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Clipping versus coiling for intracranial aneurysms

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ABSTRACT

Background and purpose: The aim of this study was to compare results of clipping and coiling for aneurysms of the anterior circle of Willis. Previous studies have not identified a clear superiority of one method over the other.

Material and methods: The study group included 165 consecutive patients. The assessment took into account the risk of death, neurological status according to the scale of the GOS and mRS, the incidence of early complications and quality of life measured by own surveys and questionnaire EORTC QLQ-C30 v. 3.0.

Results: Mean follow-up was more than four years. Early and late results of treatment after embolization and clipping for all patients did not differ. Evaluation of patients with bleeding aneurysms demonstrated better outcomes after embolization, however statistical significance was observed only in terms of symptomatic scale score of QLQ-C30 questionnaire ($p = 0.02$). For patients with non-bleeding aneurysms better outcomes were obtained after clipping, but statistical significance was found only in the early results: more excellent results in GOS score at discharge ($p < 0.03$) and fewer complications during hospitalization ($p = 0.02$).

Conclusions: Results of treatment after clipping and coiling do not differ in total for all patients, but differ depending on the presence of bleeding. Patients with bleeding aneurysms achieve better outcomes after coiling, and patients with non-bleeding aneurysms achieve better outcomes after clipping.

1. Introduction

Owing to the development of the vascular neurosurgery in the middle of the 20th century clipping has become an unrivalled method of treating intracranial aneurysms [1]. The new revolution has been brought about by the introduction of the detachable coils in 1990 by Guido Guglielmi and the Boston Scientific company briefly called GDC (Guglielmi Detachable Coils) [2]. In the following years there was a rapid development

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and popularization of the endovascular embolization in the treatment of cerebral aneurysms supported by technical progress with regard to the structure of the coils and the methods of their application. The introduction of stents, first described by Higashida in 1997, has additionally broadened the possibilities and the range of the indications as to the treatment [3]. Coiling, initially treated as a complementary method applied in cases of limited possibilities of surgical treatment, has not only become competitive but in certain fields started to substitute clipping. Contemporarily, in the majority of cases the primary aim of treating aneurysms which is the protection from bleeding may be obtained both by clipping and coiling. The advantage of the embolization is a shorter time of the procedure, a reduction of typical surgical complications such as infections or bleeding and the unnecessity of the brain compression and its aftermaths. The less permanent effect of treatment and, consequently, more frequent necessity of repeating intervention are considered to be the biggest disadvantages of coiling [4,5]. Moreover, more frequently aneurysms initially planned for endovascular treatment are eventually clipped than the other way round [6,7]. In case of certain complications after embolization, namely uncontrolled dislocation of coils from the aneurysm sack to the artery, the surgical intervention may give a chance to level the negative sequelae [8]. For these reasons, regardless of the increasing quality and rapid improvement of endovascular techniques there are no prognoses for classical surgical methods to be displaced.

The growing experience of applying both methods has allowed to elaborate certain preferences as to the choice of the treatment. The localization of the lesion plays a particularly significant role. In neurosurgery, with regard to the differences in the difficulty of accessing, a division into an anterior and posterior part of the circle of Willis has been commonly accepted. The superiority of embolization has been naturally and indisputably acknowledged for the aneurysms of the posterior part of the circle which are significantly harder to access surgically. Noticeable tendencies that differentiate the results of treatment are also formed with regard to such parameters as the size of the aneurysms, the age of the patients, their initial condition and more specific localizations, yet they contemporarily remain more as observations than certainties [4,5,9–11]. On the contrary, in case of the aneurysms located in the anterior part of the circle of Willis, there are no premises indicating the predominance of either method. Certainly, there are comparisons presenting better results after embolization; nevertheless, their critical analysis and the assessment of late results throw doubt on such unambiguous conclusions. Alike is the case of ISAT – currently the biggest and the most well-known prospective study which directly compares the results of treating bleeding aneurysms with clipping and endovascular embolization [12,13]. There are some randomized trials concerning bleeding aneurysms, however the number and quality of studies comparing the results of treatment of unruptured aneurysms is insufficient. For these reasons, apart from the aneurysms occurring in the posterior part of the circle, the choice between the endovascular embolization and clipping as the optimal form of treatment remains opened.

The aim of this research was to compare the early and late results of treating intracranial aneurysms located in the anterior part of the circle of Willis with the use of two different methods: clipping and endovascular embolization. An attempt has been undertaken to answer the question whether the results of the treatment with these methods vary and if they depend on the presence or absence of bleeding from the aneurysm.

2. Materials and methods

The assessment embraced all 165 consecutive patients treated for aneurysms located in the anterior part of the circle of Willis in the years 2003–2008. In 24 cases more than one aneurysm was treated in one patient. Twelve patients underwent more than one procedure (from 2 to 4). Three patients were excluded: two of them with non-bleeding aneurysm treated with both endovascular and surgical methods and one person with unfavourable results of simultaneous treatment of the ruptured basilar artery aneurysm.

The decision about the type of therapy was taken by the neurosurgeon on the basis of the evaluation of the condition of the patients, the results of the imaging, the opinion of the interventional neuro-radiologist and the choice of the patients themselves, if their condition allowed for a conscious consent. In some cases the choice of the method was limited by its availability. The technical limitations always concerned coiling, never clipping.

The study evaluated the outcome of patients instead of particular aneurysms. For the assessment the Glasgow Outcome Scale (GOS) [14] and the modified Rankin scale (mRs) [15] were applied. For estimating the quality of life the quality of life questionnaire EORTC QLQ-C30, version 3.0 [16,17] was employed as well as a self-created survey which included questions about the change in the overall health condition after treatment, coming back to work and other possible changes in the social functioning. The condition on the day before the intervention or the day of the intervention was assumed to be the initial condition whereas the treatment results were estimated for two periods: the condition on the last day of hospitalization and the condition after at least one year from the procedure. The grades 4 and 5 on the GOS scale and 0, 1 and 2 on the mRs scale were assumed as a "good" result. The "death" result corresponded with the grade 1 on the GOS scale and 6 on the mRs scale. Due to the expected significant majority of good results in the treatment of non-bleeding aneurysms another group has been distinguished of "very good" results embracing the grade of 5 on the GOS and 0 and 1 on the mRs scale. For the assessment of the early complications all significant, undesirable events were acknowledged, not only those which could be directly related with the given procedure. The complications which were conceived as significant were those that did not abate before being discharged and influenced the functioning of the patients.

The shortest time of observation was 19 months and the longest 94 months. The middle time was 52.2 months (SD $\pm$ 19.2), which is more than 4 years. The majority of the group (69.8%; $n = 113$) were women. The age varied from 21 to 78 years, 51.9 years on average (SD $\pm$ 10.4, median = 52 years). The examined group contained 86 patients with bleeding and 76 patients with non-bleeding aneurysms. Among 48 patients coiling was performed and among 114 patients the aneurysms were clipped.

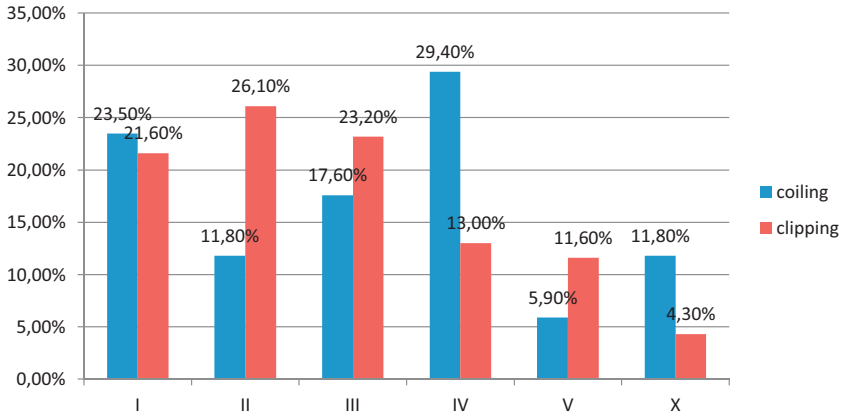

Fig. 1 – Distribution of patients in groups I–V of Hunt and Hess scale in patients with bleeding aneurysms (X – insufficient data to determine the state).

The assessment of the late results was available in 134 cases out of 162 i.e. 82.7% of the patients. Eight patients did not fill in or filled the questionnaires improperly; therefore, the estimation of the quality of life was only possible among 103 people altogether.

For the purposes of the analysis the group of 162 patients was subdivided into four groups:

A. People with bleeding aneurysms treated with endovascular embolization ($n = 17$).
B. People with non-bleeding aneurysms treated with endovascular embolization ($n = 31$).
C. People with bleeding aneurysms treated with clipping ($n = 69$).
D. People with non-bleeding aneurysms treated with clipping ($n = 45$).

The late results of the treatment were assessed among the following number of patients in each group: A = 16, B = 27, C = 55, D = 36 (134 altogether).

Before comparing the outcome the homogeneity of the above-mentioned groups of patients was checked according to their gender and age and for the bleeding aneurysms additionally according to the initial condition established with the Hunt and Hess scale.

The significance level of $p = 0.05$ was acknowledged to be relevant for the verification of the presumed hypotheses.

3. Results

3.1. *The comparison of the homogeneity of the groups*

In all sets of groups of patients divided according to the method of the treatment (coiling versus clipping) no significant differences were observed with relation to the gender and age. In the group of patients with bleeding aneurysms (A + C) a greater percentage of women was stated than in the group with non-bleeding (B + D): 78.9–61.6%, $p = 0.02$.

Table 1 – Comparison of outcome for all coiled and clipped aneurysms.

All aneurysms		Coiling *n* (%)	Clippling *n* (%)	*p*
Early outcome				
	Death	3 (6.3%)	10 (8.8%)	0.62
	Good outcome GOS (4,5)	33 (71.7%)	78 (69.0%)	0.73
	Very good outcome GOS (5)	18 (39.1%)	48 (42.5%)	0.70
	Significant complications	16 (33.3%)	27 (23.7%)	0.21
Late outcome				
	Death	7 (16.3%)	16 (17.6%)	0.85
	Good outcome GOS (4,5)	34 (79.1%)	69 (75.8%)	0.67
	Very good outcome GOS (5)	22 (51.2%)	45 (49.5%)	0.85
	Good outcome mRs (0,1,2)	34 (79.1%)	66 (72.5%)	0.41
	Very good outcome mRs (0,1)	22 (51.2%)	48 (52.7%)	0.86
	Self-assessment – without compromising	25 (78.1%)	55 (77.5%)	0.94
	Deterioration of social functioning	11 (35.5%)	27 (38.6%)	0.77
	Back to work	13 (54.2%)	20 (46.5%)	0.55
EORTC QLQ-C30 mean values	Functional scale	70.3	67.0	0.78
	Symptom scale	25.5	25.6	0.62
	Global health status	58.3	57.2	0.81

Table 2 – Comparison of outcome for bleeding aneurysms.

Bleeding aneurysms		Coiling *n* (%)	Clippling *n* (%)	*p*
Early outcome				
	Death	1 (5.9%)	9 (13.0%)	0.39
	Good outcome GOS (4,5)	7 (43.8%)	35 (51.5%)	0.58
	Very good outcome GOS (5)			
	Significant complications	7 (41.2%)	23 (33.3%)	0.55
Late outcome				
	Death	5 (31.3%)	15 (27.3%)	0.76
	Good outcome GOS (4,5)	11 (68.8%)	34 (61.8%)	0.61
	Very good outcome GOS (5)			
	Good outcome mRs (0,1,2)	11 (68.8%)	31 (56.4%)	0.37
	Very good outcome mRs (0,1)			
	Self-assessment – without compromising	6 (75.0%)	24 (64.9%)	0.57
	Deterioration of social functioning	2 (28.6%)	22 (59.5%)	0.12
	Back to work	3 (42.9%)	9 (37.5%)	0.80
EORTC QLQ-C30 mean values	Functional scale	76.8	61.6	0.22
	Symptom scale	**15.5**	**23.9**	**0.02**
	Global health status	65.8	53.8	0.12

Results that differ significantly are bolded.

In the comparison of the array of patients with embolized and clipped bleeding aneurysms (Fig. 1) among particular groups (I–V) on the Hunt and Hess scale with the use of a test for two fractions no important difference was discovered. However, comparing the array of the patients between coiling and clipping in some groups, especially II and IV, considerable differences may be observed reaching more than double. In this respect it ought to be assumed that the fact of not discovering significant differences is the effect of a too little number of patients in the examined groups rather than an actual lack of difference.

3.2. *The comparison of the results of the treatment*

After summarizing the results it has been stated that the outcomes for non-bleeding aneurysms are far better than of those with bleeding ones (B + D/A + C). Such results had been obvious and therefore the presentation of the analysis in these groups has been omitted.

For all the examined parameters no significant differences were observed between the total results of the patients with embolized and clipped aneurysms (A + B/C + D) both in the early and long-term period (Table 1).

As far as the late assessment of the patients with bleeding aneurysms, better results of the treatment were revealed among the people who had undergone embolization; still, the statistical significance was only acknowledged with regard to the medium score of the symptomatic scale of the quality of life EORTC QLQ-C30 questionnaire (Table 2).

In the assessment of the patients with non-bleeding aneurysms better results of the treatment were noticed among

Table 3 – Comparison of outcome for non-bleeding aneurysms.

Non-bleeding aneurysms		Coiling *n* (%)	Clippling *n* (%)	*p*
Early outcome				
	Death	2 (6.5%)	1 (2.2%)	0.34
	Good outcome GOS (4,5)	26 (86.7%)	43 (95.6%)	0.17
	Very good outcome GOS (5)	**16 (53.3%)**	**35 (77.8%)**	**<0.03**
	Significant complications	**9 (29.0%)**	**4 (8.9%)**	**0.02**
Late outcome				
	Death	2 (7.4%)	1 (2.8%)	0.40
	Good outcome GOS (4,5)	23 (85.2%)	35 (97.2%)	0.07
	Very good outcome GOS (5)	17 (63.0%)	27 (75.0%)	0.30
	Good outcome mRs (0,1,2)	23 (85.2%)	35 (97.2%)	0.07
	Very good outcome mRs (0,1)	17 (63.0%)	27 (75.0%)	0.30
	Self-assessment – without compromising	19 (79.2%)	31 (91.2%)	0.20
	Deterioration of social functioning	9 (37.5%)	5 (15.2%)	0.053
	Back to work	10 (58.8%)	11 (57.9%)	0.95
EORTC QLQ-C30 mean values	Functional scale	68.1	72.4	0.22
	Symptom scale	28.9	27.3	0.95
	Global health status	55.8	60.9	0.40

Results that differ significantly are bolded.

people who had undergone clipping; yet, the statistical significance was only obtained with regard to the early results: more "very good" scores on the GOS scale at the point of being discharged and less complications during the hospitalization. With regard to the late results, however, the differences in neither of the parameters obtained statistical significance though being close in some cases: more "good" scores on the GOS and mRs scales in the late assessment ($p = 0.07$) and less frequent cases of a relapse in the social functioning ($p = 0.053$) (Table 3).

4. Discussion

4.1. *The controversies in the epidemiology of the intracranial aneurysms*

Significant differences start at the stage of determining the prevalence of intracranial aneurysms. Often proclaimed the value of 5% should be treated with caution because the spread of the results calculated on the basis of autopsy or radiologic examinations is high and ranges from 0.2 to 9%. Most published results of large studies are within 0.4–6% [9,18–22]. Only the epidemiologic data concerning the subarachnoid haemorrhage (SAH) may be regarded as coherent and well documented. Fear of recurrent bleeding, which is burdened with a high, more than 70% mortality warrant preventive treatment [23,24]. On the other hand, before deciding on undertaking the treatment of the non-ruptured aneurysms, additional role is played by the knowledge of the risk of the initial bleeding which has not yet been precisely determined. The authors of the most extensive studies have calculated it at the level of 1–2% annually [21,22,25–27]. These data were shaken by the results of a multicenter study ISUIA, the first retrospective part was published in 1998 [28], and the extension including prospective part in 2003 [29]. The results of the research confirmed earlier observations that the risk of aneurysm rupture increases with its size; however, the risk concerning the small aneurysms, especially the anterior circulation, proved unexpectedly low. In the first part it was established that the annual risk of the rupture of silent aneurysms diameter up to 10 mm equals 0.05%. In the second part, cumulated, 5-year-long risk of the rupture of the anterior circle of Willis aneurysms was calculated at the value of 0% for the aneurysms smaller than 7 mm without finding a single case of bleeding in this group, 2.6% for 7–12 mm, 14.5% for 13–24 mm and 40% for 25 mm and bigger. The aneurysms of the posterior part of the circle equalled respectively 2.5%, 14.5%, 18.4% and 50%. Such unexpected results were even more surprising due to the fact that in clinical practice bleeding from the small aneurysms is not rare. The ISUIA research was currently the biggest and the most systemized attempt to assess the natural course of the intracranial aneurysms and the risk of treatment carried in accordance with the accepted standards of the Evidence-based Medicine. For this reason the announced results had wide repercussions among neurosurgeons and in many medical centres influenced the approach towards small aneurysms. Official recommendations by authorities appeared in i.a. "Stroke" in 2000 [6] suggesting that the risk of treating exceeds the risk natural course of the disease and therefore small aneurysms should not be treated at all. After a time, there is a lot of controversy about the ISUIA study. The main doubt became the dissonance between the risk of rupture of the small aneurysms and the observable in practice number of bleedings from small aneurysms which is impossible if the frequency of aneurysms do not exceed a few percent. On the basis of the American population, Winn et al. outnumbered that if such a low risk of rupture of the small aneurysms was accepted the frequency of their occurrence would need to reach not few but tens of percent to cause the approximately 30,000 cases of subarachnoid haemorrhages in the United States annually with the assumption that half of them derived from small aneurysms. [30] Down to the fact that the epidemiologic data: incidence of bleeding and the prevalence of the aneurysms have ground basis, such a low probability of rupture of small aneurysms that was claimed by the ISUIA could be regarded as unreliable. It was noticed that the inclusion of patients had been a result of a careful selection and did not reflect the profile of patients with aneurysms of the general population [31,32]. Only patients who had not undergone treatment after neurosurgical assessment were qualified for the observation. Undoubtedly observed aneurysms were considered to be safer. Most probably this was the reason why a smaller number of patients with aneurysms of the anterior cerebral artery and the anterior communicating artery complex (10%) were entered into the study than in general population (>30%). During the observation period, which lasted an average of 4.1 years 51 cases of confirmed aneurysm rupture were noticed. 534 out of the initial group of 1692 patients were excluded and submitted to treatment. Among them were, probably, patients in whom an increase of the risk of rupture was suspected due to e.g. enlargement of the aneurysm. Another 193 people were excluded due to their death. In 52 cases among them the cause of death was an intracranial bleeding and heart attack in only 14. The cause of death of 11 patients was not known. Therefore, among the overall number of 63 deceased as a result of intracranial bleeding and unknown causes in the major part the cause of death could have been ruptured aneurysms. In this respect the conclusions of the ISUIA concerning small aneurysms seem useless in clinical practice except the confirmation that intuitive assessment of neurosurgeons in choosing "safer" aneurysms is effective.

In 2004 Mocco et al. published an analysis of a number of research in the field of the natural course of unruptured aneurysms including ISUIA. By this analysis, the annual risk of rupture of 7–10 mm aneurysm is approximately 1% and increases with the increasing size [33].

Inasmuch as the morbidity rate from subarachnoid haemorrhage increases with age, an increase in the frequency of SAH should be expected due to the ageing of the population. However, the statistical reports do not confirm such findings. In the paper published by de Rooij et al. [34] it has been stated that between 1950 and 2005 the morbidity from SAH decreased by 0.6%. The data could confirm the effectiveness of the prophylaxis: better control of the arterial hypertension and a reduction in the percentage of smokers, and perhaps somewhat confirms the validity and effectiveness of preventive treatment of silent aneurysms.

4.2. *The results of the treatment in other studies and their faults*

In the majority of published studies and meta-analyzes the risk of death and morbidity after clipping rated for a few to over

a dozen percent [6]. To exemplify, King et al. [35] in 1994 claimed the postsurgical death rate at the level of 1% whereas the neurological relapse at 4.1%. Raaymakers et al. [36] in 1998 calculated respectively 2.6% and 10.9%. In the analyses better results have been observed in more recent works. The administrative data from the discharge forms in New York and California [6], however, suggest worse results of the treatment: the death rate 2.5–3% and complications rate 21.3–22.4%. In the prospective part of ISUIA the total death rate and morbidity after 1 year was estimated at the level of 15% [29]. Against this background the results of endovascular treatment seem encouraging especially those from recent years. In 2008 two prospective multicenter research were broadcasted that concerned endovascular treating of brain aneurysms. The HELPS [37] embraced people with ruptured and unruptured aneurysms noticing only 2 deceases among 218 cases of unruptured aneurysms (0.9%). In the ATENA research 739 aneurysms were treated in 649 patients [38]. The early neurological complications were stated amidst 5.4% of the patients.

So far ISAT remains the largest, most well-known, international, randomized trial directly comparing the results of the treatment of bleeding aneurysms by clipping and endovascular embolization remains ISAT [12,13]. A bad result was death and dependency of patients included in mRs scale of 3–6 points. After one year of follow-up poor outcome was observed in 30.6% of patients after clipping and in 23.7% of patients after coiling. Due to a significant difference in 2002 the recruitment was ceased at the number of 2143 patients but only 1594 of them completed a one-year observation period and the fate of the remaining 549 is unknown. The candidates were selected from among 9559 patients with SAH, which represents about 22% of the total, and only 17% of those who completed the study. After 5 years the results of treatment equalized. Among survivors 83% were independent (0–2 points on the mRs) in the coiling group, and 82% in the clipping group. A statistically significant difference was only given in the deaths: 112 (11%) after embolization and 144 (14%) after clipping. However, as Bakker et al. [39] indicated, for the calculation of the real results, the deceases from the period between the randomization and surgery should have been omitted. In this period in 17 patients awaiting coiling recurrent bleeding was noticed and 7 of them died, whereas among patients who awaited clipping, 28 cases of recurrent bleeding were noticed and 19 of them died. The difference may have resulted from a longer waiting period in case of clipping (1.7 days) than coiling (1.1 days). After subtracting the number of deaths before the treatment the difference between coiling and clipping reduced without reaching statistical significance.

In another major trial BRAT carried in a single medical centre and embracing 500 patients with SAH with the assumptions similar to ISAT, analogous results were presented. Ultimately 403 patients were assessed: death or dependence was stated among 33.7% of people after clipping and among 23.2% after embolization. What is noticeable in this case is the fact that 75 patients who were initially planned for endovascular treatment were eventually submitted for surgery mainly down to anatomical difficulties. By contrast, only four patients planned for surgery were treated endovascularily [7].

The comparisons of outcome after treatment of unruptured aneurysms remain less elaborated. In the II part of the ISUIA trial published in 2003 [29] the rate of mortality and morbidity one year after treatment was found to be 12.6% for clipping and 9.8% for coiling. The possibility of a direct comparison of the results of both groups is limited due to the initial difference between the groups and unclear qualification principles. In 1999 Johnston et al. [40] published the results of the treatment of unruptured aneurysms in university hospitals in the USA. 18.5% of patients after clipping died or were discharged not to their homes and that was only 10.6% of patients after embolization. Nevertheless the groups were again incomparable.

4.3. *The limitations of our research*

The most important seems the scarce number of testees ($n = 162$) which provides statistically weaker results after subdividing. Moreover, the research embraces material from a single centre and is strictly ground in the local realities shaped by organizational limitations, the availability of the equipment, the skills and the learning curve of the doctors performing the surgeries. The endovascular embolization was carried out by two neuroradiologists whereas the surgeries were performed by several neurosurgeons wherein the majority of the clipped aneurisms were supplied by a single, experienced surgeon.

The research was not randomized. Therefore, regardless of the homogeneity tests of the groups, the individual choice of the method of treatment could disturb the balance in relation with the unknown prognostic factors. It has to be indicated that the choice of method was often limited by its availability. The limitations always concerned coiling, never clipping. They were related to a temporal lack of staff or equipment for coiling. The embolizations were conducted only in a planned mode. In emergencies beyond typical working hours only neurosurgeons were available and in such situations the aneurysms were usually clipped. We sought as soon as possible to treat bleeding aneurysms hence emerged much larger number of subgroup of clipped bleeding aneurysms ($n = 69$) compared to coiled ones ($n = 17$).

No statistical significance was stated upon the comparison of the homogeneity of the groups; however, the distribution of the embolized and clipped bleeding aneurysms in certain groups along Hunt–Hess scale was not equal. Patients in worse condition were more often qualified for coiling. In the context of the obtained results such an array reinforces the indicated difference in favour of the embolization among patients with bleeding aneurysms.

In two patients with non-bleeding aneurysms who were excluded, coiling applied was yet ineffective and complicated. Eventually they underwent surgical treatment. In these cases the neurological relapse and decrease of the quality of life burden embolization. Therefore, if they were included in the embolized group the observed differences in the results would increase in favour of clipping.

5. Conclusions

1. The early and long-term results of treating both bleeding and non-bleeding aneurysms of the anterior part of the circle of Willis are no different.

2. Among the patients with bleeding aneurysms better results can be obtained by applying endovascular embolization.
3. Among patients with non-bleeding aneurysms better results may be obtained by applying clipping.
4. The results of the research suggest that with the lack of other circumstances as to the choice of treatment in case of the bleeding aneurysms the priority should be given to the endovascular treatment. On the other hand, in case of non-bleeding aneurysms it is clipping that should be considered first.

Conflict of interest

None declared.

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None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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