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ORIGINAL ARTICLE

Endovascular treatment of ruptured intracranial aneurysms in elderly patients: clinical features and treatment outcome

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Abstract

Management of ruptured intracranial aneurysm in elderly patients is still a major challenge in the treatment of cerebrovascular disease. This study aimed to evaluate safety and efficacy profiles of ruptured intracranial aneurysms in elderly patients treated with endovascular techniques (EVTs). We conducted a retrospective case review of 53 consecutive elderly patients with ruptured intracranial aneurysms treated by EVT between the year 2011 and 2016. The patients' angiographic outcomes, clinical outcomes, and procedure-related complications were reviewed retrospectively. Univariate and multivariate logistic analysis were applied to determine the risk factors of aneurysm recurrence and clinical prognosis. In 29 (54.7%) patients, the treatment was attempted with coiling alone. The vascular remodeled technique was applied in 24 (45.3%) patients. At a median angiographic follow-up of 9 months, 35 (67.3%) aneurysms showed stable, 9 (17.3%) were improvement, and 8 (15.4%) were recurrent. According to the multivariate analysis, the size of the aneurysm was independently associated with increased risk of aneurysm recurrence (odds ratio, 1.92; 95% confidence interval, 1.181–2.211; $p = 0.006$). High Hunt–Hess grade at admission was an independent predictor of poor functional outcome in the multivariate analysis (odds ratio, 5.93; 95% confidence interval, 1.878–33.63; $p = 0.008$). In 8 (15.1%) patients, it resulted in procedure-related complications. EVT of ruptured intracranial aneurysms in elderly patients is safe, effective, and have low recurrent rate. Recurrence after EVT for ruptured aneurysms is common in cases of large-size aneurysms. The overall clinical outcome was worst in patients presented with high Hunt–Hess grade.

Keywords Ruptured intracranial aneurysms · Endovascular techniques · Recurrence · Elderly

Introduction

As human society has to face a sustained growth in their geriatric population, treatment safety and efficacy for diseases in the elderly patient will become increasingly more important in the future. Subarachnoid hemorrhage (SAH) is the most common presentation of intracranial aneurysms. The ruptured aneurysm is a life-threatening condition that requires urgent medical attention. The incidences of SAH continue to increase with age, and some epidemiological studies have shown that a frequency of SAH is 3–4-fold higher in elderly patients [3, 13, 29, 30]. With the development of EVT in the past decade, treatment of intracranial aneurysms has become safer and more effective because of a shorter hospital stay, less infections and complications, and a lower frequency of epilepsy compared with surgery [2, 7, 28]. However, management of ruptured intracranial aneurysm in elderly patients is still a major challenge in the treatment of cerebrovascular disease in consideration of greater rigidity and tortuosity of the arteries, concomitant disease, and even life expectancy [3, 16, 29, 30]. Considering these issues, we investigated the outcome of EVT of ruptured aneurysms in our series of patients and evaluate the safety and efficacy profiles of EVT.

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Methods

Study population

This study constituted a retrospective review and analysis of clinical outcome of elderly patients, who were more than

65 years old and who were treated in the Beijing Chaoyang Hospital with ruptured intracranial aneurysms between March 2011 and December 2016. In each case, SAH was confirmed by CT scan or lumbar puncture. The intracranial aneurysm responsible for hemorrhage was revealed by digital subtraction angiography. Criteria for exclusion were when the patients' age was under 65 years old, or when the patient did not have a complete clinical and imaging material or having severe medical illness. Ultimately, 53 elderly patients with ruptured intracranial aneurysms were enrolled into our study. This study includes 21 males and 32 females, with a mean age of 73 years (range, 65–86 years). All patients were treated within 72 h of bleeding. The demographic data, morphologic features of the aneurysm, and angiographic and clinical follow-up results were retrospectively collected. This retrospective study was approved by the Institutional Review Board of Beijing Chaoyang Hospital in affiliation with the Capital Medical University.

Treatment procedure

All patients were treated under general anesthesia. Arterial access was obtained via the femoral artery with a guiding catheter. The sac of the aneurysm was accessed by a microcatheter under a roadmap guidance. Aneurysms were coiled with detachable coils by packing the aneurysm as densely as possible. To prevent coil herniation into the parent vessel in wide-necked or complex aneurysms, the balloon remodeling technique (BRT) and stent-assisted technique (SAT) was applied. BRT is more readily employed in the acute setting of SAH. However, the patient characteristics, aneurysm features, and operator's preference decided the ultimate treatment modality.

Systemic anticoagulation was achieved with intravenous heparin after the introduction of the first coil and before the placement of the stent. The activated clotting time was maintained at 2 to 3 times above the normal value throughout the procedure. Patients treated with SAT were administered with a loading dose of 300 mg aspirin and 300 mg clopidogrel at 2 h before the scheduled stenting. The individual response to antiplatelet therapy was not routinely measured during the study. Dual antiplatelet therapy was continued for at least 3 months after the procedure and aspirin indefinitely thereafter.

Outcome evaluation

Angiographic outcomes were evaluated immediately after the procedure and 6 months thereafter using computed tomographic angiography or digital subtraction angiography. Initial angiographic results were evaluated with the Raymond Roy score system as follows: complete occlusion, residual neck (aneurysmal body occlusion with minimal residual filling with coils at the neck), and body filling. On follow-up angiographic outcomes, the anatomic results were classified as stable (no interval change of occlusion degree), improvement (decreased filling in aneurismal neck or body compared with the initial result), and recurrent (any further filling of the aneurismal neck or body). At our institution, patients were scheduled for clinic follow-up at 1 month, 3 months, and 6–12 months, and annually thereafter. Clinical outcome was assessed using the modified Rankin Scale (mRS). The mRS scores dichotomized as good outcome (mRS score < 3) or poor outcome (mRS score ≥ 3). Complications, such as thromboembolic events (TEEs) and intraprocedural rupture (IPR), were evaluated carefully and recorded.

Statistical method

We analyzed the data using SPSS statistics version 19 (SPSS Inc., Chicago, Illinois). Categorical variables were presented as frequency. Continuous variables were presented as means and standard deviations. To assess associations among the outcome variables, as they are related to the input variables, the Pearson $\chi 2$ test was used to contrast associations, the odds ratio (OR) was used to measure strength of association for the categorical variables, and the non-parametric Mann-Whitney U test for two independent samples was used to compare groups of continuous variables, which were not normally distributed in this study. We used multivariate logistic regression analysis to assess the different risk factors for aneurysm recurrence and clinical outcome. Variables with significant probability values in the univariate analysis were considered as potentially independent variables in a multivariate analysis.

Data availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Results

Baseline characteristics

Our series consisted of 21 males and 32 females, with a mean age of 73 years (Table 1). Forty-seven aneurysms were located in the anterior circulation, and 6 were in the posterior circulation. The aneurysm size ranged from 2.0 to 18 mm (5.8 ± 2.7 mm). The average neck size was 4.1 ± 1.7 mm. The aneurysm was divided into 3 groups according to size (<5 mm; 5–10 mm; >10 mm). Of the 53 patients, 7 (13.2%) patients presented with Hunt–Hess grades IV–V. In 29 aneurysms, the treatment was attempted with coiling alone. To prevent coil herniation into the parent vessel in wide-necked or complex aneurysms, BRT was used in 16 patients (30.2%), and SAT was applied in 8 (15.1%) patients. The status of prehospital aspirin use was found in 6 (11.3%) patients. There was no

Table 1 Patient and aneurysm characteristics ($n = 53$)

Characteristics	
Demographics	
Age, mean ± SD, years	73.4 ± 5.6
Female, *n* (%)	32(60.4)
Smoking, *n* (%)	20(37.7)
Hypertension, *n* (%)	19 (35.8)
Diabetes, *n* (%)	8(15.1)
Aneurysm characteristics	
Hunt-Hess grade *n* (%)	
I-III	46 (86.8)
IV-V,	7(13.2)
Aneurysm size, n (%)	
< 5 mm	14(26.4)
5–10 mm	31(58.5)
> 10 mm	8(15.1)
Neck size, mean ± SD, mm	4.10 ± 1.7
Aneurysm location, n (%)	
Paraclinoid segment	5(9.4)
PcomA	13(24.5)
Anterior choroidal	4(7.5)
Carotid bifurcation	2(3.8)
AcomA	9(17.0)
ACA	6(11.3)
MCA	8(15.1)
Basilar trunk	2(3.8)
Basilar tip	4(7.5)

SD standard deiation, *PcomA* posterior communicating artery, *AcomA* anterior communicating artery, *ACA* anterior cerebral artery, *MCA* middle cerebral artery

significant difference between status of prehospital antiplatelet agent usage and clinical outcome ($p = 0.16$).

Angiographic outcomes

The immediate angiography outcomes showed that complete occlusion was achieved in 28 patients (52.8%), residual neck in 15 patients (28.3%), and body filling in 10 patients (18.9%). At a median angiographic follow-up of 9 months, one patient died because of thromboembolic event. In the remaining 52 aneurysms, 35 (67.3%) aneurysms showed stable, 9 (17.3%) were improvement, and 8 (15.4%) were recurrent. There were 8 large aneurysms (>10 mm), 4 of them resulted in recurrence (50%). Aneurysm presenting larger in size has a two-fold greater likelihood of a future recurrence than a small-size aneurysm. The following factors were tested as predictors of aneurysm recurrent: hypertension, location, aneurysms size, neck size, treatment modality, and immediate angiography outcomes. In the multivariate analyses, only the aneurysm size was statistically associated with aneurysm recurrence (odds ratio, 1.92; 95% confidence interval, 1.181–2.211; $p = 0.006$) (Table 2). Of these 8 recurrent aneurysms, 2 underwent a second embolization, and 1 underwent surgical clipping. The total retreatment rate was 5.7%. No patient presented with recurrent aneurysmal hemorrhage.

Clinical outcomes

Overall, at a median of 3.5 years follow-up, good functional status was achieved in 83.0% of the total patient population. Regarding clinical status at admission, 89.1% (41 out of 46) of the patients with Hunt–Hess grade I–III achieved good outcomes, whereas 57.1% (4 out of 7) of the patients with Hunt–Hess grade IV–V either died or had poor outcomes. According to multivariate analyses, high Hunt–Hess grade was statistically associated with poor functional outcomes (odds ratio, 5.93; 95% confidence interval, 1.878–33.63; $p = 0.008$) (Table 3).

Procedure-related complications

The overall rate of procedure-related complications occurred in 8 patients (15.1%). TEEs were found in 6 patients (11.3%). Two of them showed transient dysesthesia, which gradually improved within 6 months. Three patients showed new development of permanent neurological impairment. One patient with middle cerebral artery bifurcation aneurysm treated with SAT developed a massive ischemic stroke in the middle cerebral artery after the procedure and died 3 weeks after the procedure. Regarding treatment modality, symptomatic TEE was encountered in one patient treated with coiling alone, one patient in BRT, and two patients in SAT. IPR occurred in two patients, with one patient having coiling alone and another with SAT. The stage of IPR in the two patients occurred in early-stage coiling and then bleeding was successfully controlled in two patients by additional coiling. There was no statistical significant difference in TEE and IPR among treatment modalities (Table 4).

Discussion

Endovascular detachable coil treatment has dramatically changed the aneurysm treatment, and it is considered as an acceptable alternative option to surgical clipping [25]. However, management of ruptured intracranial aneurysm in elderly patients is still a major challenge in the treatment of cerebrovascular disease [29, 30]. This study investigated the outcome of ruptured aneurysms in elderly patient and evaluated the safety and efficacy profiles of EVT. Overall, EVT of ruptured intracranial aneurysms in elderly patients is safe and effective with a low recurrent rate.

Table 2 Results of logistic regression analysis indicating risk factors of aneurysm recurrence

Variable	Stable aneurysms ($n = 44$)	Recurrent aneurysms ($n = 8$)	Univariate P value	Multivariate P value
Hypertension, n (%)	16(36.4)	3(37.5)	0.916	
Anterior circulation, n (%)	40(90.9)	7(87. 5)	0.909	
Aneurysm size, mean ± SD, mm	5.2 ± 2.2	9.0 ± 2.7	0.003	0.006
Neck size, mean ± SD, mm	3.8 ± 1.6	5.9 ± 1.7	0.008	
Coil alone, n (%)	25(56.8)	4(50.0)	0.771	
Initial Raymond Roy score			0.779	
1	23(52.3)	4(50.0)		
2	12(27.3)	3(37.5)		
3	9(20.5)	1(12.5)		

The frequency of prehospital antiplatelet agents continues to increase with age for the prevention and treatment of thromboembolic and stoke events [21]. However, the impact of prehospital antiplatelet agents on the clinical outcome of ruptured aneurysms is still disputable. Most of the previous studies showed that patients taking antiplatelet drugs were more likely to have a worse outcome, which was attributed to increase in the amount of subarachnoid hemorrhage after an aneurysm rupture and complicate surgical procedures [24, 34]. However, other studies failed to reveal any significant effect of pre-hemorrhage due to antiplatelet use [21]. Furthermore, a recent investigation reported that impact of aspirin on the outcome was different based on age groups [24]. It was significantly improved in patients younger than 60 years, while poor outcome was found in the older group (≥ 60 years). In our present study, prehospital aspirin use was found in 6 (11.3%) patients and there was no significant difference between status of prehospital antiplatelet agents and clinical outcome ($p = 0.16$). This result should be interpreted with caution, since it is a retrospective study with a small sample in patient numbers.

Recurrence

With increasing utilization of EVT in the treatment of both ruptured and unruptured aneurysms, the issue of obliteration efficacy has become increasingly important [3]. Defining which aneurysms have a higher risk of recurrence may be important for directing initial and follow-up management. Previous studies have concluded that many morphological and clinical factors were found to be associated with recurrence after EVT [10, 20, 26, 33]. On the subject of factors affecting recurrences, there have been studies showing that there remains a shortcoming in coiling of larger aneurysm. Sluzewski et al. assessed angiographic outcome of patients with very large or giant cerebral aneurysms treated with coils [32]. They found that initial aneurysm occlusion and stability of the coil mesh over time was poor in large or giant cerebral aneurysms. In a large series of 334 patients, Chalouhi reported high rates of recurrence (39%) and retreatment (33%) for large aneurysms (> 10 mm) treated with coiling [9].

In the present study, the overall rates of aneurysm recurrence and retreatment were low (15.4 and 5.7%, respectively), suggesting that EVT is an effective and durable treatment for intracranial aneurysms in the elderly cohorts. However, aneurysm size was identified as an independent risk factor for recurrence in the multivariate analysis. Aneurysms presenting larger in size have a two-fold greater likelihood of a future recurrence than small size. An explanation for aneurysm recurrence has been attributed to suboptimal packing of these aneurysms, thrombus resolution, and coil migration into the thrombus mass.

Table 3 Results of logistic regression analysis indicating risk factors of clinical outcome

Variable	Good outcome ($n = 44$)	Poor outcome ($n = 9$)	Univariate P value	Multivariate P value
Age, mean ± SD, years	73.2 ± 5.7	74.0 ± 5.5	0.703	
Hypertension, n (%)	17(38.6)	2(22.2)	0.358	
High Hunt-Hess grade, n (%)	3(6.8)	4(44.4)	0.014	0.008
Anterior circulation, n (%)	38(88.6)	8(88.9)	0.983	
Aneurysm size, mean ± SD, mm	5.5 ± 2.6	7.1 ± 2.7	0.120	
Neck size, mean ± SD, mm	3.9 ± 1.7	4.8 ± 1.5	0.178	
Coil alone, n (%)	23(52.3)	6(66.7)	0.433	

Table 4 Procedure-related complications by treatment modality

Variable	Coil alone ($n = 29$)	SAT ($n = 8$)	BRT ($n = 16$)	P value
Symptomatic thromboembolic events, n (%)	1 (3.4)	2 (25%)	1 (12.5)	0.121
intraoperative rupture, n (%)	1 (3.4)	1 (12.5)	0 (0)	0.680

Clinical outcomes

In some literature, there was increasing evidence demonstrating that EVT of ruptured aneurysms may have better clinical outcomes in elderly patients compared with surgical clipping [4]. Cai reported the outcomes for elderly patients for ruptured intracranial aneurysms and provides strong evidence that highly favorable outcomes can be achieved in such patients with EVT [5]. In the present study, the clinical condition on admission rather than age is the major factor influencing the clinical outcome. Among elderly patients, 44 patients (83.0%) were discharged with a good clinical outcome. Of these, 89.1% (41 out of 46) of the patients with Hunt–Hess grade I–III achieved good outcomes, whereas 57.1% (4 out of 7) of the patients with Hunt–Hess grade IV–V showed poor outcomes. The results showed that age does not appear to be the determinant affecting clinical outcome, and coiling may be considered as the first choice for ruptured aneurysms in this elderly patient population. However, it still needs to be noticed that poor outcome rates remain high in elderly patients with high Hunt–Hess grade at admission.

Complications

Despite advances in endovascular technology, procedure-related complications remain common during coiling of ruptured aneurysms [17, 27, 35]. These events were associated with the most to morbidity and mortality rates. Bechan et al. reported an overall complication incidence of 14 patients (31%) with an overall death incidence of 11% in a study of 45 patients with acutely ruptured aneurysms. TEE was most prevalent at close to 20% and 5 of 45 patients had an early rebleeding, of which 4 of them were fatal [14]. In a ruptured aneurysm study, the rates of TEE and IPR were 13.3 and 3.7%, respectively, and resulted in permanent neurological deficit in 3.2 and 0.5%, respectively [11]. Gizewski et al. reported their experience in 108 patients aged 65 years or older. Their 8.3% rate of TEE and 3.7% IPR rate were relatively low [19]. In the present study, we found that TEE occurred in 8 (15.1%) patients and IPR occurred in 2 (3.8%) patients with 1.9% mortality rates.

Therapeutic modalities

SAT, as a common therapeutic modality for large, complex, and wide-necked aneurysms, improves packing density of aneurysms and promotes endothelialization at the aneurysm neck, which results in progressive aneurysm occlusion [6, 23, 28]. However, use of stents is more controversial for the treatment of ruptured aneurysms compared to unruptured aneurysms, which is mainly because of the higher procedure-related complication rate [14, 15, 31]. Bechan et al. reported that the complication rate of stent-assisted coiling with early adverse events in ruptured aneurysms was 10 times higher than that in unruptured aneurysms [1]. A study of 508 patients which underwent SAT concluded that stenting of acutely ruptured aneurysms is associated with higher hemorrhagic and thromboembolic complications compared with unruptured aneurysms (25 versus 4.7%) [6]. In the elderly series, we also found that stent-assisted coiling was associated with a higher rate of TEE (25%) and IPR (12.5%).

Furthermore, in the acute setting of SAH, many operators are reluctant to use antiplatelet drugs because of a potential need for a ventriculostomy, the possibility of a repeat aneurysm rupture, and the high likelihood of future surgical procedures. As recommended by the American Heart Association for SAH, stenting of a ruptured aneurysm is associated with higher morbidity and mortality and should therefore only be considered when less risky options have been excluded [12].

For these reasons, SAT is generally avoided in the acute setting of SAH with large and wide-necked aneurysms in favor of other endovascular techniques, such as dual catheter technique, BRT, or WEB (Woven EndoBridge) device, which do not mandate antiplatelet drugs [18, 22, 28] . Of those treatments, the WEB device is a recently developed device, which is a trasaccular flow disruptor dedicated to intracranial wide-neck aneurysm management and promoting progressive aneurysmal thrombosis [18]. In addition, microsurgical clipping can be a valuable and low-risk alternative for this special patient cohort [8]. There is no widely accepted algorithm to determine the best therapeutic strategy for a given intracranial aneurysm. The optimal strategy should be determined on a multidisciplinary decision depending on the patient characteristics, aneurysm features, and the operator's preference.

This study has a number of limitations, predominantly due to its retrospective nature, limited patient numbers from a single center, and the relatively short angiographic follow-up. Additionally, due to limited patients in the stent-assisted and balloon remodeling group, we combine the two groups together in this study, which may also have imposed a bias on the results. The findings in our report need to be validated with larger samples and longer follow-up period study.

Conclusions

In the present study, EVT of ruptured intracranial aneurysms is safe, effective, and has a low recurrent rate in elderly patients. However, in elderly patients with high Hunt–Hess grade at admission, poor outcome rates remain high. Intracranial aneurysms with large size are more likely to have a recurrence. SAT presented a higher risk of procedure-related complications in the elderly population with the acute setting of SAH.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval Approval for the retrospective study was obtained from the research ethics committee of Chaoyang Hospital affiliated with the Capital Medical University.

Informed consent All individual participants included in the study provided informed consent.

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