of endovascular treatment (EVT) that is associated with a high rate of mortality and poor outcomes. Generally, IPR is a relatively rare complication of EVT, with a reported incidence rate of 2%–5% in various case series (2,4,11,14). Although many previous studies have placed emphasis on the management and outcomes of patients with IPR (2,8,10,14), only very few studies have reported on the risk factors responsible for aneurysmal IPR. Despite its rarity, IPR is associated with a high rate of mortality and poor outcomes in up to 60% of the cases (4,10). Therefore, it is important to identify the risk factors for aneurysmal IPR to improve the

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patient outcomes. In this study, we evaluated the possible risk factors for aneurysmal IPR and discussed its management and outcomes for patients.

MATERIAL and METHODS

A total of 106 patients with cerebral aneurysm who have undergone EVT from October 2018 to October 2020 at our institute were included in this study. Cases were divided into 90 cases with ruptured aneurysm and 16 cases with unruptured aneurysm. It was found that five patients had IPR and that all of them had ruptured aneurysms with subarachnoid haemorrhage (SAH). Risk factors for IPR were evaluated, such as the aneurysm's location, size and morphological characteristics, as well as parent artery tortuosity. Patients with IPR were also compared to those without in terms of the presence of risk factors for IPR. The odds ratio (OR) was then calculated, and the chi-squared test was used to determine the p-value. Clinical outcomes were assessed using the modified Rankin scale (mRS) at 6 and 15 months and were graded as good (score: 1–3), bad (score: 4–5) or worse (score: 6, death), with a follow-up period of 16–19 months (mean: 17.2 months). Then, a literature review was conducted to discuss the possible causes of aneurysmal IPR as well as its management.

Procedure

All patients who were admitted with aneurysmal SAH or unruptured aneurysms were examined and graded clinically using the Hunt and Hess Scale (HHS) on admission. All patients underwent EVT under general anaesthesia through the right femoral route using an Infinix-i Biplane angiography suite (Toshiba America Medical Systems, Tustin, CA, USA). After femoral puncture, all patients were heparinised with a 100 IU/kg heparin bolus (activated clotting time: >300 s). Digital subtraction angiography (DSA) was performed on the region of interest in a 3D rotation view. Then, reconstructed images of 3D angiography were used to characterise the size, shape and morphology of the aneurysm. After evaluating the aneurysm, a decision was made regarding the appropriate type of procedure needed (coiling, stent/balloon-assisted coiling or a flow diverter) and hardware to be used (catheter, distal access or micro-catheter). Patients who were planned for stent-assisted coiling were given dual antiplatelet agents (300 mg of aspirin and 30 mg of Prasugrel) through Ryles tube, with intravenous Abciximab administered in a few cases. EVT was performed using high-resolution DSA and proper road map guidance carefully with check DSA after each coil placement. After ensuring satisfactory aneurysm occlusion and completing the procedure, patients were moved to the intensive care unit (ICU) and their puncture sheath was removed after 4–6 hours with compression dressing. All patients were then discharged after spending variable amounts of time in the ICU depending on their recovery rate, and all of them were followed up radiographically with DSA/computed tomography (CT) angiography or magnetic resonance angiography and their clinical outcomes were assessed using the mRS at 16–19 months.

RESULTS

Among the 106 patients who have undergone EVT, five (4.7%) had aneurysmal IPR, which is defined in our study as the extrusion of coil, micro-wire or catheter outside the aneurysmal sac with evidence of extravasation of contrast on angiography. It should be noted that all five patients with IPR had previous episodes of SAH (three males, two females; mean age: 63 years). HHS of patients on admission was (1,2-good, 3- moderate, 4,5-bad) good in 2, moderate in 2 and bad in 1 patient.

Risk Factors for IPR

Evaluating the risk factors for IPR showed that the most common location observed in IPR was Acom in three cases (60%), with an OR of 2.2, followed by one case with MCA and another with ICA-Pcom. It was observed, however, that an aneurysm located at Acom increased the risk for IPR, though statistically insignificantly (p=0.37).

Evaluation of the aneurysm's morphology revealed an irregular aneurysm shape (bi-lobed or multi-lobed) and the presence of a visible bleb or nipple, which are associated with an increased risk for IPR (OR=1.86, p=0.5 and OR=8.62, p=0.058, respectively), though statistically insignificantly.

Aneurysms that are 3.5 mm or smaller are considered to be 'small sized' for evaluating the risk of rupture. In this study, a small-sized aneurysm (≤3.5 mm) has been observed to be a statistically significant risk factor for IPR, with four patients having small aneurysms (OR=11.53, p=0.032).

We also evaluated the presence of parent artery tortuosity (ICA in our study as all IPR cases anterior circulation) as a risk factor for IPR. Arterial tortuosity generally increases the stored potential energy in delivery systems, which can indirectly lead to IPR. In this study, it was found that parent artery tortuosity is statistically significantly (p=0.048) associated with aneurysmal IPR, with four patients (80%) having this condition (OR=9.4).

It was also found that the presence of previous episode of SAH increased the risk for IPR (OR=2.12) in our study. The association is statistically insignificant (p=0.61) though all patients with IPR had SAH only because of the overall more incidence (85%) of SAH cases in our sample population. Although intra-operative hypertension may possibly increase the incidence of IPR, only one patient had a hypertension episode in our study (Table I).

Management

In this study, the causes for IPR were evident in four out of the five cases: coil mass in three patients and micro-catheter in one patient. In the remaining patient, rupture occurred while doing angiography to prepare a roadmap image before aneurysmal cannulation.

After identifying the IPR, reversal of heparinisation was performed immediately with protamine sulphate (1 mg/100 IU), and blood pressure was reduced to a permissible range (systolic blood pressure: 85–95 mmHg) by infusing Propofol. Then, the depth of anaesthesia was increased using Thiopentone or midazolam to reduce cerebral metabolism.

Primary coiling was completed in three of the five patients by gradually filling soft coils until the leak stops. One patient with a persistent leak after two coils required balloon assistance to occlude the neck and place the coil. In one patient with an ICA-Pcom aneurysm, a second micro-catheter was used and stent-assisted coiling (Enterprise 2; Codman) was performed. This patient developed parent artery thrombosis due to stenting, which resolved after the intra-arterial injection of Abciximab with development of post-operative hemiparesis, which improved partially over months.

Outcome

Post procedural CT scan revealed intra-ventricular haemorrhage in one patient, who died after two days even after placing an external ventricular drain (EVD), resulting in an overall IPR case mortality of 20%. Two patients developed hydrocephalus and required shunt procedures, which resulted in favourable recovery. Complete occlusion of the aneurysmal sac was achieved in four patients, and partial occlusion was achieved in one patient (MCA aneurysm), who was subsequently treated. Clinical follow-up with the mRS scores of the patients (mean: 17.2 months) revealed good recovery in three (60%) patients and poor recovery in one (20%) patient (Table II).

Illustrative Cases

1) A 50 years' male patient with small sized (3.4 x 2.5mm) ruptured Acom aneurysm presented with HHS 2 (case-1), had IPR with microcatheter extrusion and dye extravasation evident on DSA. Patient managed with reversal of heparinization, lowering of blood pressure and coiling continued. After completion of coiling aneurysm completely occluded. Patient was electively ventilated for 24 hours, and shifted out of ICU after extubation. Patient had good recovery and discharged on 8th day without any neurological deficit with 17 months follow up mRS score of 1 (Figure 1A-D).

2) 58 years' female presented with SAH and 4.8 x 3.6 sized multilobed right MCA aneurysm with HHS of 2 (case-4). She had IPR of aneurysm before sac cannulation while taking DSA. Exact cause of IPR not determined but postulated to be due to contrast injection pressure jet into the sac. Aneurysm was cannulated and coiling of aneurysm was done and leak stopped after 3 coil placement. Small part of neck visible after partial coiling was left due to risk of rerupture to be dealt afterwards in second intervention if required. She developed hydrocephalus on follow up CT scans and had undergone CSF diversion procedure. Her mRS score at 15.3 months is 1 showing good recovery (Figure 2A-D).

DISCUSSION

It has been reported in several previous studies that the incidence of aneurysmal IPR during coil embolisation ranges from 2% to 5% (2,4,11). In their meta-analysis, Cloft et al. mentioned that the incidence of IPR is high in cases with ruptured aneurysm (up to 7.7%), and quite low in cases with

Table I: Risk Factors for IPR of Aneurysm

Risk factor	IPR patients (n=5)	Non IPR patients (n=101)	Odd's ratio	p
Acom location	3	40	2.2	0.376
Small size (3.5 mm or less)	4	26	11.53	**0.032**
Irregular shape	3	45	1.86	0.5
Presence of bleb	4	32	8.62	**0.04**
Vessel tortuosity	4	30	9.4	**0.048**
Previous SAH	5	85	2.12	0.61
HTN	2	43	0.91	0.92

IPR: *Intraprocedural rupture,* ***SAH:*** *Subarachnoid haemorrhage,* ***HTN:*** *Hypertension.*

Table II: Patient Characteristics and Outcome

Sr. No	Age (years)	Location	Size (mm)	Cause of IPR	HHS on admission	mRS score	Outcome
1	50	Acom	3.4x2.5	Cath.	2	1	Good
2	62	Acom	3.1x3	Coil	3	3	Good
3	71	Acom	2.4x2.4	Coil	3	6	Death
4	58	MCA	4.8x3.6	ND	2	1	Good
5	74	ICA-Pcom	3.1x2	Coil	4	4	Bad

HHS: *Hunt and hess scale,* ***ND:*** *Not determined,* ***mRS:*** *Modified Rankin scale.*

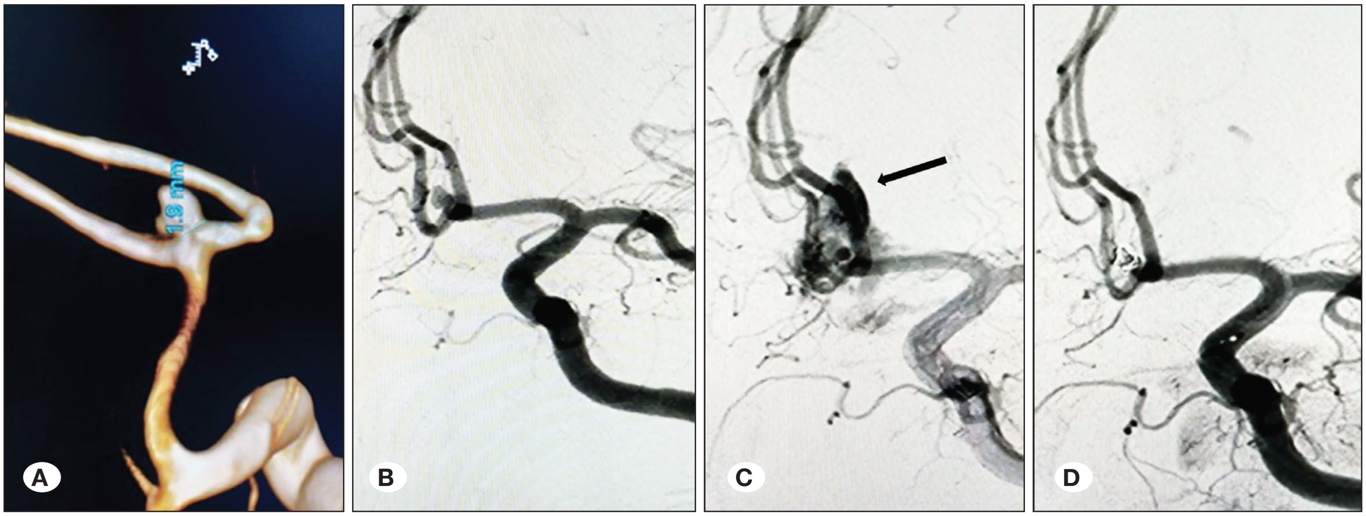

Figure 1: Illustrative case 1. Patient of ruptured Acom aneurysm with neck of 1.9mm. **A)** 3D image showing aneurysm morphology and irregular shape, **B)** DSA image of aneurysm, **C)** IPR evident with dye leak denoted by black arrow, **D)** DSA image after completion of coiling and sac occlusion.

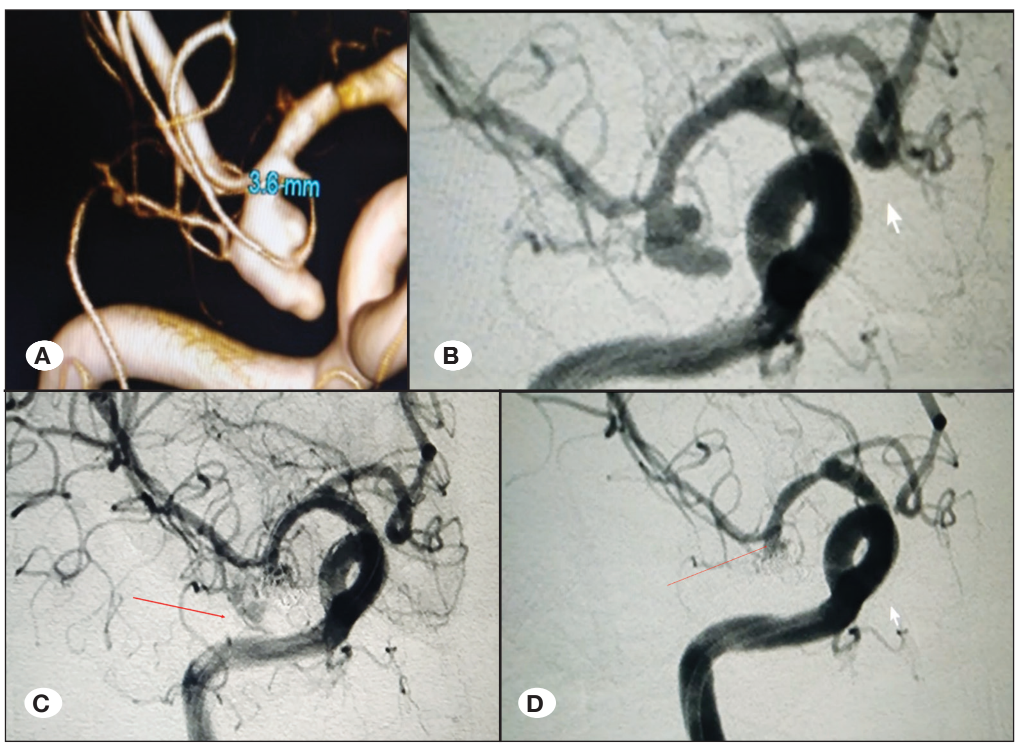

Figure 2: Illustrative case 2. Patient of ruptured right MCA bifurcation aneurysm with neck of 3.6mm. **A)** 3D image with multi-lobed irregular aneurysm with bleb, **B)** DSA image of aneurysm, **C)** IPR is evident with dye leak denoted by thick red arrow, **D)** image after completion of partial coiling with no dye leak and remaining part of neck denoted by thin red arrow.

unruptured aneurysm (ranging from 1% to 2%) (2). In our study, we found that the incidence of IPR is higher (4.9%), with all five patients with IPR having ruptured aneurysms. However, none of the patients with unruptured aneurysms were found to have IPR in our study. Such a higher rate of IPR may be explained by the large percentage of cases with ruptured aneurysms (90 out of 106) in our study.

Several previous studies have investigated the risk factors for IPR and proposed that an aneurysm located at Acom is considered an independent risk factor for IPR, with an incidence rate of 7% (5-7,17). Similar finding was observed in our study, with most patients (three out of five) with IPR having an Acom aneurysm.

According to Sujuki et al., Tsutsumi et al. and Rooij et al., small-sized aneurysms are considered a high risk factor for IPR because of the less available space for coil mass and fragile walls (16-18). In our study, similar to what has been found in previous studies, small-sized aneurysms (3.5 mm or less) were considered a statistically significant risk factor for IPR, observed in 80% of the cases.

Several previous studies like Doerfler et al., Kang et al. and Lim et al., have described irregularly shaped aneurysms and bi-lobed/multi-lobed aneurysms as risk factors for IPR (3,7,12). In our study, we also evaluated the presence of visible bleb or nipple as an independent risk factor in addition to irregular shape. As noted in our series, both of these factors increased the risk of IPR and presence of bleb or nipple have statistically significant association with IPR. Generally, high-resolution 3D reconstructed images are required for the proper identification of blebs and predicting IPR.

Other possible risk factors that have been mentioned in the literature are intra-operative hypertension, cardiac comorbidities, atherosclerosis and parent artery tortuosity (9,12). In our study, parent artery tortuosity, which results in technical difficulties during the procedure, was considered a significant risk factor for IPR, a notion that has not been much highlighted in previous studies. Arterial tortuosity increases the stored potential energy in delivery systems, which increases the jerky movements of both the micro-catheter and guidewire, thereby causing IPR. Therefore, we recommend using a long rigid sheath with soft intra-cranial support catheters (Navien, ev3, Covidien/Fargo line, Balt), which may reduce the incidence of IPR in cases of parent artery tortuosity.

As outlined in previous studies, the causes of IPR are micro-catheters, guidewires, coil mass, increased blood pressure and contrast injection jet pressure (13). In our study, the most common causes of IPR observed were coil mass in three patients (60%), micro-catheter in one patient and contrast injection jet pressure in one patient.

In all our cases of IPR, immediate reversal of heparin was performed with complete packing of the aneurysm sac as rapidly as possible to stop the leak. Heparin reversal and lowering of blood pressure have been recommended in previous studies for the management of IPR (1). However, increased thromboembolic events have been reported in IPR cases as a result of heparin reversal, necessitating the cautious use of antiplatelet agents (15). One patient in our study developed parent artery thrombosis after the completion of stent-assisted coiling and was given intravenous abciximab. Although thrombus resolution was confirmed on angiography, the patient developed neurological deficits and infarcts, which partially recovered. Therefore, it is important to consider the time of event and to take quick steps to pack the aneurysmal sac to stop the leak and, hence, achieve favourable outcomes. Many studies have reported aneurysm occlusion rates ranging from 80% to 90% in cases of IPR and emphasised the importance of partial coiling to avoid re-rupture as a result of excessive packing (15,20). In this study, complete aneurysmal occlusion was possible in four of the five patients and partial coiling was performed in one patient.

Several previous studies have reported that aneurysmal IPR is associated with a high rate of mortality (ranging from 50% to 60%) and poor outcomes (2,10,11,14). However, recently, advances in endovascular technology with the progressive development of soft coils and newer techniques have improved the outcomes of IPR cases, achieving a mortality rate of 10%–20% (1,15,19-21). In our study, the clinical outcomes of patients with IPR, measured on the mRS (mean follow-up of 17.2 months), were favourable in 60% (3/5) of the cases. Moreover, one patient with IPR died (mortality rate: 20%), and one had poor clinical outcome with severe disability.

CONCLUSION

Aneurysmal IPR is considered a rare but important complication of endovascular coiling that is associated with poor clinical outcomes. The presence of a small-sized aneurysm (<3.5 mm), the presence of bleb and parent vessel tortuosity are significantly associated with an increased risk for IPR. Whereas Acom location, irregular shape and a past episode of SAH also increase the risk for IPR, although such association has been found to be statistically insignificant in our study. Although IPR is considered a devastating complication, it is possible to obtain favourable clinical outcome by early detection and proper management with rapid aneurysmal coil packing and occlusion.

AUTHORSHIP CONTRIBUTION

Study conception and design: DKS, VP

Data collection: VP, KY

Analysis and interpretation of results: VP, KY

Draft manuscript preparation: VP

Critical revision of the article: KY, DKS

Other (study supervision, fundings, materials, etc...): VP, KY

All authors (VP, KY, DKS) reviewed the results and approved the final version of the manuscript.

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