

Clinical Outcomes After Endovascular Coiling in High-Grade Aneurysmal Hemorrhage

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ABSTRACT: *Object:* Our experience in Calgary was reviewed to determine the safety and clinical effectiveness of coiling in patients with high-grade aneurysmal subarachnoid hemorrhage (SAH). *Methods:* Patients with Hunt-Hess grades IV and V aneurysmal subarachnoid hemorrhage who underwent endovascular coiling between January 1999 and April 2009 at Foothills Medical Centre, Calgary, Alberta, Canada were reviewed. The primary outcome measure was the Modified Rankin Score after at least six months. Secondary outcome measures included extent of aneurysm occlusion and peri-procedural complications. In patients with favourable functional outcomes, Barthel's Index (BI), Re-integration to normal living index (RINL), and Zung depression scale (ZDS) were determined. *Results:* Thirty-three patients were identified (median age of 57 years; 73% female) and 69% were Hunt-Hess grade IV subarachnoid hemorrhage and 22% were grade V. Endovascular coiling resulted in absence of residual flow into the aneurysm fundus in 91%. Only seven procedure-related complications occurred with no deaths attributed to the procedure. Vasospasm, hydrocephalus, and pneumonia were the most common non-procedural complications. Average follow-up was 27 +/- 17 months. Overall mortality was 32%, but 53% of patients had good functional outcome (mRS < 3). Nine patients completed the BI, RINL, and ZDS with average BI 99 +/- 2, RINL 89 +/- 14, ZDS 33 +/- 11, suggesting minimal deficits in function and mood. *Conclusions:* Endovascular coiling in patients with high-grade subarachnoid hemorrhage is safe. While the morbidity and mortality from high-grade aneurysmal subarachnoid hemorrhage remains significant, favourable radiologic and functional outcomes can be achieved in a significant proportion of these critically ill patients.

RÉSUMÉ: *Résultats cliniques de l'embolisation endovasculaire dans l'hémorragie anévrysmale de haut grade.* *Objet :* Notre expérience à Calgary a été révisée afin de déterminer la sécurité et l'efficacité clinique de l'embolisation endovasculaire de microspires chez les patients atteints d'une hémorragie sous-arachnoïdienne (HSA) anévrysmale de haut grade. *Méthodes :* Les dossiers des patients atteints d'hémorragie sous-arachnoïdienne anévrysmale de grade IV et V à l'échelle Hunt-Hess, qui ont subi une embolisation endovasculaire par microspires entre janvier 1999 et avril 2009 au Foothills Medical Centre, à Calgary, Alberta, Canada, ont été révisés. La mesure principale des résultats était le score à l'échelle modifiée de Rankin au moins six mois après l'intervention. Les mesures secondaires de résultats comprenaient le degré d'occlusion de l'anévrysme et les complications périopératoires. Chez les patients qui ont eu des résultats fonctionnels favorables, l'indice de Barthel (IB), l'indice de réintégration à la vie normale (IRVL) et le score à l'échelle de dépression de Zung (EDZ) ont été mesurés. *Résultats :* Trente-trois patients ont été identifiés (âge médian 57 ans ; 73% de femmes) dont 69% avaient une HSA de grade IV à l'échelle Hunt-Hess et 22% une HSA de grade V. Suite à l'embolisation endovasculaire, il n'y avait aucun flux résiduel dans le fond du sac anévrysmal chez 91% des patients. Seulement sept complications reliées à l'intervention ont été observées et aucun décès n'a été attribué à l'intervention. Les complications les plus fréquentes, non reliées à l'intervention, étaient le vasospasme, l'hydrocéphalie et la pneumonie. La durée moyenne du suivi était de 27 ± 17 mois. La mortalité globale a été de 32% et 53% des patients ont eu un bon résultat fonctionnel (MRS < 3). Neuf patients ont complété l'IB, l'IRVL et l'EDZ avec des moyennes respectives de 99 ± 2 pour l'IB, 89 ± 14 pour l'IRVL et 33 ± 11 pour l'EDZ, ce qui est compatible avec des déficits fonctionnels et de l'humeur qui sont minimes. *Conclusions :* L'embolisation endovasculaire par spires chez les patients porteurs d'une HSA de haut grade est sûre. Bien que la morbidité et la mortalité dues à l'HSA de haut grade demeurent importantes, des résultats radiologiques et fonctionnels favorables peuvent être obtenus chez une grande proportion de ces patients dont l'état est critique.

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Despite recent evidence that case-fatality rates for aneurysmal subarachnoid hemorrhage (SAH) have been declining in the last 30 years,¹ it still carries an estimated mortality as high as 50% within the first six months. In the setting of severe SAH in a critically ill patient, which can be qualified as grades IV or V as described by Hunt and Hess,² the treating clinician is faced with the dilemma of pursuing aggressive medical treatment in the hopes of achieving meaningful recuperation, versus withdrawal of support for palliation if there seems no chance of a functional recovery.

Surgical clipping to secure the ruptured aneurysm in high-grade SAH is cost-effective with an estimated 30% overall survival.³

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Proponents of endovascular coiling cite the benefits of avoiding the surgical stress of craniotomy and retraction injury to the brain with consequent potential improvement in clinical outcomes. We hypothesized that endovascular coiling in patients with high-grade aneurysmal SAH could result in reduced mortality and improved functional outcome. A systematic retrospective review of all local cases of high-grade aneurysmal SAH was conducted to assess the safety and efficacy of the endovascular coiling procedure and concurrently to determine the functional outcomes of treated surviving patients with at least six months follow-up.

METHODS

Institutional research ethics review board approval and informed consent was obtained for this study. The endovascular interventional procedure log at Foothills Medical Centre in Calgary, Alberta, Canada was searched for adult patients who underwent primary endovascular coiling of a ruptured intracranial aneurysm with clinical Hunt and Hess grade IV or V. Determination of Hunt and Hess grade was based upon documentation from the emergency room and in-hospital records indicating clinical status after respiratory and hemodynamic resuscitation, but prior to external ventricular drainage. Patient risk factors such as smoking within the last year, hypertension, diabetes, and prior stroke were recorded if information was available on the clinical record. Admission head CT scans were reviewed to determine initial Fisher grade to gauge degree of bleeding in the subarachnoid space,⁴ presence of a focal hematoma, and presence of post-hemorrhagic acute hydrocephalus. The dictated procedure report of the treating endovascular specialist was reviewed for assessment of extent of aneurysm occlusion and intra-procedural complications. Hospital records were reviewed to ascertain all post-procedural medical complications, incidence of re-bleeding, and incidence of persistent hydrocephalus requiring ventriculo-peritoneal shunting during hospital stay. The incidence of vasospasm was recorded and defined by clinical evidence of neurological deficit with radiologic appearance of intracranial arterial vessel narrowing on CT angiogram or digital subtraction angiography (DSA) reported by a neuroradiologist at the time of the study. Delayed coil compaction determination was based on the interpreting neuroradiologist opinion on review of all available neurovascular imaging and was not directly re-examined for this study. Routine neuroimaging follow-up after endovascular coiling at our centre involves magnetic resonance angiogram (MRA) at six months after coiling and MRA and DSA after one year. Digital subtraction angiography may be repeated if there is evidence of coil compaction or new aneurysm formation on the yearly MRA. Modified Rankin Score⁵ (mRS) was determined based on office chart review (R.D.) after at least six months follow-up with censoring for deaths occurring after one year. Patients were classified as having a "good outcome" for a mRS of 2 or less, which represents relatively independent functional status. In such patients who had a favourable recovery, functional status was further investigated with patient questionnaires to determine Barthel's Index (BI)⁶ and Re-integration to Normal Living Index (RNLI)⁷. Barthel's Index is a measure of the functional independence of a patient and ranges from 0 (fully dependant) to 100 (completely independent). The RNLI is a

measure ranging from 0 to 100 which demonstrates the degree to which a patient has reorganized physical, psychological, and social characteristics into a harmonious whole in order to resume well-adjusted living after illness.⁸ We also screened for depression in these patients using the Zung depression scale (ZDS).⁹ Questionnaires were completed by patients at home or during follow-up clinic appointments.

Approximately 80 patients with aneurysmal SAH are treated at the Foothills Medical Centre each year. Patients with identified high-grade aneurysmal SAH typically undergo immediate intubation followed by placement of a ventriculostomy catheter if there are signs of raised intracranial pressure in the setting of acute obstructive hydrocephalus. When admission head CT scan demonstrates a large intracranial parenchymal hematoma with mass effect, we prefer to perform urgent hematoma evacuation and aneurysm clipping via craniotomy and such patients were excluded from this study. Moribund patients, especially those with brainstem findings (fixed and dilated pupils, absent corneal reflexes, absent oculocephalic reflex, or decerebrate posturing) have typically not proceeded to early intervention. After stabilization or improvement in the clinical exam is observed in the intensive care unit, we have advocated for urgent endovascular coiling of the ruptured aneurysm, usually within 24-72 hours from admission. Standard management of SAH in our institution includes administration of nimodipine, optimization of hemodynamic and fluid status, ventilatory support, repeat vascular imaging to monitor for vasospasm, and early rehabilitation.

Table 1: Aneurysm and hemorrhage characteristics in all study patients

Aneurysm Location		
Anterior Circulation		28 (85%)
Posterior Circulation		5 (15%)
Aneurysm Size		
Mean		8 mm
Range		3 – 18 mm
Fisher Grade		
I		0
II		0
III		8 (24%)
IV		25 (76%)

Table 2: Summary of non-procedure related complications after endovascular coiling in patients with grade IV or V aneurysmal SAH

Vasospasm	9 (27%)
Hydrocephalus	8 (24%)
Pneumonia	8 (24%)
Ventriculitis	4 (12%)
Urinary tract infection	3 (9%)
Intracranial hypertension	2 (6%)
Pneumothorax	2 (6%)
Aspiration pneumonitis	2 (6%)
Myocardial Ischemia	2 (6%)
Pulmonary Edema	1 (3%)
Cardiac arrest	1 (3%)
Line Sepsis	1 (3%)
Pseudomembranous colitis	1 (3%)
Sinusitis	1 (3%)

RESULTS

Thirty-three patients underwent primary endovascular coiling after presenting with grade IV or V SAH between January 1999 and April 2009. The median patient age was 57 years with a range of 20 to 85 years. More females ($n=24$) were treated than males ($n=9$). Smoking (31%, $n = 29$) and hypertension (50%, $n = 32$) were prevalent in the study population. None of the patients had a prior stroke and only two patients had diabetes mellitus type 2. Twenty-three patients (70%) had an initial Hunt-Hess grade of IV and ten (30%) had a Hunt-Hess grade of V. All patients required initial intubation and stabilization in the intensive care unit. Table 1 shows aneurysm characteristics and distribution of Fisher grades of the treated patients. The majority of aneurysms treated (85%) were in the anterior circulation and all were associated with thick subarachnoid blood. A non-surgical intracranial hematoma was observed in 20 patients (61%). Acute external ventricular drainage for control of hydrocephalus was required in 91% of all patients. Coiling was attempted in all patients within 72 hours of admission. Only two coiling attempts failed. Out of 31 patients with successful coiling, 24 had complete aneurysm occlusion, 6 had residual filling of the aneurysm neck, and 1 had some residual filling of the aneurysm fundus. No intra-procedural deaths occurred. The most dangerous complications in this series were intra-procedural re-bleeding and embolic stroke occurring in two different patients who both died within the acute hospital phase at one day and eight days post-procedure respectively. The patient who suffered intra-procedural aneurysmal re-hemorrhage died after care was withdrawn based on family wishes and thus

did not directly die from the procedural event. On the other hand, the patient with embolic stroke suffered significant neurological deficit from the intervention and this was a factor in deciding to not pursue continued aggressive medical management in this patient. Overall, seven procedure-related complications occurred including three prolapsed coils, one non-occlusive thrombus, and one femoral access site hematoma. The most common non-procedure related complications were vasospasm (27%), hydrocephalus requiring ventriculo-peritoneal shunting (25%) and pneumonia (24%) (Table 2). None of the patients suffered post-procedural aneurysmal re-bleeding. Magnetic resonance angiography follow-up was available on 28 patients and revealed a 25% rate of delayed coil compaction.

Twenty-eight patients were available at follow-up for determination of functional outcome. The mean patient follow-up was 27 ± 17 months with a range of 6 to 65 months. Three patients were lost to follow-up: one having moved to another city, one discharged from clinic after a short follow-up period, and another out-of-city patient who changed address and telephone. After at least six months follow-up, a good functional outcome ($mRS \leq 2$) was achieved in 53% of all patients (Figure) and a poor outcome was observed in 47%. Overall mortality with censoring after one year was 32%. Patients who presented with grade IV SAH had a higher proportion of good outcome (69%) when compared to patients with grade V hemorrhage (22%) ($X^2=6.651$, $p=0.010$). Mortality trended higher in grade V patients at 45% versus 26% in grade IV ($X^2 = 0.920$, $p = 0.337$) (Figure).

Nine of thirteen surviving patients who had mRS scores of 2 or less after six months completed the BI, RINL and ZDS questionnaire. The individual patient characteristics and questionnaire scores are listed in Table 3. All nine of the patients had a high level of function with BI > 90 out of 100. Quality of life was moderate to excellent in all nine patients. The mean BI score was 99 ± 2 (S.E.M.) and the mean RINL score was 89 ± 14

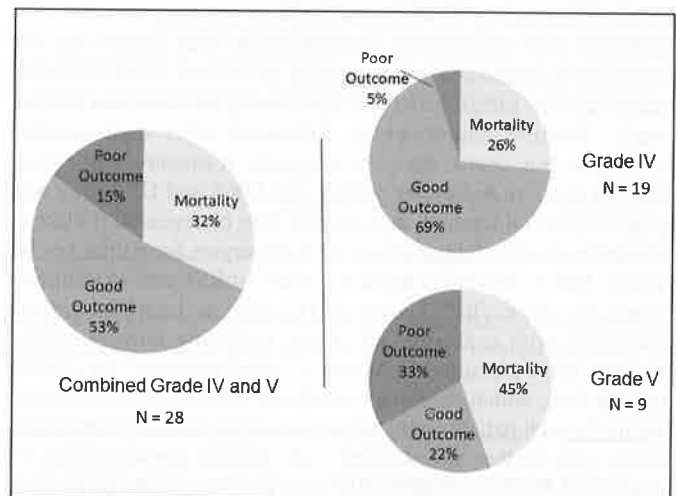


Figure: Functional outcomes as measured by modified Rankin Score after at least six months follow-up. Good outcome defined as $mRS \leq 2$ and poor outcome as $mRS > 2$.

Table 3: Barthel's Index (BI), Re-integration to normal living index (RNLI), and Zung depression score (ZDS) for patients with good functional outcome

Age	Sex	Hunt & Hess Grade	BI	RINL	ZDS
48	F	IV	100	70	41
35	F	IV	100	73.6	56
58	F	IV	100	100	26
40	F	IV	100	98.1	24
50	F	IV	100	98.1	20
59	F	IV	100	95.5	38
67	F	IV	100	100	30
60	F	V	95	66.4	38
45	F	V	100	100	27
Mean +/- SEM			99 ± 2	89 ± 14	33 ± 11

(S.E.M.). The mean ZDS was 33 ± 11 (S.E.M.) with only one patient reporting a ZDS that suggested possible mild depression (ZDS > 50).

DISCUSSION

The Foothills Medical Centre serves a population of approximately 1.5 million in southern Alberta, Canada and adjacent provinces. In the last ten years, 33 patients with high-grade aneurysmal SAH were treated by endovascular coiling of the ruptured aneurysm. Approximately 800 patients with subarachnoid hemorrhage would have occurred in this period,

but about half of patients succumb to the initial ictus of the bleed. Previous studies have reported the rate of high-grade subarachnoid hemorrhage to fall within the 20 to 40% range.¹⁰⁻¹² Therefore, between 80 and 160 high-grade subarachnoid hemorrhage patients would have been managed in hospital. Based on these estimates, the number of patients analyzed in this retrospective series represents 20-40% of the total number of patients treated for high-grade subarachnoid hemorrhage. Certainly, our patient cohort is highly selected and this limits generalization of the results of our study. Nevertheless, our selection criteria are very similar to those used in previous studies of both surgical and endovascular therapy in high-grade patients.^{13,14} Determination of initial Hunt and Hess grade was performed after cardiopulmonary and neurological stabilization in this study. The severe nature of the hemorrhages that occurred in our patient population is echoed by the high rate of external ventricular drainage in over 90% and the fact that all patients remained intubated in the intensive care unit prior to endovascular coiling.

We report a high rate of complete aneurysm occlusion (72%) and no deaths caused directly by the coiling procedure itself. This compares with a previously reported series of coiling in the setting of ruptured aneurysm which showed 70.8% complete occlusion rate of small aneurysms and 1.74% technical complication related mortality.¹⁵ The two most frequent complications in our study were vasospasm and hydrocephalus, and this is an expected finding given the high proportion of patients with intraventricular (Fisher grade IV) hemorrhage in this study. Our symptomatic vasospasm rate of 27% is similar to those previously reported for endovascular coiling in patients with all SAH grades (30-33%),^{16,17} however, it is lower than that reported for patients with high-grade SAH (37-43%).^{18,19} The range in symptomatic vasospasm in coiled patients may be influenced by numerous factors such as extent of screening for vasospasm, different intensive care unit protocols, adherence to

Table 4: Summary of studies reporting endovascular therapy for patients with grade IV or V aneurysmal SAH

Study	Number of Patients	Mean Follow up Period (months)	Favourable Outcome	Overall Mortality
Diaz and Wong, 2010	33	27	53%	32%
Pereira <i>et al.</i> , 2007	51	12	57%	35.2%
Suzuki <i>et al.</i> , 2006	111	32	35.1%	32.4%
Weir <i>et al.</i> , 2003	27	23	30%	59%
van Loon <i>et al.</i> , 2002	11	12	36%	18%
Bracard <i>et al.</i> , 2002	80	12	52.5%	37.5%
Groden <i>et al.</i> , 2001	20	17	30%	50%
Byrne <i>et al.</i> , 1999	33	6	33%	12.1%
Kremer <i>et al.</i> , 1999	40	13	40%	40%
Malisch <i>et al.</i> , 1997	9	42	0%	78%
Casasco <i>et al.</i> , 1993	9	6	44%	44%

prophylactic measures, and the specific quantity and distribution of subarachnoid blood in each population sample. The need for long-term follow-up with serial vascular imaging in survivors of high-grade SAH after endovascular coiling is highlighted by the significant rate of coil compaction with partial aneurysm recanalization (25%); although all have been asymptomatic, recurrent aneurysmal hemorrhage in the setting of coil compaction has been previously observed in one patient at our centre.

Table 4 summarizes the current and selected prior studies of high-grade SAH patients treated by endovascular coiling.^{14,18-26} Our study results of 32% mortality and a rate of good functional outcome of 53% are in line with those of previous investigators. It also compares favourably to results for surgical clipping as the International Cooperative Study on the Timing of Aneurysm Surgery showed only 11% of patients who were comatose at admission made a good recovery and 72% died.¹² Mortality rates for combined grade IV and V hemorrhage after endovascular coiling (32%) were found to be lower than those reported after surgical clipping in three historical studies (range of 34% to 52.5%)^{10,27,28} but slightly higher in two studies (range 23% to 28%).^{3,29} However, these comparisons must be interpreted with caution due to the relatively small number of patients and the heterogeneity in case selection amongst the various reported series, including ours.

The Hunt and Hess grading system has been previously reported as an important predictor of impairment of health-related quality of life after subarachnoid hemorrhage.³⁰ A higher clinical grade of SAH has been thought to portend a greater risk of mortality or disability,³¹ presumably due to greater extent of initial brain injury and more frequent complications such as hydrocephalus and vasospasm. However, the referenced study only included 20 high-grade patients who all underwent aneurysm clipping, the only method to secure a brain aneurysm in that era. Advances in endovascular technology now permit effective aneurysm therapy in a minimally invasive manner with less physiological disruption. Overall in our series, the proportion of coiled patients with good outcome (53%) outweighed that for poor outcome (15%). Our study results suggest that the axiom that clinical grade can be used to definitively predict long-term outcome may no longer be valid with modern medical care. Good functional recovery was achieved in 69% of our grade IV patients and 22% of grade V patients in our series, demonstrating that a substantial proportion of these vulnerable patients would have been denied the opportunity for a favourable outcome if they were arbitrarily refused initial aggressive treatment. This concept is also supported in a prospective cohort study by Szydelko et al³² who found lack of correlation between Hunt and Hess grade and functional outcomes after rehabilitation.

Psychosocial and behavioral deficits are common after SAH and have significant impact on re-integration into the home and community.³³ Of those functioning survivors in this report who responded to questionnaires, independent functioning and a good quality of life after at least six months follow-up was observed. These results are in accordance with those of Mocco et al³⁴ who reported a substantial proportion of high-grade patients experience cognitive recovery, increased independence, and improved quality of life. Although detailed assessment was limited to a small subset of patients in our cohort, formal

measures of quality of life suggest that favourable outcomes in function, mood, and cognition are not uncommon in survivors of this potentially devastating disease.

CONCLUSIONS

Although morbidity and mortality remain significant in patients with high-grade subarachnoid hemorrhage, judicious case selection and careful endovascular therapy permitted good functional outcomes in a significant proportion of patients in this series. Our findings suggest that aggressive intensive care and endovascular intervention in individuals with grade IV and V SAH should not be considered necessarily futile and therapeutic nihilism should be avoided in the early management of these critically ill patients.

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