Endovascular Treatment of Hunt and Hess Grade IV and V Aneurysms

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BACKGROUND AND PURPOSE: **Controversy still surrounds the question of when and how to manage cases of subarachnoid hemorrhage of Hunt and Hess grade IV and V aneurysms. Several authors are in favor of surgical treatment, reporting improved clinical outcomes and lower mortality rates. Considering that endovascular procedures are currently being increasingly used to treat aneurysms, we investigated their use in the management of subarachnoid bleeding in a retrospective review of 80 patients.**

METHODS: **Eighty patients were admitted to our hospital between October 1992 and October 1998 with subarachnoid hemorrhage of Hunt and Hess grade IV and V aneurysms. Patients received standard resuscitation treatment, nimodipine to prevent vasospasm, CSF shunt when necessary, and selective occlusion with Guglielmi detachable coil. They were subsequently followed up for at least 1 year. Aneurysm occlusion was monitored with MR angiography and/or angiography at 6 months and at 1 year.**

RESULTS: **Of the 80 patients, 42 (52.5%) did well (Glasgow Outcome Scale score of 1 or 2) (62% of the 56 patients with grade IV and 25% of the 24 patients with grade V aneurysms), seven (8.75%) presented with poor neurologic status (Glasgow Outcome Scale score of 3), and 30 (37.5%) died during the first 6 months (26.7% of the patients with grade IV and 62% of the patients with grade V aneurysms). One patient was lost to follow-up. The main causes of death were consequences of initial bleeding in the patients with grade V aneurysms and vasospasm in the patients with grade IV aneurysms.**

CONCLUSION: **The results are at least as encouraging as the outcomes reported for the surgical series and suggest that early endovascular treatment of high grade hemorrhage is a feasible option, especially because endovascular maneuvers can be performed at any time, even during vasospasm.**

Despite improved treatment regimens, high grade subarachnoid hemorrhage is still associated with a poor prognosis. Although neurosurgical referral is widely accepted for Hunt and Hess grade I and II and even grade III cases, it remains controversial for grade IV and V cases (1–8).

Recently, however, several authors have reported improved mortality and morbidity rates, especially among surgically treated grade IV cases (9, 10). Nonetheless, there remains considerable reluctance to refer these critically ill patients for early surgery because the consequences of initial treatment are among the major causes of mortality, especially in grade V cases (11, 12). In addition, surgical maneuvers may increase the risk of morbidity in a brain that is already traumatized by severe hemorrhage.

With the introduction of electrically detachable coils, endovascular treatment of aneurysms has become increasingly important (13, 14). The procedure causes no further brain trauma and can be performed at any time, even during the acute phase or during vasospasm. As a result, it has been proposed for use even for the most critical patients. We present a retrospective review of 80 patients treated between October 1992, when Guglielmi detachable coil (GDC) first became part of our clinical practice, and October 1998.

Methods

Patients and Techniques

Since 1992, all aneurysms observed by angiography at our center have been systematically included in a special register

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TABLE 1: Age of patients stratified by decade

Age (yr)	Number	Percentage
10–19	0	
20–29	3	4.75
30–39	15	18.75
40–49	15	18.75
50–59	16	20
60–69	25	31.25
70–79	6	7.5
>80	0	
Total	80	

TABLE 2: Location of aneurysms

Anterior Circulation	61	Posterior Circulation	19
Internal carotid artery	20	Vertebral artery	4
Internal carotid termination	4	Basilar artery	9
C1	12	Posterior cerebral artery	4
C2	3	Posterior inferior cerebellar artery	2
C3	1		
Middle cerebral artery	9		
Anterior cerebral artery	3		
Anterior communicating artery	29		

recording initial clinical and anatomic findings, treatment, and clinical and angiographic outcomes. For the purpose of this study, we selected all ruptured saccular aneurysms presenting as grade IV or V on the Hunt and Hess Scale at the time of initial evaluation and treated between October 1992 and October 1998. Fusiform and dissection aneurysms were excluded, as were aneurysms associated with arteriovenous malformations.

Four hundred three aneurysms detected at the time of subarachnoid bleeding were treated endovascularly during that period. Eighty (20%) patients were admitted with clinical grade IV and V aneurysms (56 patients with grade IV and 24 patients with grade V aneurysms; 58 female and 22 male patients; age range, 20–75 years) (Table 1). The 80 patients presented with 99 aneurysms; 61 patients had one aneurysm each, 16 had two each, and two had three each. In 61 cases, the aneurysms causing the subarachnoid hemorrhage were located in the anterior circulation; in 19 cases, the posterior circulation was the source of bleeding (Table 2). Twenty-two and a half percent of the cases had small aneurysms of <4 mm, and 46.25% had aneurysms of 4 to 10 mm. Eighteen (22.5%) aneurysms measured between 10 mm and 20 mm, and seven (8.75%) aneurysms were >20 mm in diameter. Aneurysm neck was average size, with a neck:aneurysm ratio between 0.5 and 1, in 46 (57.5%) patients; aneurysm neck was very small, with a neck: aneurysm ratio of <0.5, in 26 (33.5%) patients. Eight (10%) aneurysms had an unfavourable ratio of >1.

All patients received the same treatment protocol, which was as follows. At the time of admission to a neurosurgery intensive care unit, the patients were placed under neurosedation, assisted ventilation was provided, and nimodipine (2 mg/hr) was IV administered together with standard resuscitation procedures to avert possible internal organ failure. If CT indicated hydrocephalus, external CSF drainage was initiated before angiography was performed and before endovascular treatment was administered.

Cerebral angiography was performed as soon as possible, and a collegial discussion among a neuroradiologist, neurosurgeon, and neuro-intensivist regarding the appropriate management approach immediately ensued. Endovascular treatment was always performed as soon as was feasible. Fifty (62.5%) patients were treated during the first 3 days after admission, generally within the first 24 hr. The remaining patients were treated later, either because they had been referred by another hospital or because they were too critically ill to undergo the procedure (Table 3).

TABLE 3: Treatment delay

Treatment Delay			Clinical Status (1 year)				
			Excellent	Good	Fair	Poor	Death
<72 hr	50	62.5%	17	7	5	0	21
3–7 days	12	15%	3	5	0	0	4
8–14 days	6	7.5%	3	2	0	0	1
15–30 days	10*	12.5%	3	1	1	0	4
>30 days	2	2.5%		1	1		
Total	80*		26	16	7	0	30

* One patient lost to follow-up.

Treatment of the aneurysm was systematically accompanied by continuous perfusion of 20 to 40 IU of heparin per kg of body weight/hr from the start of angiography. No antagonist was administered at the end of the procedure to eliminate residual circulating heparin. During treatment for the aneurysm, 300 mg of papaverine was systematically perfused through a guiding catheter into the internal carotid or vertebral artery leading to the aneurysm.

The procedure always began by inserting a 6F guiding catheter into the carotid or vertebral artery. The aneurysm was then selectively catheterized with a 2.1- or 1.8-French microcatheter. GDC (Target Therapeutic, Freemont, CA) were used exclusively.

After locating the site of the aneurysm, the ideal position for coil placement was identified and visualized in two planes with 2D or 3D angiography. Once in place and before detachment, coil position was assessed by seriography. Final position was monitored by 2D or 3D angiography. Non-magnified angiographic views of the whole carotid or vertebral artery were always assessed for possible thromboembolism, and the arterial or venous phases were studied. During hospitalization, patients underwent CT one or more times each. Transcranial Doppler ultrasonography was systematically used to screen for vasospasm.

Patients returned to the neurosurgery intensive care unit for the postoperative period, where they received symptomatic resuscitation in addition to low molecular weight heparin in the form of two daily injections during the first week, subsequently reduced to one injection per day. Preventive vasospasm treatment always consisted of IV administered nimodipine and, if appropriate, moderate arterial hypertension and hypervolemia. Symptomatic vasospasm was treated with angioplasty and papaverine.

Patients were followed up by the neuroradiologist while in the hospital and were then reviewed clinically 6 weeks to 2 months after discharge. Clinical status was reassessed by the neuroradiologist when the patient returned at 6 months for MR angiography and at 1, 3, and 5 years, when angiography was performed. MR angiography was performed in 3D time of flight. Source images and maximum intensity pixel reconstructions were used for assessment of the presence of flow. Initial and subsequent occlusion criteria were as follows: total occlusion, total occlusion of both sac and neck; subtotal occlusion, neck partially visible without sac opacification; and partial occlusion, even minimal sac opacification (15). Total and subtotal occlusion were considered satisfactory outcomes not requiring further treatment. Partial occlusion was considered unsatisfactory, and those cases were referred for repeat endovascular or surgical treatment.

TABLE 4: Clinical outcome versus Hunt and Hess grades

	Glasgow Outcome Scale (1 year)					
Hunt and Hess	Excellent	Good	Fair	Poor	Death	Total
IV	21	14	5	0	15	56*
V	5	2	2	0	15	24
Total	26	16	7	0	30	80

* One patient lost to follow-up.

TABLE 5: Clinical evolution

Glasgow Outcome Scale	Hospital Discharge	6 weeks	6 months	1 year
I (excellent)	12	18	25	26
II (good)	10	15	16	16
III (fair)	32	16	8	7
IV (poor)	0	0	0	0
V (death)	26*	3	1	0
Total	80	52†	50	49

* Three treatment failures.

† One patient lost to follow-up.

Results

Results of Aneurysm Management

Total occlusion was obtained at first procedure in 24 (30%) patients, subtotal occlusion in 43 (53.75%), and partial occlusion in 10 (12.5%). The procedure could not be performed on three (3.75%) patients.

The 49 surviving patients were followed up according to our treatment protocol requiring MR angiography and, if necessary, angiography at 6 months and at 1 year. At 6 months, occlusion was judged to be satisfactory in 37 (75%) patients (16 total occlusion, 21 subtotal occlusion). At 1 year, occlusion was considered to be satisfactory in 44 (89%) patients (25 total occlusion, 19 subtotal occlusion), nine of whom had undergone repeat endovascular treatment.

Clinical Results

Twenty-six (32.5%) patients died during the initial phase. These included the three patients for whom the procedure proved unfeasible and 23 treated patients (29% of all patients treated). Six patients died during the first 6 weeks after discharge, and one died during the intervening 6 months. In summary, 30 of the 80 patients (15 of the 56 patients with grade IV and 15 of the 24 patients with grade V aneurysms) died as a result of the consequences of ruptured aneurysms or secondary complications (37% of all patients and 35% of those treated). At 1 year, 42 (54.5%) patients treated endovascularly were in good clinical condition (Table 3). Outcomes differed with clinical grades assessed at time of entry; 62% of the 56 patients presenting with Hunt and Hess clinical grade IV had achieved good outcomes at 1 year (Glasgow Outcome Scale score of 1 or 2) as compared with only 29% of the 24 patients with Hunt and Hess clinical grade V. Sixty-two percent of the patients with grade V aneurysms died, compared with 27% of the patients with grade IV aneurysms (Table 4).

Treatment was initiated as early as possible. It is our practice to perform angiography and administer treatment as soon as is feasible, unless the patient's clinical, hemodynamic, or respiratory condition is too severe to sustain subsequent intensive resuscitation. Fifty (62.5%) patients were treated during the first 3 days. Good clinical outcomes were achieved in 46% of the cases, and 42% of the patients died (Table 5). Clinical outcomes were better for the patients treated between days 3 and 14. These patients responded best to resuscitation. Patients treated after that time interval did less well because, although they survived the initial period, their conditions at the time of admission had been too critical to justify treatment.

Vasospasm was frequently observed on transcranial Doppler ultrasonograms and/or angiograms of patients with severe hemorrhage. Fifteen patients presented with vasospasm and late onset ischemic complications (10 observed after treatment of the aneurysm and five observed before treatment). Clinical outcomes for these patients were often poor, and the complications of vasospasm were diagnosed late, at the time of patient presentation. Of the 15 patients with symptomatic vasospasm, only five had no deficit at the time of discharge from the hospital. Six had mild deficits, and four died. The five patients whose vasospasm was detected during the procedure to treat the aneurysm received papaverine and underwent angioplasty. Our specific vasospasm protocol, consisting of papaverine and angioplasty, was administered to the other patients who had already received papaverine infusion during the endovascular procedure. This was often commenced fairly late, however, based on transcranial Doppler ultrasonographic evidence of high blood flow, deteriorated patient condition, and/or CT evidence of ischemia.

Four clinical complications occurred after endovascular treatment of the aneurysms. Two were transient ischemic attacks, and two were episodes of stroke. These latter cannot be unequivocally attributed to the procedure, however, because both patients presented with vasospasm at the time of the procedure.

Early rebleeding occurred in two cases, one on the day of treatment and the second after 3 days. Both patients died. The first, an elderly patient, had been treated endovascularly in an attempt to achieve stablization before referral for surgery. Subtotal occlusion had been achieved in the second patient, but thromboembolism during the procedure mandated high dose anticoagulant treatment during the immediate postoperative period. None of the 49 surviving patients whose follow-up extended beyond 1 year experienced rebleeding.

The complications of the endovascular procedure are presented in Table 6. There was one case of coil rupture, which induced no clinical complication. Three ruptured aneurysms were observed. Two produced no clinical consequences, and the patients proceeded to achieve good clinical outcomes. The third

TABLE 6: Technical complications

Complication	No. of Cases	Consequence
Coil rupture	1	No clinical consequence
Aneurysm rupture	3	No clinical consequence
Embolic projections	7	Transient ischemic attack (2) Stroke (2)

patient was not a candidate for endovascular treatment and was referred for surgery 3 days later.

The most frequent complication was thromboembolism. Seven (9%) of the 77 patients treated endovascularly presented with thromboembolic complications at the time of angiography. Treatment was simple: arterial pressure elevation, intra-arterial papaverine perfusion, and administration of heparin for four patients. One patient underwent mechanical thrombolysis, with a guidewire and microcatheter being passed through the clot. Two patients were treated in situ with urokinase (900,000 IU). Treatment was successful in six of the seven cases, and vessel patency was reestablished. Four of these seven patients died, however. One experienced rebleeding, as described above, and the other three died as a result of the consequences of the initial subarachnoid bleeding. Clinical outcomes were satisfactory in three cases, despite limited ischemic motor deficit sequelae in two cases.

Discussion

Conservative treatment of these cases usually affords very poor results. In their 1968 grading scale, Hunt and Hess (16) estimated a mortality rate of 78.7% (71% for patients with grade IV and 100% for patients with grade V aneurysms). These disastrous outcomes have been confirmed by other studies (6, 8, 17) and vary both with age and initial clinical grade. Grade IV has a much better prognosis than does grade V (9, 18). Hutchinson et al (11) reported a different outcome according to the early response, especially to the withdrawal of sedation.

Although early treatment of grade I and II aneuryms is now generally accepted, controversy remains regarding the advisability of early treatment of grade IV and V aneurysms. The high mortality and morbidity rates associated with the initial bleeding have been major arguments against early treatment in the more severe cases. More recently, however, several authors have shown mortality benefits from early treatment of aneuryms in these patients. Zentner et al (17) reported mortality rates of 29% for their patient group undergoing early treatment and 95% for their non-treated group. Lee et al (12) reported a 23% mortality rate for their early treatment group, compared with a 46% mortality rate for all 166 patients. These results are corroborated by Duke et al (9), Gumprecht et al (10), Seifert et al (6), and Weir and Aronyk (8).

The initial mortality rate (29%) for our case material was largely the same as that for the series undergoing surgery. Other studies with sufficiently large numbers of patients with grade IV and V aneurysms treated endovascularly have reported higher mortality rates (40% reported by Kremer et al [19]) or slightly lower mortality rates (14, 22). Viñuela et al (14) reported an overall mortality rate of 21% (11.6% for the 69 patients with grade IV and 34.6% for the 26 patients with grade V aneurysms). In a study of 21 patients with grade IV and 12 patients with grade V aneurysms, Byrne et al (22) reported a lower mortality rate (12% at 6 months) and exceptional results for such critically ill patients.

Improvements in survival rates have been achieved, especially for patients with grade IV aneurysms. Lee et al (12) reported that in patients with grade IV aneurysms, rebleeding is as important a cause of death as the consequences of the initial hemorrhage, whereas the effects of the initial bleeding remain the main cause of death in patients with grade V aneurysms (91.8%). It follows that grade IV cases benefit most from treatment of their aneurysms. In their study on early treatment of prevalently grade IV cases, Duke et al (9) and Gumprecht et al (10) reported significant improvement in mortality rates. Although this was most marked in patients with grade IV aneurysms, a lower mortality rate was also observed for patients with grade V aneurysms, especially for patients undergoing endovascular procedures. This improvement was less evident in the surgical series.

Although survival rates have improved as a result of early treatment of aneurysms, the same cannot be said for the subsequent quality of life. Cesarini et al (1) reported only a small increase in good outcomes after treatment and a marked increase in the number of severe residual deficits. In contrast, our series shows a large number of satisfactory or excellent outcomes (52%) at 6 months and at 1 year, with only 8.75% of patients not achieving self-sufficiency. Zentner et al (17) and Le Roux et al (20) reported that satisfactory outcome is closely correlated to initial clinical grade, with 50% of patients with grade IV aneurysms achieving good outcomes compared with only 22% to 24% of patients with grade V aneurysms. Our results confirm this finding. Of our 80 patients, 62% of the 56 patients with grade IV aneurysms achieved satisfactory outcomes compared with only 25% of the 24 patients with grade V aneurysms.

The findings presented by most authors suggest that treatment should be initiated during the first 3 days after admission. Duke et al (9) even argued that treatment should commence within the first 24 hr and be the most effective possible, treating the aneurysm and administering vasospasm prevention, considering the particularly high prevalence of this complication in this patient population (1).

The incidence of vasospasm reported in the literature varies. Some neurology centers report high rates of vasospasm among their endovascularly treated cohorts, whereas others report more vasospasm among surgically treated patients. In our experience, symptomatic vasospasm was similar for both surgically and

endovascularly treated groups (21). The problem is rather that vasospasm is often diagnosed too late in patients with grade IV and V aneurysms when ischemic lesions are already established. Systematic investigations to detect cerebral ischemia, such as xenon-enhanced scanning, single photon emission CT, and diffusion-perfusion MR imaging, performed in addition to transcranial Doppler ultrasonography should allow earlier detection of vasospasm, immediate patient referral for angioplasty, and thereby fewer complications. In our series, vasospasm was a particularly frequent and feared complication.

The main aim of early treatment of aneuryms is to prevent rebleeding, which is the main cause of death, especially for patients with grade IV aneurysms. Endovascular treatment has been widely reported to prevent rebleeding, although some cases of rebleeding (four of 259 cases) were reported by Byrne et al (22). Although the rebleeding reported by Byrne et al occurred some time after the first episodes, the only rebleeding observed in our study occurred during the early phase and in concomitance with particular technical conditions. We have observed no cases of late onset rebleeding during the follow-up period.

The reason for abstaining from or delaying surgery is the difficulty of operating on a brain that is already turgid and traumatized by hemorrhage. The endovascular approach avoids direct mechanical brain trauma. Moreover, we have found no marked difference in survival rates between the endovascularly treated and surgically treated series, although Viñuela et al (14) and Byrne et al (22) reported slightly better survival rates for the endovascular group. Because mortality is often the result of the consequences of the first bleeding, this minimal difference in mortality rates is understandable. More importantly, however, the endovascular series should present fewer neurologic deficits because of the absence of direct mechanical brain trauma. We hope that larger studies will address this issue in the future.

Conclusion

Early endovascular treatment of grade IV and V aneuryms seems a viable alternative to surgery. It is a procedure that can be performed in the emergency setting regardless of the patient's clinical condition and is compatible with aggressive resuscitation maneuvers. Clinical outcomes have proved to be at least as good as those obtained by surgery, with a higher number of patients enjoying very satisfactory recovery.

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