Original Article Application and outcomes of endovascular treatment of coil embolization on ruptured intracranial aneurysms with daughter sacs

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Abstract: This study aimed to evaluate the feasibility and efficacy of coil embolization in patients with ruptured intracranial aneurysms (IANs) with daughter sacs (DS). A total of 56 patients with ruptured IAN in poor-grade subarachnoid hemorrhage (SAH) were enrolled. IAN was categorized into three groups according to the position of DS, including Type D, B, and N. Coil embolization was performed on 50 patients with IAN of Type D and B. Parent artery occlusion (PAO) and partial stent-supported coil embolization (SCE) were selectively performed on the left 6 patients with IAN of Type D and B was achieved with preserved blood flow in parent arteries, which exhibited 67.9% total occlusion, 14.3% subtotal occlusion, and 7.1% incomplete occlusion. Subtotal occlusion was also achieved by PAO and partial SCE in BTO-positive patients with IAN of Type N. The final follow-up visit showed favorable outcomes in 47 patients (83.9%), severe disability in 8 patients (14.3%) and one dead (1.8%). The recurrence rate of IAN was 19.6% during follow-up. Endovascular treatment with coil embolization was feasible and effective in patients with ruptured IAN with DS in poor-grade SAH.

Keywords: Intracranial aneurysms, daughter sacs, subarachnoid hemorrhage, rupture, coil embolization

Introduction

Intracranial aneurysm (IAN) is a common and serious cerebrovascular disorder characterized by localized dilation or ballooning of blood vessels [1]. In clinic, IAN is always located at the bifurcation of internal carotid-posterior communicating artery and anterior cerebral-anterior communication artery, and emerged in single by increased tension against the weakness aneurysmal walls [2]. According to statistics, the mean prevalence of IAN was 5%-10% all over the world [3], and approximately 71% IAN could lead to a fatal subarachnoid hemorrhage (SAH) due to rupture [4]. Although the risk of rupture is relatively low, rupture IAN could seriously threaten people's lives with a high mortality rate of 25%-50% [5]. Moreover, about 40%-60% of survivors may suffer severe disability [2]. Therefore, ruptured IAN is considered to be a serious clinical problem which urgently needs to be solved.

SAH, induced by ruptured IAN, is one of the main reasons for increased preference of endovascular treatment [6]. Endovascular treatment of ruptured IAN was firstly recognized in 1974 by the use of detachable balloons for aneurysm embolization [7]. However, the use of detachable balloons is limited by restricted safety and effectiveness [8]. In 1991, controlled detachable coils were emerged and revealed to be able to directly embolize ruptured IAN [9]. Moreover, Guglielmi detachable coils (GDC) approved by the Food and Drug Administration in 1995 was recognized a valid alternative treatment for IAN with poor candidate for traditional surgical clipping [10]. Meanwhile, the deployment and detachment of GDC is easy to control regardless the morphology, size, location and status (ruptured or unruptured) of IAN [11]. As reported, the feasibility of GDC embolization was 96%, and a good mid- and long-term stability was exhibited [12]; GDC is feasible in

96.9% ruptured IAN cases with a mortality rate of 1.4% and morbidity of 8.6%; GDC is a highly safe procedure with low intervention-related morbidity (0.5%) and mortality (3.5%) [13]. Although endovascular treatment with GDC is confirmed effectively in embolization of ruptured IAN, the outcomes could also be affected by the treatment plan, imaging, operative techniques, and the management of complications [13]. In addition, the recurrence of aneurysms due to improper healing still remains the major drawback of the coiling treatment [14].

Reorganization of the blood clot covering the rupture site of IAN could always result in lumen extension and emerge as a secondary out pouching (daughter sacs, DS) [15]. In intracalvarium, ruptured IAN with DS (IAN+DS) at the "presumed" rupture site is also commonly encountered [13]. Although coil embolization is illustrated to be effective in the treatment of ruptured IAN [16], related studies on IAN+DS are still limited. The accurate identification and evaluation on the structure and distribution of IAN+DS are not only helpful to the therapeutic options of endovascular methods, but also contribute to the improvement of outcomes. In this study, IAN+DS was firstly identified and categorized by angiogram according to the position of DS. Then selective aneurysmal embolization with detachable coils were performed on patients with IANs of different type. Functional outcomes of these patients were finally assessed, including perioperative complications, disability degree and recurrences. Our finds may provide valuable information for clinical diagnosis and therapy of ruptured IAN+DS with poor-grade SAH, and reveal clinical outcomes of coil embolization.

Material and methods

Subjects

In this prospective cohort study, a total of 56 patients (26 males and 30 females) with aneurysmal SAH induced by ruptured IAN at age of 24 to 66 years (mean 47.8 ± 9.51) were consecutively selected from the department of Neurosurgery in Shanghai Jiaotong University School of Medicine from January 2011 to June 2014. These patients had been suffered from SAH for more than twice with an interval of 3 to 12 days (7 \pm 2.6). In addition, these patients either met the criterion of Glasgow coma scale

(GCS) score \geq 8 [17], or exhibited recovery possibility through operations of ventricle drainage or evacuation of intracranial hematoma combined with decompressed craniotomy with stable vital signs (GSC < 8).

Angiography

A 6-vessel cerebral digital subtraction angiography (DSA) was performed in all patients after their admission to reveal the characteristic and distribution of IAN+DS in cerebral arteries. According to the position of DS, IAN was categorized into three groups, including Type D (DS directly connect with the aneurysmal dome), Type B (DS directly connect with the aneurysmal body), and Type N (DS directly dilate in the proximity of the aneurysmal neck).

Endovascular treatment

Endovascular treatment was performed on patients with ruptured IAN+DS in Poor-grade SAH (World Federation of Neurological Surgeons grades IV and V) [18] after 6-72 hours of latest symptom onset. Among these patients, 50 patients with daughter sacs at directly connect with the aneurysm dome and body were treated with selective aneurysmal embolization with detachable coils (GDC) as previously described [12], and the remaining 6 patients with IAN of Type N were selectively performed with balloon occlusion test (BOT) [19], parent artery occlusion (PAO) (with the use of detachable coils) [20] or partial stent-supported coil embolization (SCE) as previously described [21]. Besides, dehydration therapy, triple-H therapy and therapy on postoperative complications were selectively given to all enrolled patients.

Outcomes

Functional outcomes of patients treated by coil embolization were assessed using the Glasgow outcome scale (GOS) [22]. Favorable outcome was identified by high scores of GOS with mild and moderate disability, and unfavorable outcome was identified by severe disability, persistent vegetative state, or even dead. Besides, perioperative complication was identified within 30 days of endovascular treatment. The average follow-up of these patients was 49 \pm 15.4 months with a range from 6 to 72 months, and all clinical outcomes were blindly assessed by 2 neurosurgeons.

	Total (n=56)	Туре В	Type D	Type N
Age (years)				
Mean	47.8 ± 9.51	41.2 ± 7.46	47.6 ± 8.32	44.3 ± 6.72
Range	24-66	35-52	41-66	24-53
Gender, n (%)				
Male	26 (46.4)	9	15	2
Female	30 (53.6)	11	15	4
IAN+DS location, n (%)				
Anterior circulation (%)	46 (82.1)	16	25	5
At the internal carotid artery (ICA)	19	8	9	2
At the middle cerebral artery (MCA)	10	2	6	2
At the anterior cerebral artery (ACA)	17	6	10	1
Posterior circulation (%)	10 (17.9)	4	5	1
Distal to P1 segment of posterior cerebral artery (PCA)	10	4	5	1
Mean aneurysms size, mm	3.1-5.8	3.4	3.2	3.6
Mean daughter sacs size, mm	2.1-15.4	2.2	1.6	4.2

Table 1. Basic information and clinical feature of patients with ruptured intracranial aneurysms of
three types

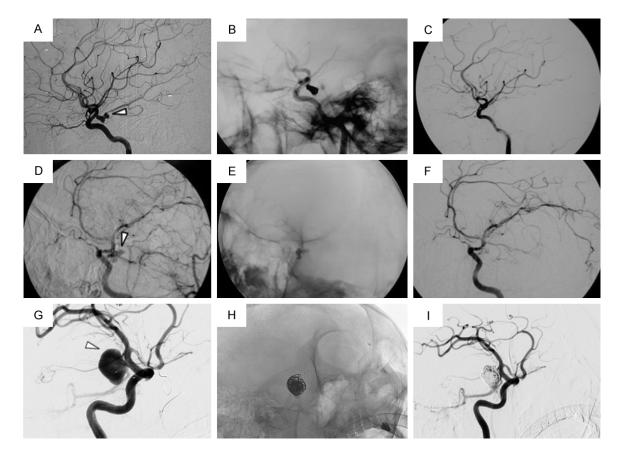


Figure 1. Case 1: Intracranial aneurysm (IAN) of Type D in the right posterior communicating artery (PCoA) observed by lateral projection of right internal carotid artery (ICA) angiogram (A); Only aneurysmal sac was occluded with 5 coils (B); Preserved ICA and total occlusion of IAN and daughter sacs (DS) without recanalization after 1 year of treatment (C). Case 7: IAN of Type B in the left PcoA observed by lateral projection of left ICA angiogram (D); IAN and DS were embolized with 6 coils (E); Preserved Left ICA parent artery and total occlusion of IAN and DS without recanalization after 1 year of treatment (F). Case 12: IAN of Type N in the right PcoA observed by lateral projection of right ICA angiogram (G); IAN and DS were embolized with 8 coils assisted by a neuroform stent at 4×15 mm (H); Preserved parent artery and total occlusion of IAN and DS without recanalization after 1 year of treatment (I). White arrow represents the position of DS.

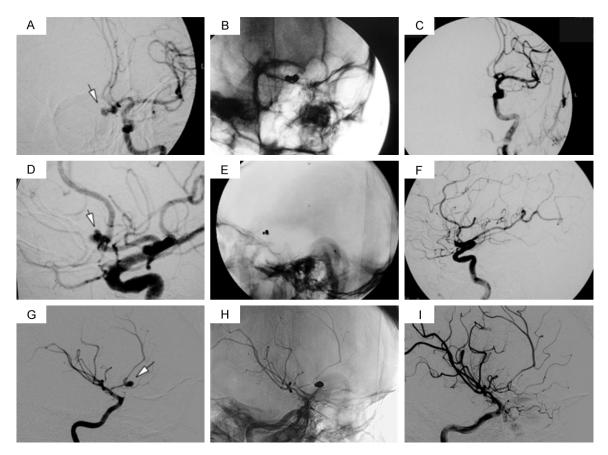


Figure 2. Case 21: Intracranial aneurysm (IAN) of Type D in the anterior communicating artery (AcoA) observed by left internal carotid artery (ICA) angiogram (A); IAN and daughter sacs (DS) were embolized with 6 coils (B); Preserved parent artery and total occlusion of IAN and DS without recanalization after 1 year of treatment (C). Case 17: IAN of Type B in the left AcoA observed by left ICA angiogram (D); IAN and DS were embolized with 4 coils (E); Preserved parent artery and total occlusion of IAN and DS without recanalization after 1 year of treatment (F). Case 13: IAN of Type N in the AcoA observed by left ICA angiogram (G); IAN and DS were embolized with 4 coils (H); Abnormal vessel spasm in bilateral anterior artery (I). White arrow represents the position of DS.

Results

The basic information and clinical feature of enrolled patients were shown in **Table 1**. A total of 59 IANs were observed in 56 patients by DSA, which located in the anterior (IAN=48, DS=46) and posterior (IAN=11, DS=10) circulation. The size of IANs ranged from 3.1 to 5.8 mm and the size of DSs ranged from 2.1 to 15.4 mm. In anterior circulation, 19 IAN+DSs at the internal carotid artery (ICA) (**Figure 1**), 10 at the middle cerebral artery (MCA) (**Figure 3**), and 17 at the anterior cerebral artery (ACA) were observed (**Figure 2**). Besides, IAN+DSs distal to P1 segment of posterior cerebral artery (PCA) were all observed in posterior circulation (**Figure 3**).

For these patients with IANs of Type D (Figure 1C) and Type B (Figure 1F), successful coil

embolization was achieved with preserved blood flow in parent arteries. Angiographic outcomes showed 67.9% (n=38) total occlusion (100%) with no residual IAN, 14.3% (n=8) subtotal occlusion (95-99%) with minimal filling of IAN, and 7.1% (n=4) incomplete occlusion (< 95%) with marked filling of IAN. Besides, subtotal occlusion was achieved by PAO in 4 BTOpositive patients with IAN of Type N (**Figure 1H**). IANs of the other two BTO-positive patients were also successfully occluded by partial SCE (subtotal occlusion) (**Figure 3C**).

After the surgery of coil embolization, various perioperative complications emerged and immediately treated appropriately. The surgery parameters and outcomes were shown in **Table 2**. In details, 16 (28.6%) acute hydrocephalus, 2 (7.1%) aggravation of cerebral hernia, 32

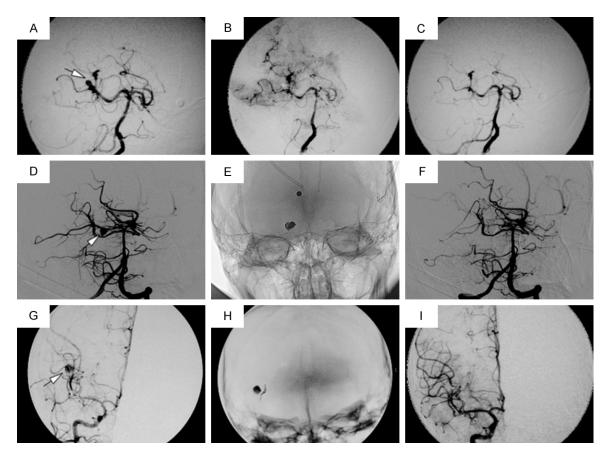


Figure 3. Case 20: Intracranial aneurysm (IAN) of Type D in the P3 segment of right posterior cerebral artery (RPCA) observed by anteroposterior projection of right internal carotid artery (ICA) angiogram (A); IAN and daughter sacs (DS) were embolized with 5 coils (B); Preserved parent artery and occlusion of IAN and DS without recanalization after 1 year of treatment (C). Case 16 (dead): IAN of Type N in the P1 segment of RPCA observed by anteroposterior projection of left vertebral artery angiograpm (D); IAN and DS were embolized with 5 coils (E); part of the parent artery was occluded (F). Case 11: IAN of Type N in the M2 segment of RMCA observed by anteroposterior projection of right ICA angiogram (G); An endovascular short segmental internal trapping (10 mm) of the right pericallosal artery was embolized using several coils (H); Completely obliterated IAN and maintenance of retrograde manner through compensated cortical vessels (I). White arrow represents the position of DS.

(57.1%) pulmonary infection, and 9 (16.1%) symptomatic vasospasm were treated by ventricular external drainage, decompressive craniotomy, tracheotomy and 3H therapy, respectively. At the final follow-up visit, favorable outcomes were found in 47 patients (83.9%), and unfavorable outcomes were exhibited on the left 9 patients, including 8 (14.3%) severe disability and 1 (1.8%) dead. A patient treated by PAO was died 4 days after the procedure due to aneurysm re-bleeding. Besides, the recurrence of IAN was found in 11 patients (19.6%) during follow-up.

Discussion

As ruptured IAN was always accompanied with DS, it is necessary to distinguish IAN from DS

before the application of endovascular treatments [15]. In clinic, angiography was helpful in precise visualization of the aneurysm neck, shape, and size of IAN+DS, which could direct the treatment plan and avoid unexpected difficulties [13]. In this study, DSA was firstly performed in all patients after their admission, and a total of 59 IANs located in the anterior and posterior circulation were identified by delayed opacification and delayed washout and retention of contrast medium [1]. Meanwhile, IANs were categorized into three groups according to the position of DS as a weak portion adjacent to the dome, body or aneurysmal neck. Among these types, type D seemed to have a greater tendency to form and rupture than type B and type N due to the location of DS on aneurysmal dome [13]. The finds of angiography were illus-

	Total (n=56)	Туре В	Type D	Туре N
Operative type, n				
Aneurysmal embolization with detachable coils (GDC)	50	20	30	0
Balloon occlusion test (BOT)	4	0	0	4
Parent artery occlusion (PAO)	4	0	0	4
Partial stent-supported coil embolization (SCE)	2	0	0	2
Operative time, min	63	52	55	135
Intraoperative blood loss, mL	62	66	56	78
Postoperative complications, n				
Acute hydrocephalus	16	8	6	2
Aggravation of cerebral hernia	2	1	0	1
Pulmonary infection	32	11	17	3
Symptomatic vasospasm	9	2	5	2
Length of hospital stay, day	23.3	25.2	22.6	21.3
Outcome, n (%)				
Favorable	47 (83.9)	16	27	4
Unfavorable	9 (16.1)	3	4	2
Recurrence rate, n (%)	11 (19.6)	2	5	2

 Table 2. The surgery parameters and outcomes of patients with ruptured intracranial aneurysms of three types

trated to be helpful in the direction of treatment options for ruptured IAN+DS in clinic.

As known, patients with poor-grade SAH were always high-risk in surgery because a fragility and unstable wall of IAN [23]. Meanwhile, IAN+DS was always accompanied with fragile tissues developed from gradually reorganizing clot surrounding the point of ruptured IAN, which exhibited the characteristics of loose connective tissue, not well-formed sacs and surrounded clots [15]. Therefore, IAN+DS was easy to rupture in the process of surgical dissection wrapping or vascular reconstruction in a limited surgical field and anatomical variations, particularly in a swollen brain after SAH [13]. In order to avoid direct mechanical trauma, endovascular treatments began to use to manage SAH at acute phase owing to its minimal invasiveness and no dissection of adjacent vessels [13]. In this study, successful coil embolization of IAN with preserved parent arteries was achieved in most patients, which indicated aneurysmal embolization with detachable coils was effective in occlusion of ruptured IAN+DS. However, there were still several cases not completely occluded, and some aspects were still needed to pay attention during the procedure of endovascular treatment due to weak angioarchitecture of IAN. Firstly, perforation of coils could occur due to the pressure applied to IAN wall on the loop of the first coil, which should be prevented by a detachable coils that is slightly smaller than the measured size of IAN. Secondly, small coils with a high degree of shape memory may exhibit a tendency to damage the weakened area of initial rupture, which should be prevented by a soft 2D coil. Thirdly, the movement of coils should be attended as not to advance to the DS or penetrate the fragile wall. Besides, irregular IAN may limit the application of detachable coils, which was always associated with late recurrence due to subtotal occlusion, and increased difficulty in therapy due to mutual occlusion of IAN [13].

DS was known to be easily formed in patients suffered SAH for more than twice with poorgrade of WFNS (IV or V), and high morbidity and mortality of disastrous rebleeding always occur in the treatment process of SAH [24]. To avoid secondary rupture of IAN+DS, definitive surgery should be performed immediately. As it is usually difficult to embolizate IAN of type N due to its characteristics of wide necks and complicated geometry, endovascular adjunctive techniques were always performed [25]. For example, the application of intracranial stent was a feasibility and efficacy technique in the management of IAN of type N [26]. Stent was a scaffold for coils, which could be sent through a

microcather to cover the neck of the aneurysm, thereby pack the aneurysm with coils through the stent interstices [27]. In this study, 2 BTOpositive patients with IAN of type N were successfully subtotal embolizated by partial SCE, which illustrated the efficiency of stent on coiling embolization. However, stent could not be used in the segment of intracranial artery because of small diameter and vasospasm in patients with poor-grade SAH [28]. If a negative result of BOT on the parent artery was obtained, proximal PAO may be an alternative. Besides, a balloon was only used to control the blood flow in vessels of patients with rupture IAN in this study. The abandonment of balloon-assisted coiling (BAC) may be explained by stable microcatheter in IAN and its risk in rupture [13].

In conclusion, coil embolization was feasible and effective in the treatment of ruptured IAN+DS in poor-grade SAH, which exhibited favorable outcomes (83.9%). However, coil embolization was still accompanied with high incidence of perioperative complications and recurrence rate of IAN (19.6%). Moreover, this study was still limited by insufficient subjects, and "pseudoaneurysmal" dilatation of AN was not surgically explored or confirmed by histopathological analyses (AN with pseudoaneurysm may be mistaken for AN+DS) [13]. Further researches on new therapeutic methods on ruptured IAN+DS with favorable outcomes, less perioperative complications and low recurrence were still needed in a large population.

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Disclosure of conflict of interest

None.

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