Journal of Clinical Neuroscience xxx (2012) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

A single-centre experience and follow-up of patients with endovascular coiling of large and giant intracranial aneurysms with parent artery preservation

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ARTICLE INFO

Article history:
Received 21 February 2011
Accepted 29 March 2011
Available online xxxx

Keywords:
Balloon
Endovascular therapy
Embolization
Giant intracranial aneurysm
Stent

ABSTRACT

Large and giant aneurysms are some of the most challenging vascular pathologies in the central nervous system. Their peculiarities make the surgical and endovascular approaches difficult and frequently limit them by posing risks and complications. Endovascular coil embolization of these lesions is being used increasingly as an alternative. Here we report the clinical experience and follow-up results of the endosaccular packing of 102 consecutive patients with 106 large or giant aneurysms to assess the efficacy and safety of this method. Embolization was completed by packing the aneurysm sac with a variety of commercially available coils. Primary endosaccular coiling, balloon-assisted coiling and stent-assisted coiling were used. The technical feasibility of the procedure, procedure-related complications, angiographic results, clinical outcome and follow-up angiography were evaluated. During admission, immediate angiography demonstrated complete occlusion in 48.1%, neck remnant in 28.3%, and incomplete occlusion in 23.6%. Procedure-related morbidity and mortality was 7.5% and 2.8%, respectively. A favorable clinical outcome (Modified Rankin Scale score of 0–2) was observed in 88.2% of patients (average follow-up time, 56.5 months). No re-hemorrhage of a treated aneurysm occurred. Angiography follow-up was obtained in 77.5% (79/102) patients (average follow-up time, 38.1 months). The overall recanalization rate was 29.6%. Comparison of occlusion class immediately after treatment and at last follow-up showed that 80.2% of the 81 aneurysms (in 79 patients) were stable or had improved. Five stent-assisted aneurysms that were not completely occluded initially had converted to complete occlusion on last follow-up. Nineteen recanalized aneurysms underwent successful re-embolization. No procedural complication was seen at retreatment. We conclude that in treating large and giant intracranial aneurysms, endovascular coiling with parent vessel preservation is a safe and effective technique.

1. Introduction

Endovascular coiling of intracranial aneurysms has been progressively more accepted worldwide. The recent publication of a multicenter randomized trial showing improved safety and clinical outcome of patients treated with endovascular methods as compared with open clipping has accelerated this trend.[1] The results of this trial have increased the numbers of patients referred for endovascular treatment and thereby further emphasized the need for effective treatment of intracranial aneurysms.

Large (15–25 mm) and giant (>25 mm) intracranial aneurysms remain a therapeutic challenge both surgically and endovascularly because of their size, propensity for intraluminal thrombosis, calcification, neck dimensions, involvement of perforator arteries, and proximity to cranial nerves and the brainstem. Endovascular coil embolization of these lesions is an increasingly used alternative to surgical clipping. We report our clinical experience regarding treatment with endosaccular packing for large and giant cerebral aneurysms, highlighting the technical feasibility, complications and follow-up results.

2. Methods and materials

2.1. Patients

This retrospective analysis includes 102 consecutive patients with 106 large or giant aneurysms who underwent endosaccular embolization at our department from January 2000 to December 2008. Therapeutic alternatives were discussed between the neurosurgical and neurointerventional teams. Informed consent from the patients and institutional review board approval were obtained. The medical records, radiographic studies and endovascular procedure reports were reviewed. Patient and aneurysm characteristics are shown in Table 1. All aneurysms were wide necked; and 21 aneurysms were partially thrombosed, as confirmed on CT scan or MRI.

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doi:10.1016/j.jocn.2011.03.038

Table 1
Characteristics of 102 consecutive patients with 106 large or giant aneurysms treated with endosaccular embolization

No. of patients	102
Age (years)	
Mean	52.9
Range	18–71
Gender	
Female	71
Male	31
Ruptured aneurysms (%)	65 (61.3)
Hunt and Hess grade	
I	21
II	23
III	17
IV	4
Unruptured aneurysms (%)	41 (38.7)
Mass effect	15
Incidental	11
Previous SAH	6
TIA	9
Aneurysm location (%)	
Anterior circulation (%)	85 (80.2)
ICA	66
MCA	12
AcomA	7
Posterior circulation (%)	21 (19.8)
BA	12
VA	5
VB junction	4
Aneurysm size (%)	
Large	75 (70.8)
Giant	31 (29.2)
Maximum dimension (mm)	
Mean	17.2
Range	15–31
Aspect ratio (dome/neck)	
Mean	2.4
Range	1–6.2

Large = 15–25 mm; giant, >25 mm.
AcomA = anterior communicating artery, BA = basilar artery, ICA = internal carotid artery, MCA = middle cerebral artery, SAH = subarachnoid hemorrhage, TIA = transient ischemic attack, VA = vertebral artery, VB = vertebrobasilar.

2.2. Endovascular treatment procedures

All procedures were performed under general anesthesia. When the use of a stent was planned, patients with unruptured aneurysms were premedicated with antiplatelet therapy consisting of aspirin 300 mg and clopidogrel 75 mg for 3 days before the procedure, and patients with subarachnoid hemorrhage (SAH) were treated with aspirin (300 mg) and clopidogrel (225 mg) via nasogastric tube after induction of general anesthesia. All patients received systemic heparinization to raise the activated clotting time (ACT) to about 300 s and continuous intravenous infusion of nimodipine (2 mg/hour) to prevent vasospasm during the procedure. A full three- or four-vessel cerebral angiogram was performed to permit a complete evaluation of the aneurysm, measure the aneurysm neck, width, and height, and measure the parent artery proximal and distal to the aneurysm. A 6F or 8F sheath was introduced into the right femoral artery following a standard Seldinger puncture. A 6F or 8F Envoy guiding catheter (Johnson & Johnson, New Brunswick, NJ, USA) was then guided into either the cervical internal carotid artery (ICA) or the vertebral artery, depending on the location of the aneurysm. The microcatheters were the Prowler series (Johnson & Johnson) or Excelsior SL-10 or Excelsior 1018 (Boston Scientific/Target Therapeutics, Natick, MA, USA). Embolization was completed by packing the aneurysm sac with a variety of commercially available coils. At the beginning, the aneurysms were framed using three-dimensional (3D) coils – Orbit Complex (Cordis, Miami Lakes, FL) or Microplex coils (Terumo, Tokyo, Japan). The inner space was usually packed with fibered (Nexuscoil series, ev3, Irvine, CA, USA) or bioactive coils (Matrix coils (Boston Scientific) and HydroCoils (Terumo). Forty aneurysms were coiled directly without a stent, among which 23 were treated by the balloon-assisted remodeling technique[2,3]; 66 aneurysms underwent stent-assisted coiling,[4–6] among which coronary stents were used in four, a Wingspan stent (Boston Scientific) in one, and Neuroform stents (Boston Scientific) in the other 61 aneurysms. After the procedure, patients were moved to the neurosurgery intensive care unit for monitoring and received low-molecular weight heparin calcium 4000 IU every 12 hours for the following week. Nimodipine was administered to all patients. Clopidogrel (75 mg/day) was taken orally for an additional 30 days, and aspirin (100 mg/day) was taken for 6 months for patients in whom a stent was used.

2.3. Evaluation and follow-up

The technical feasibility of the procedure, procedure-related complications, angiographic results, and clinical outcome were evaluated. Clinical follow-up data were collected at clinic visits, follow-up angiography, or by telephone interview. For all patients, 6-month, 1-year, 3-year and 5-year follow-up angiograms were recommended. Complications recorded included intraprocedural rupture, thromboembolism, coil or stent migration, rehemorrhage of the treated aneurysm, parent vessel stenosis, and perforating branch occlusion. For each patient, the pre- and post-embolization and follow-up (if possible) angiograms were reviewed and compared by two senior endovascular neurosurgeons not involved in the procedure. Occlusion grade was classified as: class 1, complete occlusion (no contrast filling of the aneurysmal sac); class 2, neck remnant (residual contrast filling of the aneurysmal neck); or class 3, residual flow (residual contrast filling of the aneurysmal body).[7] At follow-up, an aneurysm was considered recanalized if a previously totally occluded aneurysm had a partial recurrence of the neck and/or the sac, or if a subtotally occluded aneurysm had an increasing neck remnant or residual aneurysm. Clinical outcome was graded according to modified Rankin score (mRS) scale: excellent (mRS 0–1), good (mRS 2), poor (mRS 3–4) and death (mRS 5).

2.4. Statistical analysis

The Statistical Package for the Social Sciences software version 11.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. A chi-squared test was used for comparisons of incidences. A $P < 0.05$ was considered statistically significant.

3. Results

3.1. Technical feasibility and complications

The initial post-procedure angiogram revealed: class 1, complete occlusion, in 51 aneurysms; class 2, neck remnant, in 30 aneurysms; and class 3, residual flow, in 25 aneurysms (Table 2). A total of 21 complications occurred, among which 12 were in large aneurysms and nine in giant (Table 3). Procedure-related morbidity was 7.5% and procedure-related mortality was 2.8%.

Of eight thromboembolic events, three aneurysms were primary endosaccular coiled, and five were stent-assisted coiled. The patients were managed with local intra-artery administration of abciximab or urokinase and the clot was mechanically disrupted with a microwire immediately. Complete or partial recanalization

Table 2
Immediate angiographic occlusion results of 106 large or giant aneurysms in 102 consecutive patients treated with endosaccular embolization

Strategy	No.	Class 1	Class 2	Class 3
Primary endosaccular coiling	17	3	8	6
Balloon-assisted coiling	23	14	5	4
Stent-assisted coiling	66	34	17	15
Aneurysm				
Large	75	40	23	12
Giant	31	11	7	13
Overall	106	51	30	25

Table 3
Procedural-related complications in 106 large or giant aneurysms in 102 consecutive patients treated with endosaccular embolization

Complication	No.	Morbidity	Mortality
Intraprocedural rupture	3	1	2
Thomboembolism	8	4	1
Vasospasm	4	2	0
Coil protrusion	3	0	0
Artery dissection	2	0	0
Stent migration	1	1	0
Total	21	8	3

Results include patients with more than one complication.

was achieved in seven instances: two patients recovered completely, three patients developed residual mild neurological deficit and independent daily activity; one patient developed left hemiplegia and became dependent; and one patient (Hunt–Hess grade III) died from infectious complications despite receiving intensive medical management. Recanalization of the lower trunk of the right middle cerebral artery failed in a 42-year-old man with a ruptured posterior communicating artery (PcomA) aneurysm (Hunt–Hess grade I). Fortunately, he did not develop any neurological deficit. A 58-year-old woman with a ruptured PcomA aneurysm (Hunt–Hess grade I) developed a thrombus in the left ICA terminus at the end of the primary endosaccular coiling procedure. Intra-arterial injection and mechanical disruption failed to open the vessel. Subsequently, mechanical dilation with balloon angioplasty was performed at the thrombosed segment, and near-complete recanalization was achieved. The patient recovered well without any deficit.

Vasospasm occurred in four ruptured aneurysms. Two aneurysms were located at the PcomA, one at the anterior communicating artery and one at the basilar tip. The angiograms showed obvious vasospasm. The patients were managed with immediate local administration of nimodipine and papaverine. After they were returned to the intensive care unit, standard medical management for vasospasm was continued, including calcium channel blockers and hypertensive, hypervolemic, and hemodilution therapy. Three patients resolved well and had no or mild deficit. A 58-year-old woman with a ruptured left paraclinoid ICA aneurysm (Hunt–Hess grade III) required a balloon-assisted coil embolization. Vasospasm was noted in the left supraclinoid ICA, and after immediate management, the angiogram showed completely resolved vasospasm. However, decreased level of consciousness occurred 24 hours after treatment. A CT scan showed a left cerebral hemisphere infarction, and cerebral angiography revealed diffuse severe bilateral anterior and posterior circulation vasospasm. An emergent decompressive craniotomy was performed. This patient underwent a long recovery with right hemiparesis and expressive aphasia, and was then discharged to a specialised nursing facility.

3.2. Clinical outcome

A total of six patients died during the trial: three as a result of procedure-related complications, one patient with acute SAH (Hunt–Hess grade IV) died because of the severity of their initial hemorrhage during hospitalization, and two died from other diseases. Of the 96 surviving patients, clinical follow-up was obtained from <1 month to 82 months (mean: 56.5 months). The mRS score was excellent in 59 patients, good in 31 patients, and poor in six patients at last follow-up (Table 4).

3.3. Angiographic outcome at follow-up

Angiography was performed at follow-up in 79 patients with 81 coiled aneurysms. A follow-up angiogram was obtained from 2 months to 68 months (mean: 38.1 months), and 58 of the 79 patients (73.4%) had >1 year of follow-up.

Comparison of occlusion class immediately after treatment and at last follow-up showed that 80.2% of the 81 aneurysms were stable or had improved and that 19.8% had worsened (Table 5). Of note, five stent-assisted coiled aneurysms had converted to class 1 at last follow-up. Of these 81 aneurysms, 24 (29.6%) of the follow-up angiograms demonstrated recanalization (Table 6): 19 underwent successful re-embolization and the remaining five patients' angiograms showed an increasing remnant neck on the 3-month follow-up examination, but appeared stable on subsequent follow-up. Therefore, re-embolization was not considered for them. No procedural complication occurred at re-treatment.

4. Discussion

The natural history of large or giant cerebral aneurysms is grim because the diagnosis is associated with high morbidity and mortality rates, with 2-year survival rates reported to be as low as 20%.[8] Treatment is generally considered because of this poor prognosis. The peculiar characteristics of these lesions demand

Table 4
Clinical outcomes in 102 consecutive patients with 106 large or giant aneurysms treated with endosaccular embolization

Modified rankin score	With SAH	Unruptured aneurysms	Overall
Excellent	33	26	59
Good	23	8	31
Poor	5	1	6
Death	4	2	6

SAH = subarachnoid hemorrhage.

Table 5
Comparison of angiographic outcome occlusion class in 79 patients with 81 coiled aneurysms immediately after treatment and at last follow-up

Strategy		Class (%)		
		Improved	Unchanged	Worse
Overall	81	5 (5.4)	60 (65.6)	16 (29.0)
Primary endosaccular coiling	12	0	8	4
Balloon-assisted coiling	17	0	13	4
Stent-assisted coiling	52	5	39	8
Immediate angiographic result		Improved	Unchanged	Worse
Class 1	38	0	29	9
Class 2	22	3	12	7
Class 3	21	2	19	0
Aneurysm size		Improved	Unchanged	Worse
Large	53	5	42	6
Giant	28	0	18	10

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Table 6
Recanalization rates at follow-up of 81 aneurysms treated with endosaccular embolization

Strategy	Recanalized (%)
Primary endosaccular coiling	6 (50.0)
Balloon-assisted coiling	8 (47.1)
Stent-assisted coiling	10 (19.2)
Immediate angiographic result	Recanalized (%)
Class 1	9 (23.7)
Class 2	7 (31.8)
Class 3	8 (38.1)
Aneurysm size	Recanalized (%)
Large	11 (20.8)
Giant	13 (46.4)
Overall	24 (29.6)

complex treatment objectives which can be summarized as: (i) prevention of hemorrhage; (ii) prevention of thromboembolic complications; and (iii) relief of mass effect. The mainstay of treatment for intracranial aneurysms is surgery.[9] Techniques that range from the isolation of the aneurysm with direct clipping to sacrifice of the parent artery with bypass surgery have been part of the surgical armamentarium available for the treatment of these lesions. However, endovascular therapy has evolved as a safe and effective alternative for selected intracranial aneurysms with significant evolution in equipment, embolization technique and endovascular decision-making. Three endovascular treatment options are available: parent-vessel occlusion,[10] the use of a covered stent,[11] and endosaccular embolization with detachable coils.[12] A mainstay of endovascular treatment for these lesions has been parent vessel occlusion with or without bypass surgery. However, there are many patients who demonstrate an inability to tolerate test balloon occlusion (TBO) and who, as a result, are not candidates for parent vessel occlusion. In addition, there remains a 5% to 10% risk of serious stroke with associated morbidity/mortality despite tolerated TBO.[13] Exclusion of aneurysms from the circulation with preservation of the parent vessel is therefore preferred. The use of covered stents placed across the aneurysm neck proved to be effective and safe, but it is not always possible. Selective endosaccular packing of cerebral aneurysms with detachable coils was introduced in the early 1990s. From then on, balloon- and stent-assisted coiling techniques, as well as better coil designs, have greatly improved the ability to coil large and giant aneurysms and still preserve the parent vessel. In light of the small number of large and giant aneurysms and the recent evolution of coils and stents, there is limited knowledge about clinical and angiographic follow-up outcome for endosaccular packing of these lesions with different strategies.

4.1. Comparison of different strategies

In our series, the rate of complete and nearly complete occlusion (class 1 and class 2) was 76.4%, which is much higher than that reported by Gruber et al.[12] and Sluzewski et al.[14] The follow-up data in our series are also encouraging. The overall recanalization rate was 29.6%. When stent-assisted coiling was compared to balloon-assisted coiling, the complete occlusion rate did not show a statistical difference ($P = 0.298$, chi-squared test), however our data suggest that the incidence of recanalization is significantly lower in the stent-assisted coiling group ($P = 0.028$, chi-squared test). This result suggests that a stent placed across the aneurysm neck may prevent recanalization. The role of the stent is not only to provide a permanent scaffold across the aneurysm neck to prevent coil prolapse into the parent artery, but also to alter the dynamics of blood flow and to reduce flow into the aneurysm, which may be conducive to thrombosis in the aneurysmal sac and prevent delayed coil compaction. Two main options are practiced for stent-assisted coiling techniques: (i) the stent is placed before the coiling microcatheter is introduced into the aneurysm through the struts of the stent (sequential technique); (ii) first the coiling catheter can be placed within the aneurysm sac, and then the stent is positioned and immediately deployed across the aneurysm neck, which may cage the catheter between the vessel wall and stent (jailed technique or parallel technique) (Fig. 1). We prefer the latter because difficulties have been reported in the sequential technique when accessing the aneurysm for coiling after initial stent placement. This leads to the potential hazard of rupturing the aneurysm, especially when the parent artery is tortuous, or a closed-cell stent is used. Furthermore, if the microcatheter is forced out of the aneurysm during coiling, re-entrance through the stent struts may be challenging and hazardous.

4.2. Aneurysm recanalization

The goal of aneurysm treatment should be permanent exclusion of the aneurysm from the circulatory system to prevent rupture or re-rupture. The International Study of Unruptured Intracranial Aneurysms documented a rupture risk for giant aneurysms of 6.4% in the cavernous segment of the carotid artery, 40% in the anterior circulation, and 50% in the posterior circulation over a 5-year period.[15] Although aneurysm recanalization must be acknowledged as a failure of treatment of these aneurysms, prevention of hemorrhage is a significant objective to be achieved. The risk of rupture after occlusion of large and giant aneurysms can be substantially reduced. In our series, not a single treated aneurysm underwent re-hemorrhage during follow-up, despite incomplete occlusion and recanalization. However, aneurysm follow-up angiography and re-embolization, if necessary, should still be done, especially for giant aneurysms and those showing incomplete occlusion. We observed 24 instances of aneurysm recanalization on follow-up angiograms, 15 (62.5%) of which were not initially completely occluded (class 2 or class 3). Of note, recanalization of giant aneurysms was statistically higher than that of large ones ($P = 0.017$, chi-squared test). Recently, Renowden et al.[16] and Henkes et al.[17] reported a complication rate of 2% to 3% in their large series of re-treatment of previously embolized aneurysms. In our series, no adverse event was shown on follow-up angiograms or occurred during retreatment with detachable coils. Thus, follow-up procedures are safe, and the risk from retreatment with detachable coils does not negate the advantages of initial use of coil embolization. Patients should be made aware during initial treatment discussions that large and giant aneurysms may require multiple treatments and will certainly require a significant course of long-term follow-up.

4.3. Mass effect

Another common presentation of large and giant aneurysm is mass effect on adjacent structures. The pulsation of the aneurysmal mass caused by haemodynamic stress is considered the main reason for most of these symptoms. Satoh et al., who examined embolization rates using aneurysm models constructed of glass tubes, showed that the maximum percentage of volumetric occlusion was 32.0% to 33.3%, even though the aneurysms were packed as tightly as possible with coils.[18] In a recent study, volumetric occlusion for HydroCoil, bare platinum coils and Matrix coils were 76%, 31% and 23%, respectively.[19] Shrinkage of approximately 57% of initial volume after 18 months of endosaccular coiling has also been reported.[20] Based on these results, mass effect symptoms will probably improve with the shrinkage of aneurysms after embolization. In our series, 69% of our patients presenting with symptoms of

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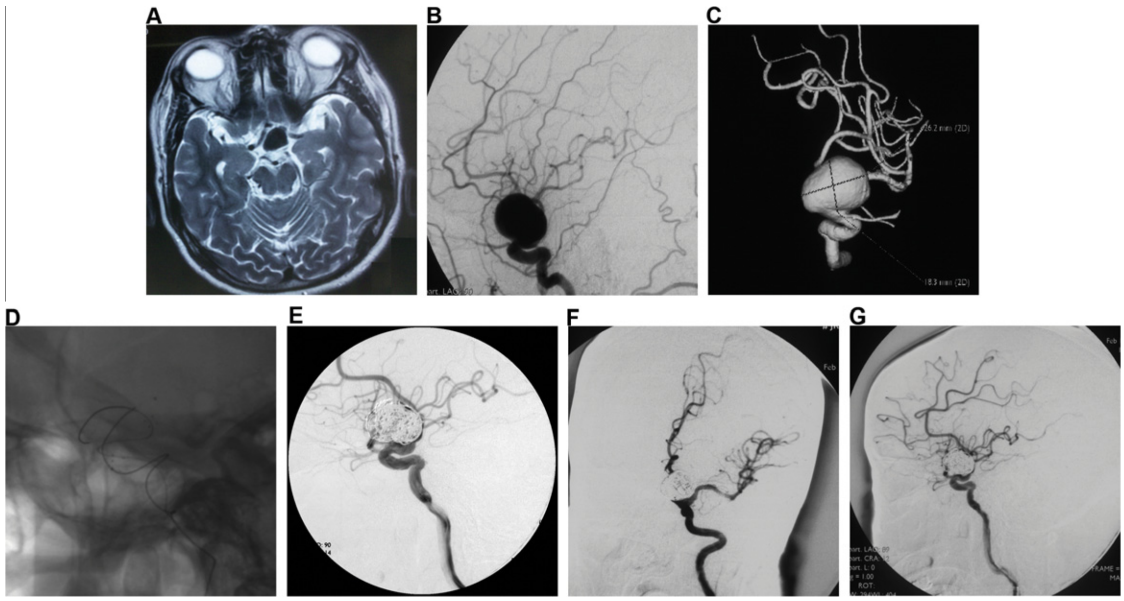

Fig. 1. A giant ophthalmic segment aneurysm was treated by stent-assisted coiling. (A) A preoperative axial T2-weighted MRI showing a partially thrombosed intracranial aneurysm; (B) a left carotid angiogram and (C) a three-dimensional reconstruction showing a giant left ophthalmic segment aneurysm; (D) the aneurysm was coiled with the parallel technique and the coiling catheter was caged between the vessel wall and the stent; (E) a postprocedural angiogram showing complete occlusion; (F, G) 14-month follow-up angiogram showing obliteration of the aneurysm, with a patent parent vessel.

mass effect improved. Gruber et al. also reported that 45.5% of patients with symptoms of neural compression improved after endosaccular embolization of giant and very large aneurysms.[12] In non-giant aneurysms, improvement of symptoms secondary to mass effect have been reported in 73% of instances.[21]

4.4. Complications and adverse effects

The overall procedure-related complications, morbidity and mortality were 19.8%, 7.5% and 2.8%, respectively, with a cumulative excellent or good clinical outcome rate of 88.2%. This is a better outcome than open surgical series. There was no statistically significant difference between giant aneurysms and large ones ($P = 0.105$, chi-squared test) in procedural complication rates. Most of our complications occurred during the first half of our trial.

Thromboembolism is usually the main cause of a procedure-related adverse event.[22] Qureshi et al.[23] reported that thromboembolism comprised nearly half of all complications (6/16). Park et al. observed nine thromboembolic events among 27 complications during coiling of 118 ruptured aneurysms.[24] In our series, eight thromboembolic events occurred, leading to one death and four neurologic deficits, which was acceptable compared with most publications. This low rate of thromboembolic events was achieved with adequate heparinisation, a short duration of endovascular manipulation, and prevention of embolus into the circulation. In addition, based on our experience, the use of some bioactive coils in conjunction with a stent should be avoided, as these coils accelerate thrombus formation and may possibly increase the risk of in-stent thrombosis. Partially thrombosed aneurysms can be coiled using the balloon remodeling technique, and the stent can then be delivered across the aneurysm neck at the end of the procedure. Once thromboembolism has been noted, local intra-artery administration of abciximab or urokinase and mechanical disruption of the clot with a microwire are necessary. Sometimes mechanical dilation with balloon angioplasty can be achieved.

Because of a prolonged post-treatment antiplatelet regimen, if there is any evidence that the patient in whom a stent is used will need an external venricular drain (EVD) due to SAH, this should be done before interventional therapy. On the basis of our experience, this might not only prevent a fatal increase of intracranial pressure, but may also reduce subsequent bleeding complications if the patient is on a significant anticoagulation and antiplatelet regimen. However, in our series, three patients received an EVD. Protamine chloride and desmopressin were used to reverse the anticoagulation and antiplatelet drugs before surgery. Fortunately, there were no surgical complications or difficulties due to abnormal intraoperative bleeding during the operation. Taking into account relatively more ischemic events, a more aggressive anticoagulation and antiplatelet therapy should be used after the procedure.

4.5. Limitations of our work

We acknowledge that the principal weakness of our study is the retrospective design, allowing the results to be confounded by physician bias on patient selection. Because there was no randomized comparison to other therapeutic approaches, including surgical procedures, parent artery occlusion, trapping, or flow-diverter stent placement, our data can not address the relative superiority or inferiority of this approach to large and giant intracranial aneurysms, and can portray only a snapshot of current techniques and their associated results. Large and giant intracranial aneurysms remain one of the most challenging vascular lesions in the central nervous system. The therapeutic approach to these lesions requires a sophisticated understanding of their unique anatomy and hemodynamic features, an extensive comprehension of the treatment strategies, and a keen decision-making process to individualize the treatment for any specific lesions.

5. Conclusion

We conclude that endovascular coiling with preservation of the parent artery is a safe and effective technique for the minimally invasive treatment of large and intracranial aneurysms. Follow-up results were encouraging. Nevertheless, additional, large series with long-term follow-up are necessary to determine the durability of these promising results.

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Please cite this article in press as: Gao X et al. A single-centre experience and follow-up of patients with endovascular coiling of large and giant intracranial aneurysms with parent artery preservation. *J Clin Neurosci* (2012), doi:10.1016/j.jocn.2011.03.038