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AJNR Am J Neuroradiol published online 12 January 2012
http://www.ajnr.org/content/early/2012/01/12/ajnr.A2881

Published January 12, 2012 as 10.3174/ajnr.A2881

ORIGINAL RESEARCH

Age-Related Complications Following Endovascular Treatment of Unruptured Intracranial Aneurysms

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BACKGROUND AND PURPOSE: The factors that led us to do the research for this paper was a desire to see if elderly patients did as well as non-elderly patients during endovascular intracranial aneurysm treatment. By doing this research, we could better stratify the most appropriate treatment for each patient with an aneurysm. The purpose of this study was to determine whether the incidence of procedural complications was greater in the elderly, defined as patients older than 65 years of age, compared with nonelderly patients undergoing elective endovascular treatment for intracranial aneurysms.

MATERIALS AND METHODS: A retrospective review was performed in patients undergoing elective endovascular treatment of intracranial aneurysms between 2000 and 2010 at 1 institution. "Minor complications" were defined as those resulting in minimal or no loss of function that resolved before dismissal; "major complications" were complications that resulted in loss of function or complications that required a subsequent invasive therapy. Major complications were further stratified into those with and without neurologic disability, defined as an mRS score of >3. *T* tests and χ^2 analyses were used to compare groups.

RESULTS: Three hundred fifty-five patients underwent 394 endovascular procedures treating 75 aneurysm recurrences and 319 untreated aneurysms. One hundred eight (30%) were elderly. There was no significant difference in the rate of complications in the elderly compared with the nonelderly (33% versus 26%, respectively; $P = .18$). Major complications were significantly more prevalent in the elderly than in the nonelderly (17% versus 7.4%, respectively, $P = .004$). Major complications with neurologic disability were also significantly more prevalent in the elderly compared with the nonelderly (8.2% versus 1.8%, respectively, $P = .004$).

CONCLUSIONS: Major functional complications were markedly more common in the elderly compared with the nonelderly.

ABBREVIATIONS: CI = confidence interval; mRS = modified Rankin Scale; NIS = Nationwide Inpatient Sample

Endovascular treatment with coiling has been established as a mainstay therapy of intracranial aneurysms. A number of studies suggest that endovascular therapy may be as effective as surgical clipping in treating unruptured aneurysms.[1-5] Although it is the preferred choice of treatment for unruptured intracranial aneurysms in general, it remains unclear whether endovascular coiling should be used in the elderly population. Advanced age has been reported to increase the risk of complications following such procedures as carotid stent placement[6,7] as well as surgical clipping of intracranial aneurysms.[8] Elderly patients may appear better suited for endovascular therapy than open surgery because they have an increased number of comorbidities compared with younger patients, making them poor surgical candidates.[9,10] However, it is not clear whether advanced age alone increases the risk of complications in patients undergoing endovascular aneurysm therapy.[11]

The purpose of this study was to determine the incidence of complications in patients undergoing elective endovascular therapy for intracranial aneurysm and whether complications were more frequent in elderly patients compared with younger patients.

Received February 26, 2011; accepted after revision August 8.

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http://dx.doi.org/10.3174/ajnr.A2881

Materials and Methods

We performed a retrospective review of patients undergoing elective endovascular treatment for all intracranial aneurysms at our institution, a large tertiary referral center, between January 2000 and January 2010, following approval by the Mayo Clinic institutional review board. Elective treatment was defined as treatment for either an unruptured aneurysm or retreatment of a previously treated aneurysm. When deemed necessary to achieve aneurysm obliteration, balloon-assisted and stent-assisted coiling was performed. Data collected on each patient included age; sex; number, size and location of aneurysms; presence of symptoms referable to the target aneurysms; comorbidities; type of treatment; treatment outcomes; intraprocedural medications; number of coils used; and procedural complications.

A "complication" was defined as any condition arising within 30 days of the endovascular procedure that necessitated further evaluation or treatment. Complications were stratified into 2 categories, minor and major. A "minor complication" was defined as a complication that resulted in minimal or no loss of function and resolved before dismissal; major complications were complications that resulted in loss of function (temporary or permanent) or complications that required a subsequent invasive therapy. "Major complications"

were further characterized into 2 categories: complications that resulted in unresolved neurologic deficits at dismissal and complications without neurologic deficits at dismissal. An "unresolved neurologic deficit" in major complications was defined as a neurologic deficit at the time of dismissal that was ≥3 on the mRS.[12,13] mRS score was determined by retrospectively evaluating postprocedure neurology examinations. "Elderly patients" were defined as those patients older than 65 years of age at the time of treatment. Although there is considerable variation in the literature regarding the definition of elderly, the age of 65 was chosen because it falls in the median age cutoff among publications examining coiling in elderly patients and was used in the literature reports of major studies, including the International Subarachnoid Aneurysm Trial, as the cutoff for elderly.[14-16]

Endovascular Treatment

Patients were treated under general anesthesia. Typically, a 6F guiding catheter (Envoy; Cordis, Miami Lakes, Florida) or a 5F guiding sheath (Shuttle, Cook, Bloomington, Indiana) was placed in the carotid or vertebral artery. Heparinization was administered to achieve an activated clotting time of >250 seconds. Various endovascular coil devices were used, usually bare platinum coils. Aneurysms were packed as densely as possible.

Statistical Analysis

Continuous and ordinal data were presented as means (range). Nominal data were presented as counts (percentage). Baseline comparisons of continuous data were between groups by using the Student *t* test, while nominal data were compared by using a χ^2 or Fisher exact test when appropriate. Multivariate analysis was performed to identify independent risk factors for the development of complications by using multiple logistic regression adjusting for age, sex, number of aneurysms, largest diameter of aneurysms, and location of aneurysms and whether patients were symptomatic and the type of procedure performed. A *P* value <.05 was considered statistically significant. A 95% CI was calculated when applicable. All statistical analyses were performed by using JMP, Version 5.1 software (SAS Institute, Cary, North Carolina).

Results

Patient Population

Three hundred fifty-five patients (76% female; 95% CI, 72%–80%) were identified. These patients underwent 394 elective endovascular treatment sessions during the time period studied. The mean age of patients was 57 years (range, 6–87 years). Of the 355 patients, 108 were elderly (30%; 95% CI, 26%–35%). Elderly patients were noted to have increased prevalence of hypertension and hyperlipidemia, but this is expected in an elderly population. It was also observed that the elderly population had a significantly larger average aneurysmal size (Table 1).

Three hundred nineteen procedures (81%; 95% CI, 77%–85%) involved treatment of previously untreated unruptured aneurysms, while in 75 procedures (19%; 95% CI, 15%–23%), patients were being treated for recurrence of previously treated aneurysms. Fifty-three patients (13%; 95% CI, 10%–17%) had a history of subarachnoid hemorrhage, while 39 patients (9.9%; 95% CI, 7.0%–13%) had a family history of subarachnoid hemorrhage. Of the 394 procedures, patients displayed symptoms related to their intracranial aneurysms before 105 of the 394 endovascular treatment sessions (26%; 95% CI, 22%–31%). The most common symptoms included headache, diplopia, gait instability, vertigo, hearing loss, weakness, transient ischemic attack, and seizures. The mean length of admission for all patients undergoing endovascular therapy of intracranial aneurysms was 2.0 days, and the median length of stay was 1 day (range, 1–19 days).

Table 1: Demographic comparisons[a]

	Elderly	Nonelderly	*P* Value
Age	70.7 ± 4.7	50.7 ± 10.2	
No. of men	30 (24.6%)	64 (23.5%)	.89
HTN	74 (60.6%)	124 (45.6%)	.006
Hyperlipidemia	58 (47.5%)	73 (26.8%)	.001
Heart disease	41 (33.6%)	56 (20.6%)	.007
Diabetes	10 (8.9%)	20 (7.4%)	.84
COPD	25 (20.4%)	54 (19.9%)	.893
GU	2 (1.6%)	5 (1.8%)	1.000
Only 1 aneurysm	92 (75.4%)	167 (61.4%)	.008
Aneurysm size (mm)	9.7 ± 5.4	6.3 ± 3.5	.001

Note:—HTN indicates hypertension; COPD, chronic obstructive pulmonary disease; GU, genitourinary.
[a] As expected, elderly patients had more comorbidities than nonelderly patients, particularly hypertension and hyperlipidemia. However, with an elderly population, these 2 comorbidities are expected to be increased in prevalence.

There were single intracranial aneurysms in 259 procedures (66%; 95% CI, 61%–70%) and 135 procedures (36%; 95% CI 30%–39%) involving patients with multiple intracranial aneurysms. The largest number of aneurysms in 1 patient was 8 ($n = 3$). Of the 394 primary aneurysms treated, 36% (95% CI, 31%–41%) were located in the internal carotid artery, 22% (95% CI, 18%–26%) were located in basilar artery, 15% (95% CI, 11%–19%) were located in the anterior communicating artery, 9.1% (95% CI, 6.2%–12%) were located in posterior communicating artery, 8.1% (95% CI, 5.4%–11%) were located in middle cerebral artery, 4.3% (95% CI, 2.3%–6.3%) were located in the posterior cerebral artery, 2.5% (95% CI, 1.0%–4.0%) were located in the anterior cerebral artery, 1.8% (95% CI, 0.5%–3.1%) were located in the supraclinoid internal carotid artery, and 1.5% (95% CI, 0.3%–2.7%) were located in the superior cerebellar artery.

The mean number of aneurysms treated per patient was 1.06, while the maximum number treated during 1 procedure was 3 ($n = 3$). The mean diameter of the largest aneurysm treated during each procedure was 7.4 mm (range, 1–30 mm). Aneurysms were treated by coiling in 279 procedures (71%; 95% CI, 66%–75%), balloon-assisted coiling in 81 procedures (21%; 95% CI, 17%–25%), stent placement and coiling in 9 procedures (2.3%; 95% CI, 0.8%- 3.8%); and coiling was attempted but failed in 25 procedures (6.3%; 95% CI, 3.9%–8.8%).

Complications

Complications developed following 110 procedures (28%; 95% CI, 23%–32%). Sixty-nine minor complications (18%; 95% CI, 14%–21%) in 394 procedures were identified, representing 63% (95% CI, 54%–72%) of all complications. The most common minor complication was asymptomatic intravascular thrombus or embolus, which occurred in 30 patients (7.6%; 95% CI, 5.0%–10%) in 394 procedures. Other com-

Table 2: Major and minor complications in elderly and nonelderly patients[a]

	All Patients	Nonelderly Patients	Elderly Patients	*P* Value
No. of Patients	355	247	108	
No. of Procedures	394	272	122	
Minor complications	69 (18%)	50 (18%)	19 (16%)	.56
	CI, 14%–21%	CI, 14%–23%	CI, 9.1–22%	
Major complications	41 (10%)	20 (7.4%)	21 (17%)	.004
	CI, 7.4%–13%	CI, 4.2%–10%	CI, 11%–24%	
Major complications without neurologic deficit	26 (6.6%)	15 (5.5%)	11 (9.0%)	.19
	CI, 4.2%–9.1%	CI, 2.8%–8.2%	CI, 3.9%–14%	
Major complications with neurologic deficit	15 (3.8%)	5 (1.8%)	10 (8.2%)	.004
	CI, 1.9–5.7%	CI, 0.2–3.4%	CI, 3.3%–13%	

[a] All CIs are in 95% intervals.

Table 3: Comparison of previously ruptured aneurysms and unruptured aneurysms[a]

	Previously Ruptured	Unruptured	*P* Value
No. of procedures	319	75	
Age (yr)	55.1 ± 13.5	57.6 ± 12.5	NS
Percentage of women	77	77	NS
No. of aneurysms	1.1 ± 0.4	1.05 ± 0.24	NS
Size of aneurysm	5.9 ± 4.1	7.9 ± 4.5	.0005
Number of coils	4.3 ± 3.3	5.5 ± 3.5	.00072
Major complications	14	27	.10
Minor complications	17	52	.24

Note:—NS indicates not significant.
[a] Although the number of coils and size of aneurysm varied between unruptured aneurysms and previously ruptured ones, there was no difference in the complication rate between the 2 groups.

mon minor complications included hematoma formation at the vascular access site ($n = 10$, 2.5%; 95% CI, 1.0%–4.1%), misplaced coils that were retrieved ($n = 10$, 2.5%; 95% CI, 1.0%–4.1%), urinary retention ($n = 7$, 1.8%; 95% CI, 0.5%–3.1%), cardiac arrhythmias ($n = 3$, 0.8%; 95% CI, −0.1%–1.6%), and neck pain ($n = 3$, 0.8%; 95% CI, −0.1%–1.6%).

Of the 110 complications, 41 were major complications (10.4% of all 394 procedures; 95% CI, 7.4%–13%). Patients experienced 26 (6.6% of all procedures; 95% CI, 4.1%–9.1%) major complications that did not result in neurologic deficits at dismissal. These included temporary neurologic deficits that resolved before dismissal ($n = 13$, 3.3%; 95% CI, 1.5%–5.1%), subarachnoid hemorrhage ($n = 8$, 2.0%; 95% CI, 0.6%–3.4%) resulting in hydrocephalus and ventricular shunt placement in 3 patients, acute anemia requiring transfusion ($n = 3$, 0.8%; 95% CI, −0.1%–1.6%), and seizures ($n = 1$, 0.25%; 95% CI, −0.2%–0.7%); 1 patient had an occlusion of the common femoral artery requiring thrombectomy (0.25%; 95% CI, 0.2%–0.7%).

Fifteen (3.8% of all procedures; 95% CI, 1.9%–5.7%) patients had major complications with neurologic deficits. Thirteen patients (3.3% of all procedures; 95% CI, 1.5%–5.1%) had ischemic infarctions that resulted in neurologic deficits at dismissal. Two patients (0.5%; 95% CI, −0.2%–1.2%) had fatal ischemic infarctions (Table 2).

No difference was noted in the complication rate or demographics of patients who were undergoing treatment for unruptured aneurysms or previously treated ruptured aneurysms (Table 3). Similarly, there was no difference in complication rates between patients on anticoagulation therapy and those not on anticoagulation therapy (Table 4).

Table 4: Effect of anticoagulation therapy on complications[a]

	Anticoagulation Therapy Prior to Procedure	No Anticoagulation Therapy Prior to Procedure	*P* Value
No. of patients	123	271	N/A
Minor complications	23	46	.67
Major complications	10	31	.37

Note:—N/A indicates not applicable.
[a] No effect was noted on complications between patients on anticoagulation and those not on anticoagulation therapies.

Age-Related Risk Factors for Complications

Age older than 65 years was not a significant risk factor for complications overall ($P = .18$, Table 5). Rates of minor complications were not significantly different between nonelderly and elderly patients ($P = .56$). However, both major complications overall (7.4 versus 17% for nonelderly and elderly patients, respectively, $P = .004$) and major complications associated with neurologic deficit (1.8% versus 8.2% for nonelderly and elderly patients, respectively, $P = .004$) were significantly more prevalent in the elderly compared with nonelderly patients (Table 5).

Discussion

In the current study, we demonstrated that elderly patients undergoing elective endovascular intracranial aneurysm treatment do not have a greater overall complication rate compared with nonelderly patients. However, major complications, particularly major complications associated with neurologic deficits, occurred at a significantly greater rate in the elderly population compared with the nonelderly population, with elderly patients having such complications 4 times as frequently as nonelderly patients. One potential explanation for this observed difference in major complication rates is that the "vascular reserve" of elderly patients is compromised; thus, any type of ischemic insult may lead to symptoms that might be subclinical in younger patients.[17]

Asymptomatic diffusion abnormalities are common after coil embolization, occurring in >50% of patients in many series.[18] Furthermore, elderly patients have tortuous vasculature and atherosclerotic disease in the aortic arch and intracranially, making them prone to complications.[19] While these explanations cannot be proved in the current series, the fact that other neuroendovascular procedures, including carotid stent placement, appear relatively poorly tolerated in elderly patients lends credence to the concept of diminished vascular reserve.[17,19] Although these 2 articles[17,19] on this subject had

Table 5: Patients with major complications and unresolved neurologic deficits

Sex	Age of Patient (yr)	Location of Ischemic Event	Clinical Findings	mRS Score
Female	74	Right posterior occipital infarct, bilateral thalamic infarcts, and right medial temporal infarct	Vision loss, gait imbalance, lower extremity weakness	5
Female	65	Left middle cerebral infarct	Nausea, vomiting, headache, right hand tingling, and dysmetria	3
Female	80	Right posterior cerebral infarct	Urinary retention, left-sided weakness	3
Female	50	Posterior inferior cerebellar infarct	Gait imbalance and lower limb weakness	3
Female	51	Anterior cerebral infarct	Right-sided weakness	3
Female	74	Pontine and left midbrain infarct	Right-sided hemiparesis, dysarthria, ataxia	4
Female	76	Bilateral cerebellar, right pons, and cerebral peduncle infarcts	Left lower extremity weakness and dysarthria	5
Female	65	Right cerebellar and paramedian left cerebellar infarcts	Facial weakness and right hemi-ataxia, right 6th and 7th cranial nerve palsies	4
Male	37	Subarachnoid hemorrhage, multiple infarcts	Severe anoxic brain injury resulting in death	6
Female	43	Ophthalmic artery occlusions	Decreased left eye visual acuity	3
Female	73	Multiple infarcts	Death	6
Male	66	Watershed left frontal and parietal lobe infarcts	Right lower extremity weakness, blurry vision, right homonymous hemianopsia	4
Male	66	Left paracentral lobule infarct	Generalized right-sided lower extremity weakness	3
Female	73	Anterior cerebral occlusion by coil	Left lower extremity weakness	3
Female	47	Middle cerebral embolization by coil	Right upper extremity weakness	3

different age cutoffs for the elderly (70 and 80, respectively), the idea of diminished vascular reserve can be applied to elderly patients in general, because it is a gradual phenomenon. The findings of elevated risk of major complications indicate that elective coiling in the elderly should be carefully considered, especially given the relative risk of spontaneous hemorrhage and potentially shorter life expectancy than in younger patients.

Relatively few previous studies have examined the complication rate of elderly patients undergoing elective endovascular aneurysm treatment. Most of these previous studies have focused on treatment of elderly patients with ruptured aneurysms.[15,16,20] Gonzalez et al[11] reported 97 elderly patients, defined as older than 70 years of age, who had undergone elective aneurysm treatment. In that study, it was determined that being elderly carried no additional risk during coiling. However, the study had no comparison between nonelderly and elderly patients; thus, it could not determine whether coiling had a higher rate of complications within the elderly group. The overall major complication with neurologic deficits rate that we observed was 3.8%, which is comparable with the 3% found by Ross and Dhillon[21] in their study of aneurysms. That study did not examine complications not involving permanent neurologic deficits, and we could not compare the other types of complications to this study or others.

Our mortality rate of 0.5% in the elderly group is lower but comparable with the rate of 1.3% observed by van Roojj and Sluzewski.[22] Furthermore, the mortality rate in our elderly group was similar to that of the 0.8% found in the NIS.[23,24] Also in the NIS, it was noted that patients aged 65–79 years had a significantly increased mortality rate compared with patients younger than 65 years of age, as shown in the current study.[23]

This retrospective trial had several limitations. First, it remains possible that with complete follow-up and prospectively defined outcomes, risks might have been higher in both groups than we determined with retrospective data analysis. Second, we defined the elderly as patients older than 65 years of age, while other studies have used different age thresholds. A third limitation was in the observation that the elderly population had an average aneurysmal size larger than that in the nonelderly population, perhaps biasing results because larger aneurysms are more prone to complications such as rupture or lack of compaction.[25] Further study may be warranted between elderly and nonelderly cohorts with similar aneurysmal sizes.

Disclosures: David Kallmes—*Research Support (including providing of equipment or materials)*: NFocus, Sequent, ev3, MicroVention, Cordis, *Consultant*: ev3, *Details*: development of educational materials.

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