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Original Article

Unruptured Intracranial Aneurysms in Elderly Patients: Results of Surgical and Endovascular Treatment

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SUMMARY

Background: Management of unruptured intracranial aneurysms (UIA) in elderly patients is controversial, taking into consideration their limited life-expectancy and existing comorbidities. With advances in endovascular techniques, we decided to evaluate treatment results in this population and to assess results in surgically and endovascularly treated cases.
Methods: Thirty six elderly patients, aged ≥ 70, with the total of 39 aneurysms, were treated. The possibility of endovascular treatment was considered as the first option and surgical treatment as the second method of intervention.
Results: No patient died and no patient became bedridden after the procedures. In surgical group (14 UIA), deterioration was observed in five cases at the time of discharge, but persisted in only two cases at follow-up. In endovascular group (25 UIA), deterioration was observed in one case at the time of discharge and persisted at follow-up. Endovascular techniques included coils placement alone in nine (36%) procedures, coiling with stent placement in five (20%) procedures and stent placement alone in eleven (44%) procedures. Follow-up DSA revealed no treatment effect in three patients after stent placement alone (12% of endovascularly treated aneurysms). Of these, two patients were successfully retreated with second flow-diverting stent placement and one patient refused retreatment.
Conclusion: Treatment of elderly patients with UIA is relatively safe and effective. Worse short-term and long-term outcomes were observed among the operated compared to embolized patients. In patients treated with stent placement alone, treatment failure and the need for the next stage of embolization in some cases should be taken into account.

1. Introduction

The rationale for the treatment of unruptured intracranial aneurysms (UIA) in the elderly patients is still matter of debate because of their limited life expectancy combined with not negligible risk of treatment.[1–3] However, a therapeutic intervention in physically and mentally healthy older persons may be justified, especially in the face of the ever-increasing human lifespan.[2,4,5] Furthermore, psychological discomfort resulting from the presence of an aneurysm threatening with hemorrhage is similar at all ages and it is difficult to define a clear upper age limit from which no treatment should be undertaken.[6] Nonetheless, it should be aware that the risk of complications seems to be higher in this group of patients.[3,7,8] Large prospective series assessing treatment results of UIA in the elderly are lacking.[2] In the face of developing endovascular techniques, we decided to evaluate treatment results in this age group of patients and to assess results in surgically and endovascularly treated cases.

2. Materials and methods

2.1. Subjects

The clinical and radiological data of elderly patients, defined as 70 years old and more, who were treated for UIA in 2010–2016 were reviewed retrospectively. Only patients treated surgically or endovascularly were included in this series. Aneurysm size was defined as the largest diameter measured on three-dimensional reconstruction of computed tomography angiography (CTA) or digital subtraction angiography (DSA) images. Patients with an aneurysm larger than 5 mm in diameter, with symptomatic aneurysms, with enlarging aneurysm in serial CTA imaging and with an aneurysm with a daughter sac were qualified for treatment. In our approach to the treatment of UIA we consider the possibility of endovascular treatment as the first option and surgical treatment as the second method of intervention. In addition, we qualify all posterior circulation aneurysms for endovascular procedures.

Surgical and endovascular procedures were carried out under general anesthesia. The aim of coiling was to obtain maximal packing of the aneurysm, until not a single coil could be placed inside and contrast agent did not fill aneurysm sac. In some cases, balloon-

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assisted or stent-assisted coiling were used to prevent possible coil herniation to parent vessels. In some patients, flow-diverting stents were deployed, especially in cases with wide-neck aneurysms or with larger size aneurysms. During surgical procedures all aneurysms were clipped with the idea of achieving optimal positions of the clips. Aneurysms with atherosclerotic changes were clipped with leaving a bit of the aneurysm neck in order to avoid parent vessels stenosis or occlusion. In the endovascular treatment group, immediate angiographic results at the end of procedures were noted.

Periprocedural morbidity was defined as a deterioration of preprocedural neurological deficits or occurrence of new permanent deficits after surgical or endovascular treatment. Postprocedural mortality was defined as all-cause mortality occurring within 30 days after of the procedure.

The modified Rankin Scale (mRS) was used for evaluation during long-term follow-up.[9] The long-term status of the patients was determined on the basis of observations in an outpatient clinic, examinations during follow-up hospitalizations or by telephone interviews with patients or their relatives. All cases treated by endovascular coiling had follow-up DSA performed at 6 months and all cases treated by stent placement had follow-up Dyna-CT performed at 3 months and follow-up DSA at 6 months after the procedure. Depending on the results of these examinations, some of the patients had further follow-up studies in the form of DSA, Dyna-CT or magnetic resonance angiography (MRA). Patients treated with stent placement received dual antiplatelet therapy (clopidogrel and acetylsalicylic acid) until follow-up Dyna-CT, i.e. for three months after the procedure.

2.2. Statistical analysis

Data were analyzed using the Statistica software, version 12.0 (StatSoft, Tulsa, OK). The analyses included basic descriptive statistics, the Student t-test, and contingency tables with the Pearson Chi-square test and the exact Fisher test. p-value of less than 0.05 was considered statistically significant.

2.3. Ethics

Our study is a retrospective analysis and in our institution according to our country law this type of research does not require Institutional Review Board approval. We obtained a statement from the IRB Committee that the study is exempt from such an approval (decision number: AKBE/148/2018). All patients gave written informed consent for the procedures. A consent for publication was not required and all identifiable information are not included in the manuscript.

3. Results

3.1. Study group

Of 36 elderly patients treated during study period, 34 had a single UIA, including 13 patients (five men and eight women) who were treated surgically and 21 patients (four men and seventeen women) who were treated by endovascular intervention. Two patients had multiple aneurysms. One woman had two aneurysms, the first aneurysm treated by an endovascular intervention and second aneurysm treated surgically, and another woman had three aneurysms, all treated by an endovascular intervention, each one during a separate session. Thus, the subject of the analysis is the treatment of 39 unruptured intracranial aneurysms. The average age was 73.3 years (range: 70–81 years). Duration of the medical history ranged from five days to six years, with the mean of 295 days and the median of 142 days. Almost half of UIAs were discovered incidentally (n = 17, 47.2%) and in the remaining aneurysms headache was the most common reason for a diagnostic procedure - Table 1.

There were 35 anterior circulation aneurysms, including 14 (40%) treated surgically and 21 (60%) treated endovascularly, and four posterior circulation aneurysms, all treated endovascularly. The MCA bifurcation and ICA-PcomA were the most frequent locations (Table 2). All two patients with cavernous ICA aneurysms were symptomatic. Diplopia and oculomotor nerve paresis or diplopia and abducens nerve paresis with trigeminal nerve dysfunction were observed in these cases, respectively. There were two aneurysms with the largest diameter < 5 mm, twenty seven with the largest diameter in range 5–12 mm, eight with the largest diameter in range 12–25 mm, and two with the largest diameter > 25 mm. There was no significant difference (p = 0.600) in size between operated (mean 9.81 mm) and embolized aneurysms (10.82 mm), although the largest aneurysms were embolized. Aneurysms in the posterior circulation were treated only endovascularly, while MCA aneurysms were mostly treated surgically (Table 2). Neurological deterioration after the procedures was not related to the size of aneurysm (p = 0.514). Regarding the location of the aneurysms, postprocedural deterioration was statistically more frequently observed in cases of MCA bifurcation aneurysms (MCA bifurcation location vs. other locations, p = 0.007).

3.2. Surgical group results

During surgical procedures, all aneurysms were clipped with

Table 1
Presenting symptoms.

Presenting symptom	Number of patients (%)
Discovered incidentally	17 (47.2%)
Headache	9 (25%)
Oculomotor palsy	5 (13.9%)
Abducens palsy	1 (2.8%)
Epileptic seizures	1 (2.8%)
Prior SAH from another aneurysm	3 (8.3%)

Table 2
Location of aneurysms and the method of treatment depending on the location.

Location of aneurysm	Number of cases	Treated endovascularly	Treated surgically
ICA-PcomA	8	6 (75%)	2 (25%)
ICA bif.	2	2 (100%)	0
ICA-opht.	2	2 (100%)	0
ICA cavernous	2	2 (100%)	0
ICA-hypoth. sup.	2	2 (100%)	0
MCA bif.	12	2 (16.7%)	10 (83.3%)
AcomA	7	5 (71.4%)	2 (28.6%)
VA-PICA	1	1 (100%)	0
VB junction	2	2 (100%)	0
BA bif.	1	1 (100%)	0

ICA-PcomA: Internal Carotid Artery-Posterior communicating Artery, ICA bif.: Internal Carotid Artery bifurcation, ICA-opht.: Internal Carotid Artery - Ophthalmic Artery, ICA cavernous: cavernous segment of Internal Carotid Artery, ICA-hypoth. sup.: Internal Carotid Artery - Superior Hypophyseal Artery, MCA bif.: Middle Cerebral Artery bifurcation, AcomA: Anterior communicating Artery, VA-PICA: Vertebral Artery - Posterior Inferior Cerebellar Artery, VB junction: Vertebrobasilar junction, BA bif.: Basilar Artery bifurcation.

optimal positions of the clips. Complete clipping was achieved in 13 of 14 aneurysms, and the remaining aneurysm was clipped with leaving a bit of the neck due to atherosclerotic changes to maintain vessels patency.

No patient died and no patient became bedridden. A deterioration of preoperative neurological deficits or occurrence of new deficits after the operation was observed at the time of discharge in five cases: four patients with MCA bifurcation aneurysms had aphasia and one patient operated for an ICA-PcomA aneurysm had a motor deficit and oculomotor nerve paresis. No patient was lost to follow-up, which average duration was 30 months. During the follow-up, aphasia resolved in three patients and remained unchanged in the remaining patient, and the postoperative motor deficit observed in one patient improved during the follow-up. Preoperative and long-term follow-up clinical status according to mRS is shown in Table 3.

3.3. Endovascular group results

The following embolization techniques were used: coils placement alone in nine (36%) procedures, coiling with stent placement in five (20%) procedures and stent placement alone in eleven (44%) procedures. In all cases with stent placement alone flow-diverting stents were used.

Endovascular coiling resulted in nine cases of complete obliterations with no contrast filling in the aneurysmal sac and five cases with small residual necks. In 11 cases with stent placement alone, partial thrombosis of aneurysmal sac was observed in two cases and delayed contrast stagnations in the aneurysmal sac was observed in nine cases at the end of the procedures.

No patient died and no patient became bedridden. Neurological deterioration in the form of aphasia was observed in only one case with location of the aneurysm in MCA bifurcation. Healing problems at the access site to the femoral artery occurred in four cases and included a hematoma in one case and a pseudoaneurysm in three cases.

No patient was lost to follow-up. The mean duration of follow-up was 31.5 months (median: 29 months). Aphasia observed postoproceduraly in one case improved considerably during long-term follow-up. Preprocedural and follow-up clinical status according to mRS in the endovascular group is presented in Table 4.

Follow-up DSA were performed in all cases. A total of 28 follow-up DSA (1.12 per aneurysm, 1.22 per patient) and 19 other vascular examinations, i.e. Dyna-CT and MRA (0.76 per aneurysm, 0.83 per patient) were undertaken. Follow-up imaging confirmed successful treatment in all nine cases with a complete obliteration of the aneurysm sac after coiling. Of five cases with a residual neck of aneurysm, follow-up imaging showed a complete obliteration of aneurysms in two cases and no change of the residual neck in three cases. At the follow-up imaging in the group of 11 cases with stent placement alone: complete thrombosis of the aneurysm sac was observed in five cases, unimportant contrast filling at the base of the aneurysm, stable at subsequent controls, was observed in three cases and contrast filling of the aneurysm sac with no change of the aneurysm size was observed in three cases. Of the latter three cases with aneurysm contrast filling (12% of endovascularly treated aneurysms), two patients were successfully retreated with second flow-diverting stent placement and one patient refused retreatment.

A deterioration of preprocedural neurological deficits or occurrence of new deficits immediately after procedures was observed significantly more frequently after the surgical treatment (in 5 of 14 aneurysms) compared to the endovascular treatment (in 1 of 25 aneurysms) ($p = 0.016$). When comparing patients condition at follow-up in relation to the condition before the procedures, long-term treatment outcomes as evaluated by the mRS were also significantly better in the endovascular group compared to the operated patients ($p = 0.014$). The change in the patient condition was not dependent on the aneurysm site (anterior vs. posterior circulation) (p = ns) and the aneurysm size (p = ns).

4. Discussion

Our series demonstrated that the treatment of elderly patients with UIA is relatively safe with favorable results. Both treatment approaches, i.e. surgical and endovascular, are effective with no postprocedural mortality. Morbidity in the surgical group was higher than in the endovascular group. It should be noted that neurological deterioration observed immediately after procedures resolved or improved during further follow-up in most cases and the vast majority of patients were independent at follow-up evaluation. In the majority of embolized aneurysms, successful treatment was observed in follow-up DSA, although among patients with stent placement alone, treatment failure was observed in some cases. In these patients, the next stage of treatment was necessary with second flow-diverting stent placement.

Nowadays management of elderly patients with unruptured intracranial aneurysms is still matter of debate. Increasing availability of imaging studies has led to increased detection of UIA also in the elderly group. Patients with UIA are affected by a potentially devastating disease, and preventing aneurysm rupture by a surgical or endovascular intervention is considered the most effective strategy for lowering mortality and morbidity rates associated with SAH.[2,10] However, all currently used therapies carry some risk and therefore treatment recommendations require careful and judicious consideration of the natural history of UIA, especially that treatment risks are thought to be higher in the elderly patients.[2,3,7]

Focusing on influence of an increasing patient age as a risk

Table 3
Preoperative and follow-up clinical status according to mRS in surgical group.

Status according to mRS	Number of cases (%)	
	Preoperatively	At follow-up
0	8 (57.1%)	10 (71.4%)
1	6 (42.9%)	2 (14.3%)
2	0	1 (7.15%)
3	0	1 (7.15%)
4	0	0
5	0	0
6	-	0

mRS: modified Rankin Scale.

Table 4
Preprocedural and follow-up clinical status according to mRS in the endovascular group.

Status according to mRS	Number of cases (%)	
	Preproceduraly	At follow-up
0	17 (68%)	20 (80%)
1	8 (32%)	5 (20%)
2	0	0
3	0	0
4	0	0
5	0	0
6	-	0

mRS: modified Rankin Scale.

factor of hemorrhage, studies reveal an unclear pattern with some investigators noting direct relationship, while others noted no or even inverse relationship. A long-term study by Juvela et al.[10] showed that the patient age at the time of diagnosis was a significant inverse predictor for subsequent aneurysm rupture. The relative risk with increasing age in this study was 0.97 per year with the 95% confidence interval of 0.93–1.0. It is important to point out that most patients in this cohort had a history of subarachnoid hemorrhage from another aneurysm. On the other hand, in a prospective study performed in Japan (Unruptured Cerebral Aneurysms Study; abbr. UCAS), age over 70 years was not found to be an independent predictor of aneurysm rupture.[11] Similarly, the patient age did not affect rupture rates in International Study of Unruptured Intracranial Aneurysms (abbr.ISUIA) in the subgroup of patients with no history of SAH from another aneurysm. However, in the subgroup of patients with previous SAH from another aneurysm older age was a predictor of rupture.[8] Also, in the meta-analysis based on 4706 patients, age above 60 years was a risk factor for UIA rupture with relative risk of 2.0 in comparison to youngers.[12] In the recent report that summarized the UCAS I and UCAS II study results, Japanese authors[13] in multivariate analysis showed that in elderly patients, the subgroup of patients older than 80 years old had a twice higher risk of aneurysm rupture compared to patients between 70 and 80 years of age. De Rooij et al.[14] also found in a meta-analysis, that incidence of SAH clearly increases with age. In addition, these authors noted that a gender difference of higher SAH incidence in women compared to men appears at the age of 55 years and increases thereafter. In summary, intuition suggests, that because some UIA enlarge with time,[10] the elderly people should be more likely to have larger size aneurysms, and therefore older age should be a risk factor for hemorrhage. On the other hand, the majority of discovered UIA do not rupture over a patients' lifetime.

A discrepancy between chronological and biological age exists in people and this phenomenon becomes greater in the elderly. This makes difficult, if not impossible, to define a cut-off age limit for an intervention in case of UIA. The unknown further life expectancy for a specific patient causes the intention of treating UIA justifiable even at an advanced age.[1,4,5,15] Of course, the decision to treat older individuals will be reasonable if the risk of complications is relatively low (within acceptable ranges), similarly to other age groups.[1,4,5,15] Individual decisions should be based on the assessment of risks and benefits, including comorbidities which may influence outcome. We should also not underestimate the fact that the awareness that aneurysm rupture could lead to death can have a negative impact of quality of life.[6] The mortality rate after SAH is high, around 42–60%,[10,16,17] with about 50% of survivors having moderate to severe disability.[17]

In contrast to surgery, endovascular morbidity and mortality are less dependent on the patient age.[2,4,7] The International Study on Unruptured Intracranial Aneurysms (ISUIA) demonstrated that age was a strong predictor of poor outcome in the surgical group but not in the endovascular group.[8] Surgery is considered more invasive and is associated with a greater risk for the elderly patients because many of them are in a poor general condition, with many comorbidities that are poor prognostic factors in case of a major surgery. Moreover, the elderly patients are more likely to have atherosclerotic and calcified adjacent arteries which also increases the surgical risk. Endovascular therapy is associated with lower rates of morbidity and mortality compared to surgery, particularly in patients in a poor general condition or with numerous risk factors.[2,3] However, it could be true only for short-term results, without taking into account the mortality and morbidity in the endovascular group due to subsequent retreatment of incompletely coiled or recanalized aneurysms. Retreatment, which is almost exclusively necessary after endovascular treatment leads to a bias against surgery.[18] The risk of recanalization, especially of incompletely coiled aneurysms, causes the question of the durability of endovascular treatment in the long term and its efficacy in preventing SAH. Indeed, incomplete aneurysm occlusion after an endovascular treatment is frequently observed and residual or recurrent filling is detected in between 15% and 50% follow-up angiograms.[19–21] Failure to achieve complete occlusion seems to be closely related to the size and location of the aneurysm and is particularly observed in large aneurysms and in posterior circulation aneurysms. Retreatment of endovascularly treated UIA is performed on average in 10% of patients.[19] Also in our series, we found no treatment effect in three (12%) of the embolized patients (more precisely in patients who had been stented only), requiring re-embolization which was successfully performed in two cases (the third patient refused further treatment).

A meta-analysis of the surgical treatment of UIA in patients in all ages showed that mortality was observed in 1.7% of cases with 99% confidence interval from 0.9% to 3.0% and an unfavorable outcome, including death, occurred in 6.7% of cases with 99% confidence interval from 4.9% to 9.0%.[22] A prospective multicenter study that focused on UIA patients treated by endovascular approach (ATENA) showed the 1-month mortality rate of 1.4% and morbidity rate of 1.7%.[23] It is easy to notice that endovascular treatment is characterized by a lower morbidity and similar mortality. However, in the ATENA trial, endovascular treatment failed in 4.6% of patients, post-procedural aneurysmal occlusion was complete only in 59.0%, neck remnant was observed in 21.7%, and aneurysm remnant was observed in 19.3% patients.[23] The rate of immediate neurological complications is higher among the elderly patients undergoing surgery compared to the endovascular intervention (10.3% vs. 3.5%)[24] and this difference becomes more prominent as the patients age increase. Using the National Inpatient Sample, Brinjikji et al.[7] found that coiled patients between 65 and 79 years of age had a lower in-hospital mortality (0.8% vs. 2.0%) and were less frequently discharged to long-term facilities (6.9% vs. 26.8%) compared to clipped patients, which was even more pronounced in the group of patients above 80 years of age, in whom in-hospital mortality was 2.4% in the endovascular arm versus 21.4% in the surgery arm and discharge to long-term facilities was in 9.8% versus 33.5% of cases, respectively. In that study, no differences in the in-hospital mortality was seen only in subgroup of patients younger than 50 years of age (0.6% vs. 0.6%), but less frequent discharge to long-term facilities was also observed among them in coiled cases (3.5% vs. 8.1%).

Thus, for the elderly patients, especially those older than 80 years, endovascular intervention seems to be a better option based on short-term outcomes if treatment of UIA is indicated.

Our study has some limitations. First, it was done retrospectively and therefore susceptible to potential biases. Second, it included a relatively small number of patients. Third, we defined the elderly population as patients aged 70 and above, and the specific age threshold used can have an impact on the results.

Conflict of interest statement

The authors declare that the research was conducted in the absence of any financial and non-financial relationships that could be construed as a potential conflict of interest.

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