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Clinical Article

Predictor and Prognosis of Procedural Rupture during Coil Embolization for Unruptured Intracranial Aneurysm

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Objective : The objectives of this study was to determine the incidence and outcomes of procedural rupture (PR) during coil embolization of unruptured intracranial aneurysm (UIA) and to explore potential risk factors.

Methods : This retrospective study evaluated 1038 patients treated with coil embolization between January 2001 and May 2013 in a single tertiary medical institute. PR was defined as evidence of rupture during coil embolization or post procedural imaging. The patient's medical records were reviewed including procedure description, image findings and clinical outcomes.

Results : Twelve of 1038 (1.1%) patients showed PR. Points and time of rupture were parent artery rupture during stent delivery (n=2), aneurysm rupture during filling stage (n=9) and unknown (n=1). Two parent artery rupture and one aneurysm neck rupture showed poor clinical outcomes [modified Rankin Scale (mRs) >2] Nine aneurysm dome rupture cases showed favorable outcomes (mRS ≤2). Location (anterior cerebral artery) of aneurysm was associated with high procedural rupture rate ($p<0.05$).

Conclusion : The clinical course of a patientwith procedural aneurysm rupture during filling stage seemed benign. Parent artery and aneurysm neck rupture seemed relatively urgent, serious and life threatening. Although the permanent morbidity rate was low, clinicians should pay attention to prevent PR, especially when confronting the anterior cerebral artery aneurysm.

Key Words : Procedural rupture · Intracranial aneurysm · Endovascular · Unruptured.

INTRODUCTION

The prevalence of intracranial unruptured aneurysm has been reported as 3.2% in the general population[21]. Although previously reported annual rupture rates are low[22], preventive treatments are widely accepted and performed. When coil embolization was approved as a treatment for intracranial aneurysm surgical treatment was the only option[3]. Over the next 2 decades various coil embolization techniques have been applied worldwide.

Coil embolization has some benefits in treating an intracranial aneurysm. It can be performed without major craniotomy. Therefore it is less influenced by a patient's general medical condition and can easily meet the patient's preference. The symptomatic complication rate was not inferior to surgical treatment[4]. A higher thromboembolic complication rate has been described but most thromobembolic events are asymptomatic and does not usually influence cognitive functions[10,12,18].

Although procedural rupture (PR) accounts for a small percentage (0.5−4%) of complications during coil embolization but can be disastrous with severe morbidity or mortality (20−40%)[2,17]. However, conclusions are hindered by the relatively small study populations and heterogeneous nature of the patients with ruptured and unruptured intracranial aneurysms[2,17,23]. PR during coil embolization for aneurysms with subarachnoid hemorrhage (SAH) cannot demonstrate the outcomes of procedural rupture due to the renowned poor outcome of the preexisting SAH[15].

We reviewed more than 1000 consecutive cases of coil embolizations for unruptured intracranial aneurysms performed at our institution over the past 12 years to identify the incidence and outcomes of PR and to explore potential risk factors of PR.

MATERIALS AND METHODS

We retrospectively reviewed all unruptured saccular aneurysm cases treated with coil embolization in a tertiary academic

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hospital between January 2001and May 2013. This consisted of 1086 aneurysm coil treatment procedures in 1038 patients. Exclusion criteria were ruptured aneurysms, mycotic aneurysms, and dissecting aneurysms. Data collected from medical records and imaging findings included age, sex, size, and location of aneurysm, type of endovascular procedure, type of rupture, postprocedural management, and clinical status of PR patients until the latest follow-up. Demographic characteristics were documented and video file records were reviewed to identify PR during procedure and/or postoperative imaging. The aneurysm size was documented from the operative notes during the coil embolization and/or procedural imaging. Aneurysm locations were categorized as anterior cerebral artery, middle cerebral artery, distal internal cerebral artery, posterior circulation, and multiple according to their location.

PR was defined as angiographic visualization of the extravascular leakage of contrast medium or identifiable SAH on post procedural computed tomography (CT) and/or magnetic resonance imaging (MRI). In our strategy, We performed immediate postprocedural CT and MRI according to physician's or patient's preference or any neurologic deterioration. PR was investigated with respect to timing, location of rupture, and clinical outcomes. PR was categorized as procedural parent artery rupture (PPAR) and procedural aneurysmal rupture (PAR) according to rupture site (Fig. 1). In one case where the rupture site was not identified during procedure, hemorrhage was assumed to be PAR. Out of concern that PPAR might result from a mechanism other than PAR, statistical analyses were performed regarding for PAR solitarily. Modified Rankin Scale (mRS) was used to assess clinical outcomes after PR.

Procedure

All aneurysm coiling procedures were performed using a commercially available biplane angiographic unit equipped with an image-intensifier. Rotational angiography, followed by three-dimensional image reconstruction by volume rendering, was performed before embolization in all patients. Final angiograms in the frontal and lateral projections and working projections were acquired at the end of each procedure in order to rule out distal branch occlusions. All patients were treated while under general anesthesia and systemic heparinization was administered after placement of the femoral introducer sheath.

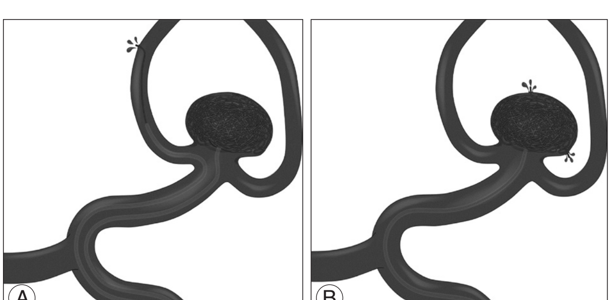

Fig. 1. Schematic images demonstrating type of rupture in this study. Types of rupture were categorized into two types–procedural parent artery rupture (A), procedural aneurysm (dome or neck) rupture (B) during coil embolization.

In line with our embolization protocol, 3000 IU/60 kg of heparin was administered as an intravenous bolus injection, followed by an additional 1000 IU with routine activated coagulation and thromboplastin time check. After embolization, heparin injection was continued for 24 hours in patients treated with stent assisted coil embolization and for selected cases without stent assisted coil embolization. All aneurysm embolizations were performed using commercially available detachable coils including hydrogel-coated coils, Guglielmi detachable coils, or other bare platinum coils. Each femoral puncture site was closed using a commercially available closing device. Balloon, stent, or catheter assisted coil embolization has been chosen for coil embolization of aneurysms with an unfavorable configuration. Procedure related factors such as embolization methods (conventional or adjunctive device, such as balloon or stent assisted technique) were also included.

Statistical analyses

Univariate and multivariate statistical analysis was performed to explore the potential risk factors of PAR. Frequency comparison was performed using the Fisher exact test. Multiple logistic regression test was used for multivariate analysis. Differences were considered significant at $p<0.05$. Statistical analysis was performed with SPSS 20.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Among 1086/1038 saccular aneurysm/patients coil embolization, 34 (3.2%) cases were retreated. Baseline characteristics of the patients are described in Table 1. All data for each variable of interest were fulfilled. PR occurred in 12 patients (1.1%). Rupture points of these patients were parent artery (n=2), aneurysm itself (n=9), and unknown rupture site (n=1). Eleven PRs were identified during coil embolization and one PR was identified on a post-procedural CT. Two parent artery ruptures probably occurred during the stent delivery procedure (Fig. 2). Nine aneurysm ruptures occurred during filling stage after frame coil insertion. Among 10 cases of aneurysm rupture, eight occurred in the aneurysm dome area, one occurred in the aneurysm neck, and one was unknown (Table 2).

Additional coil insertion was performed in all cases with aneurysm rupture. Protamine sulfate was applied in the patients with aneurysm neck rupture because of procedural difficulties during additional coil insertion in the rupture point. Postprocedural CT of the Patient with aneurysm neck rupture showed extensive subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH) and intraventricular hemorrhage (IVH). Except this patient, 8 out of 9 aneurysm rupture showed mild to moderate subarachnoid hemorrhage.

Contrast leakage of one parent artery rupture was stopped spontaneously with thrombus formation. Other parent artery rupture showed prolonged contrast leakage despite of protamine sulfate and proximal balloon occlusion. Postprocedural CT showed extensive ICH, IVH, and SAH in both patients.

Two patients with parent artery rupture and one with aneurysm neck rupture received subsequent craniectomy with hematoma removal but showed poor outcome at latest follow up. After 3, 19, and 39 months of follow-up, mRS of these patients were 5, 4, and 4, respectively.

Among 8 patients who experienced aneurysm dome rupture during filling stage and one patient with unknown rupture site, 1 patient received a external ventricular drainage temporarily and three patients received serial spinal tapping for the coexisting hydrocephalus. Nevertheless none of the patients required permanent shunting. After 34 months (median, range 4–59) of follow-up, morbidity or mortality were absent (mRS=0), except for one patient (mRS=2) complicated by subsequent ischemic insult on the parent artery.

Among 10 patients with aneurysm rupture, six were anterior cerebral artery aneurysms and the location of aneurysm was the only associated factor of PAR (anterior cerebral artery vs. others=6/184 vs. 4/854, p=0.003 Fisher-exact test). Other variables such as age (<65 vs. ≥65, p=0.500), sex (p=0.382), aneurysm size (<10 mm vs. ≥10 mm, p=0.397) or usage of stent or

Table 1. Baseline characteristics of the patients

Characteristics	Value (No. of procedural aneurysm rupture)
Gender (male/female)	312/726 (2/8)
Age	57.1±10.1 (mean±standard deviation)
Location of aneurysm	
Distal ICA	624 (2)
ACA	184 (6)
MCA	53 (0)
Posterior circulation	130 (1)
Multiple	47 (1)
Coil technique	
Simple	690 (7)
Balloon assisted	52 (0)
Stent assisted	296 (3)
Aneurysm size	
<10 mm	899 (8)
≥10 mm	139 (2)
Retreatment	34 (0)

ICA : internal cerebral artery, ACA : anterior cerebral artery, MCA : middle cerebral artery

Fig. 2. Digital subtracted angiography showed contrast leakage (arrow) at distal anterior cerebral artery after stent deployment.

Table 2. Detailed information of the patients with procedural rupture

	Age (year)/ sex	Location of aneurysm	Size (mm)	Technique	Rupture point	Follow up periods (months)	mRS at latest follow up	Note
1	57/F	A-com	5.1	Simple	Dome	121	2	Subsequent infarct ACA
2	52/F	Basilar tip	4.0	Simple	Dome	59	0	Serial spinal tapping
3	57/F	A-com	4.3	Simple	Dome	31	0	NC
4	61/F	A-com	4.3	Simple	Dome	38	0	NC
5	62/F	A-com	9.2	Stent assisted	Parent artery	39	4	Craniectomy hematoma removal
6	65/F	A-cho	10.1	Stent assisted	Dome	37	0	EVD
7	47/F	A-com	3.9	Simple	Dome	36	0	Serial spinal tapping
8	53/M	A-com	3.8	Simple	Neck	25	5	Craniectomy hematoma removal
9	74/F	A-com	4.7	Stent assisted	Parent artery	20	4	Craniectomy hematoma removal
10	78/F	A 2/3	3.9	Simple	Dome	10	0	NC
11	71/F	P-com	10.2	Stent assisted	Dome	7	0	Serial spinal tapping
12	53/F	Ophthalmic (bilateral)	7.1	Stent assisted	Unknown	7	0	NC

A-com : anterior communicating artery, A-cho : anterior choroidal artery, ACA : anterior cerebral artery, NC : no comment, EVD : external ventricular drainage

Table 3. Uni- and multivariate analysis results for risk factor of aneurysmal rupture during coil embolization

	Univariate analysis	Multivariate analysis	Odds ratio	95% confidence interval	
				Lower	Upper
Male gender	0.382	0.160	3.189	0.633	16.058
Age (≥65)	0.500	0.883	1.110	0.277	4.445
Size of aneurysm (mm) (≥10 vs. <10)	0.397	0.336	0.449	0.088	2.293
Technique					
Stent assisted vs. others	0.572	0.379	0.507	0.112	2.299
Aneurysm location					
ACA vs. Others	0.003	0.000	13.333	3.125	55.556

not (p=0.572) did not show statistically significant difference. Multivariate analysis supported the results of univariate analysis. The ACA location was the only associated factor with procedural aneurysm rupture (p<0.001; odds ratio, 13.333; 95% CI 3.125−55.556). Aneurysm size did not show statistical significance in uni- and multivariate analyses in this study (Table 3).

DISCUSSION

In our case series eight aneurysm dome ruptures occurred during filling stage. Fortunately, all of these cases and unknown site leakage cases showed favorable outcomes with independency at the latest follow up. However one aneurysmal neck rupture showed poor outcome. This may reflect different in flow dynamics during coil embolization. Flow arrest identified by contrast stasis at the distal portion (dome area) of aneurysm from coil material is frequently identified during coil embolization[1,8]. Hwang et al.[8] reported that 73.1% of contrast stasis was located at the dome area. Rupture of these areas can be benign due to spontaneous thrombus formation. Thrombus formation can be facilitated by low flow rate and foreign material at the dome portion of aneurysm even after frame coil insertion[16]. Therefore, extravasation might be minimal in PR at the dome area during the filling stage. However the neck portion of aneurysm can be considerably influenced by a parent artery flow rather than the dome portion by coil material, especially given a loosely packed aneurysm status[11]. Technical difficulty of additional coil insertion conducted in the neck area may also be a reason of prolonged blood leakage. When PR occurs in a loosely packed neck position these factors may cause huge extravasation of blood and poor clinical outcomes.

Most previous studies on PR focused only on aneurysm rupture during coil embolization[2,6,17]. But our results show that parent artery injury can actually occur and seems to trigger more disastrous complications. Aneurysmal ruptures can be corrected in selected cases by an endovascular technique, such as additional coil insertion or temporary flow arrest using balloon[17,23]. Distal parent artery perforation may be difficult to control through the endovascular technique in our experience and could result in poor clinical outcomes. Therefore excessive precaution is essential when approaching the distal angulated portion, especially when using adjunctive device. Development of a safer stent delivery system seems necessary in manipulating the distal vascular territory.

Interestingly, 8 of 12 PR, and 6 of 10 PAR events occurred in ACA. This may reflect the difficult anatomical characteristics for endovascular coil embolization of the ACA aneurysm, such as unfavorable dome neck ratio and acute ICA-A1 angle[5]. Previous studies on coil embolization for ACA aneurysm also demonstrated high risk of rupture[20]. Additionally the surgical manipulation of this area remains challenging due to the fact of multiple vital perforating arteries and high risk of premature rupture[7], which makes it difficult to say if substitutional surgical method can be preferred. Also ACA located aneurysm had high risk of rupture even small sized aneurysm if left untreated[9,14,19,22]. To the best of our knowledge, there is no absolute guideline in treating ACA aneurysms. An interdisciplinary approach to ACA aneurysm is needed and a more careful procedure is required. Further prospective controlled studies comparing the outcomes between treatment modality and risk factors in treating ACA aneurysms could increase better understanding and may help determine appropriate treatment strategy.

All PARs occurred during the filling stage in this study. This finding reflects a technical limitation. During aneurysm selection and frame coil insertion, an experienced operator can see and predict the motion of microcatheters, microwires, and coil material. Detached coil materials could block the operator’s view and the additional coil could be influenced by previously inserted coils, restricting prediction of the location and direction mode of action of additional coil which can be a cause of PAR.

Our study showed relatively favorable outcomes when comparing with recently published studies focusing on PR[13,23]. One of the reasons might have resulted from the inclusion criteria of this study. We only included patients with unruptured aneurysms excluding ruptured aneurysms based on the hypothesis that a ruptured aneurysm could be anunfavorable candidate to elucidate the outcomes of PR. Since SAH itself can lead to morbidity in 25% of the patients[15].

The present study has several limitations that should be noted. In particular, it is limited by its retrospective nature. Not all of the patients received immediate postprocedural CT or MRI, which means that the patients with silent or mild symptomatic PR not identified during procedure could have been missed. Patients were treated with heterogeneous devices which can influence our results. Other factors, such as vascular tortuosity, connective tissue disease and other medical conditions that possibly influence the risk of rupture and clinical outcomes were not considered in this study.

CONCLUSION

PR can result in a disastrous outcome in treating unruptured intracranial aneurysms. PPAR and rupture at the neck portion of the aneurysm seemed to result in poor clinical outcome, nevertheless PARs during the filling stage seems to have a relatively benign course. We should pay more attention when treating ACA aneurysms to avoid PR. Further studies regarding detailed risk factors and outcomes of endovascular treatment and clipping is required to improve our understanding and to set balanced interdisciplinary treatment strategies.

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