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EARLY AND LONG-TERM RESULTS OF ENDOVASCULAR TREATMENT OF CEREBRAL ANEURYSMS

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Introduction. Postoperative angiographic examinations after endovascular treatment of cerebral aneurysms may demonstrate unstable results, both in the form of recurrence formation, and in the form of increased degree of occlusion with initially incomplete occlusion of the aneurysm sac. Cerebral aneurysm recurrences represent an important medical and social problem comparable in terms of hemorrhage risks with nonoperated aneurysms.

Aim. To estimate the early and long-term results of endovascular treatment of patients with cerebral aneurysms operated on using different endovascular techniques.

Materials and methods. The present study included 167 patients (48 men and 119 women) with 195 cerebral aneurysms aged from 18 to 75 years who were operated on using endovascular techniques at the neurosurgical department No. 3 of the Russian Research Neurosurgical Institute named after Prof.A. L. Polenov from 2013 to 2016. The average age of the patients was 52 ± 12 years, the minimum age was 18 years, and the maximum age was 75 years. The choice of endovascular treatment method in the patients included in the study was based on anatomico-topographic and morphometric features of aneurysm, as well as taking into account the period of aneurysmal disease course.

Results. The study of data of control angiographic examinations after endovascular treatment of patients with cerebral aneurysms showed that in the remote postoperative period the degree of aneurysm occlusion may differ from that initially achieved. The probability of aneurysm recurrence after its isolated occlusion with coils may reach 13.1% already in 6 months after surgical treatment, 31.7% after 12 months and 22.3% after 36 months, averaging 22.5% ($p < 0.05$).

Conclusion. The personalized approach in choosing optimal surgical tactics for the treatment of patients with cerebral aneurysms allows to achieve stable radical aneurysm occlusion, to decrease the incidence of postoperative complications and aneurysm recurrences in the long-term postoperative period.

Keywords: cerebral aneurysm, endovascular occlusion, detachable spirals, balloon-assist, stent-assist, deflecting stent

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INTRODUCTION

Cerebral aneurysms are pathological local protrusions of the artery wall and become one of the main causes of intracranial hemorrhage, which occurs more often in people of working age [1, 2]. A complicated course of aneurysmal disease can lead to development of a severe, persistent neurological deficit or death [3]. In recent decades, including due to active introduction of techniques of endovascular occlusion of cerebral aneurysms, significant progress has been made in treatment of patients with this cerebrovascular pathology. The achievements of recent years have made it possible to expand the scope of endovascular techniques to almost all types and localization of cerebral aneurysms creating a direct alternative to microsurgical treatment [4, 5]. The results of large international randomized trials, such as the International Subarachnoid Aneurysm Trial (ISAT) and the Barrow Ruptured Aneurysm Trial (BRAT), have demonstrated better clinical outcomes in endovascular treatment of patients during acute period of subarachnoid hemorrhage as compared with microsurgical techniques; meanwhile among the advantages have been noted lower risks of operation on patients initially being in a serious condition, having severe somatic status, severe neurological deficit caused among other things by aneurysm rupture, as well as the possibility of chemical angioplasty for treatment and prevention of cerebral vasospasm [6, 7].

The gradual accumulation of data on the long-term results of endovascular occlusion of aneurysms made it clear that the achieved radical result of turning off the aneurysm from bloodstream may be short-lived and the eliminated risks of intracranial hemorrhage may resume in some cases [8–11]. At the same time, most reports that describe hemorrhage

from previously occluded aneurysms indicate a more severe course of the disease that more often leads to deep disability and death [12–14].

Thus, it is obvious the necessity and actuality of studying the causes of recurrence of cerebral aneurysms after endovascular interventions as well as optimization of tactics of the endovascular treatment depending on the risk factors of recurrence.

The aim of the study was to evaluate the early and long-term results of endovascular treatment of patients with cerebral aneurysms operated using various endovascular techniques.

MATERIALS AND METHODS

The present study included 167 patients (48 men and 119 women) with 195 cerebral aneurysms aged 18 to 75 years, operated using endovascular methods of treatment from 2013 to 2016 on the basis of neurosurgical Department No. 3 of the V.L. Polenov Russian Research Neurosurgical Institute – branch of the Almazov National Medical Research Center of Ministry of Health of Russia. The average age of the patients was 52 ± 12 years (from 18 to 75 years).

It should be noted that out of 195 aneurysms, 76 (39%) manifested themselves as intracerebral hemorrhage, other neurological symptoms (mass-effect, thromboembolism from the aneurysm sac) – 19 cases (9.7%) and 100 (51.3%) aneurysms were asymptomatic and randomly detected. 169 (86.7%) cerebral aneurysms were occluded by detachable spirals including those with the use of assisting techniques of which in 64 (37.9%) cases the aneurysm was turned off from the bloodstream using detachable spirals without additional assisting techniques, in 41 (24.2%) cases balloon assistance was used, in 64 (37.9%) – stent-assistance was used. In 26 (13.3%) cases a reconstruction of the parent artery with a flow diverter stent was performed.

The choice of endovascular treatment method for patients included in the study was based on the anatomo-topographic and morphometric features of the aneurysm, as well as taking into account the period of aneurysmal disease.

ASSESSMENT OF PRIMARY ANGIOGRAPHICTHE RESULTS OF THE CONDUCTED SURGICAL TREATMENT

The analysis of angiograms performed at the end of surgical treatment evaluated the radicality of aneurysm shutdown from bloodstream, the safety of arterial branches involved in the aneurysm, the absence of sagging coils of spirals into the vessel lumen, the presence of stagnation of the contrast agent in the aneurysm sac (if stenting techniques of the parent artery were used), the position of the implanted stent. The aneurysm occlusion class was evaluated according to the Raymond–Roy Occlusion Classification (RROC, 2006) and Cekirge–Saatci (Cekirge–Saatci, CSC, 2016) classifications.

Of the 195 cerebral aneurysms, 169 (86.7%) were occluded by detachable spirals, including those with use of assisting techniques, of which in 64 (37.9%) cases the aneurysm was turned off from bloodstream using detachable spirals without additional assisting techniques, in 41 (24.2%) cases the balloon assistance was used, in 64 (37.9%) – the stent-assistance. In 26 (13.3%) interventions, reconstruction of the parent artery with a flow diverter stent was performed. Total shutdown of aneurysm from bloodstream was achieved in 101 (58.8%) cases, subtotal – in 52 (30.8%), partial occlusion was performed in 16 (9.4%) cases ($p < 0.05$) (Fig. 1).

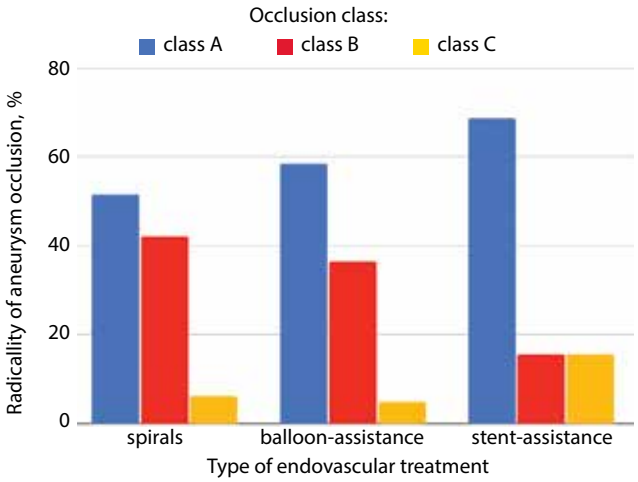

Fig. 1. *Raymond–Roy initial radicality of cerebral aneurysm occlusion*

There was an increase in the primary radicality of surgical treatment aimed at turning off the aneurysm from bloodstream using assisting techniques (odds ratio (OR) 1.726; 95% confidence interval (CI) 0.917–3.251; $p < 0.05$). With stent assistance, the radicality rates are higher as compared with the group without assisting techniques – 68.8 and 51.6%, respectively (OR = 2.067, 95% CI 1.005–4.250, $p < 0.05$). In all 26 cases of using flow diverter stents, remodeling of the parent artery (class IVA according to CSC) was achieved.

According to our data, unfavorable factors preventing the achievement of total occlusion of aneurysm by detachable spirals, including when there was used balloon assistance, were wide (more than 6 mm) neck and large (15–25 mm) size of aneurysm ($p < 0.005$), while favorable – the size of neck in the range of 3–6 mm and its usual (4–15 mm) size ($p < 0.005$).

EVALUATION OF LONG-TERM ANGIOGRAPHIC RESULTS OF SURGICAL TREATMENT

We considered the data of selective cerebral angiography performed no earlier than 6 months after the surgical intervention to be long-term results. The analysis of control angiograms took into account the dynamics and completeness of the aneurysm shutdown from the bloodstream using the specified classifications RROC (2006) and CSC (2016).

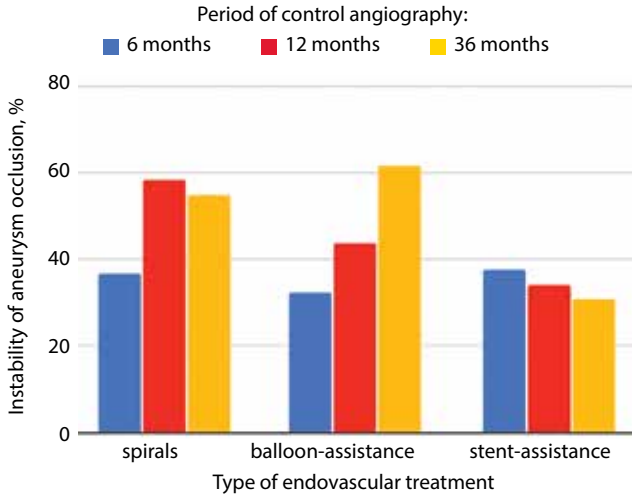

Fig. 2. *Unstable occlusion result in the long-term postoperative period*

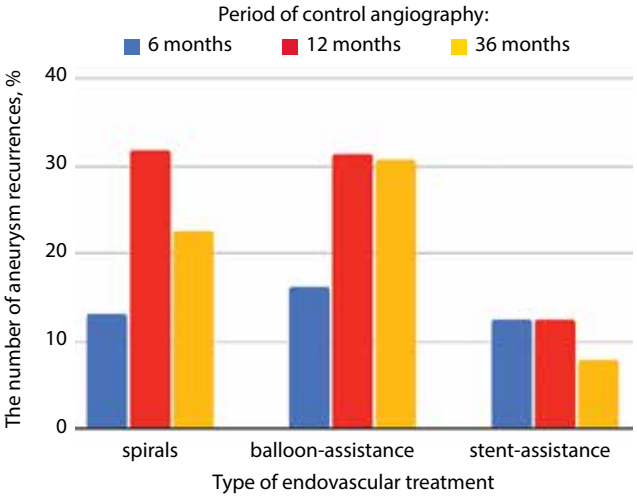

Fig. 4. *Frequency and duration of recurrence of cerebral aneurysms*

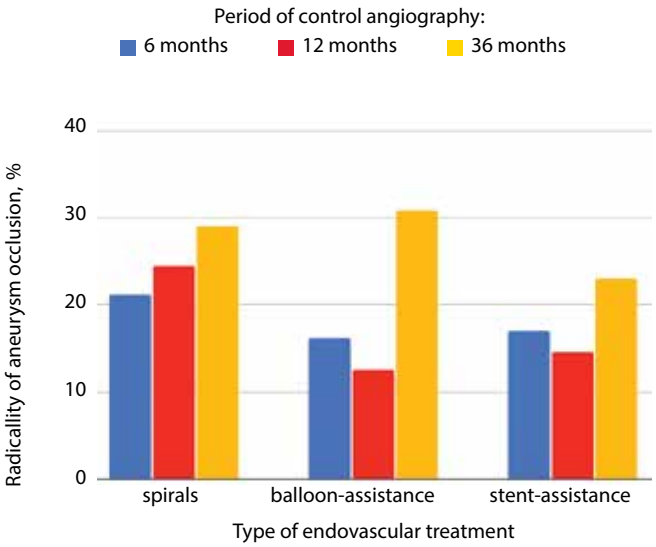

Fig. 3. *Increase of radical occlusion in the long-term postoperative period*

The analysis of control angiograms showed that the result of occlusion may be both stable and unstable, in the latter case it may be caused by both an increase in the occlusion degree of initially non-radically switched-off aneurysm and due to formation of recurrence (Fig. 2). The data obtained indicate high frequency of unstable occlusion of cerebral aneurysms in cases when used isolated occlusion by detachable spirals (36.8, 58.5 and 54.8% after 6, 12 and 36 months, respectively), balloon assistance (32.3, 43.7 and 6% after 6, 12 and 36 months) or stent assistance (37.5, 34.2 and 30.7% after 6, 23 and 36 months). Subtotal occlusion in our series turned out to be the most unstable type of occlusion (RROC class II) ($p < 0.05$).

We analyzed the increase in radical occlusion in long-term postoperative period (Fig. 3).

It was found that the average increase in radical occlusion in the long-term period with the use of isolated aneurysm occlusion by detachable spirals was 24.8% (21.1, 24.4 and 29% after 6, 12 and 36 months, respectively), with balloon assistance – 19.8% (16.2, 12.5 and 30.8% after 6, 12 and 36 months), with stent assistance – 18.1% (14.6, 23 and 18.1% after 6, 12 and 36 months) at $p < 0.05$.

When analyzing the data of control postoperative angiograms, an assessment of the timing and frequency of recurrence formation was carried out (Fig. 4).

It was revealed that average frequency of recurrence after the use of isolated aneurysm occlusion by detachable spirals was 22.5% (13.1, 31.7 and 22.6% after 6, 12 and 36 months, respectively), with balloon assistance – 26.1% (16.2, 31.3 and 30.8% after 6, 12 and 36 months), stent – assistance – 10.8% (12.5, 12.2 and 7.7% after 6, 12 and 36 months) ($p < 0.05$).

ASSESSMENT OF RECURRENCE FORMATION RISKS

A statistical analysis of anatomo-topographic, morphometric characteristics of the aneurysm and its supporting vessel was carried out to identify risk factors for the formation of aneurysm recurrence after endovascular treatment. According to the data obtained, localization of aneurysm, involvement of bifurcation, inclusion of arterial branches, bending of the artery, presence of diverticula do not have a statistically significant effect on the recurrence risk.

When analyzing aneurysm morphometric characteristics, it was found that statistically significant predictors of aneurysm recurrence after endovascular occlusion are large size (15–25 mm) of the aneurysm ($p = 0.043$) and its height (distance from the neck to the dome) more than 6 mm ($p = 0.037$).

The analysis of dependence of recurrence risks on the method of endovascular treatment used was carried out. According to the data obtained, the risk of aneurysm recurrence is 1.83 times higher when detachable spirals are employed without use of assisting techniques ($p = 0.028$), and also 2.03 times higher if class II radicality according to RROC is achieved ($p = 0.011$).

In addition, it was found that another predictor of recurrence is a transferred intracerebral hemorrhage from an aneurysm ($p = 0.017$).

Thus, reliable predictors of aneurysm recurrence after endovascular treatment according to our data are as follows: large aneurysm size ($p < 0.05$), its height is more than 6 mm ($p < 0.05$), the use of detachable spirals without employment of assisting techniques ($p < 0.05$), subtotal aneurysm occlusion (class II according to RROC) ($p < 0.05$), suffered intracerebral hemorrhage from aneurysm ($p < 0.05$).

The analysis of our data confirms the need for long-term angiographic control of radicality of the aneurysm shutdown from bloodstream for timely detection of their recurrence and repeated surgical intervention in order to prevent possible rupture of the aneurysm.

Based on the data obtained showing that initially incomplete occlusion plays a leading role in formation of aneurysm recurrence, we have developed an algorithm for differentiated selection of patients for endovascular treatment (Fig. 5).

One of the determining factors is the anatomo-morphometric characteristics of aneurysm, on the basis of which the possibility of radical shutdown of the aneurysm from bloodstream using detachable spirals is evaluated. Such characteristics of aneurysm include baggy-spherical shape, narrow unstrung neck, single-chamber structure and the absence of involvement of arterial branches in the neck and aneurysm sac.

DISCUSSION

The main goal of treatment of patients with cerebral aneurysms is the prevention of intracranial hemorrhage. Having a lower primary radicality as compared with microsurgical clipping, the endovascular treatment has a number of advantages, such as possibility of performing surgical treatment of aneurysms that are difficult to access for microsurgery, low invasiveness during treatment, low risks of local purulent-septic complications, as well as shorter duration of inpatient treatment [6, 12, 15–17].

Gradual accumulation of data on long-term results of aneurysms endovascular occlusion have made it possible to understand that the achieved radical result of turning off the aneurysm from bloodstream may be short-lived and, in some cases, the eliminated risks of intracranial hemorrhage may resume [5, 8, 9–11, 18, 19].

According data by L. Pierot et al., the use of isolated occlusion of aneurysms by detachable spirals makes it possible to achieve total shutdown of the aneurysm from bloodstream only in half of cases [20]. In our series of 64 aneurysms occluded by spirals without use of assisting techniques in 33 (51.6%) cases aneurysms were turned off from bloodstream totally, in 27 (42.2%) – subtotally and in 4 (6.2%) – partially. Thus, the primary results of endovascular isolated occlusion of aneurysms by detachable spirals achieved by us are comparable with the data presented in the literature.

According to G.M. Debrun et al., in order to achieve radical occlusion of an aneurysm using only spirals, the aneurysm must have the following characteristics: baggy-spherical shape, normal size, narrow neck, absence of diverticula [21]. According to our data, the favorable characteristics of aneurysm contributing to its radical shutdown from bloodstream when using detachable spirals without assisting techniques are the dimensions of its neck in the

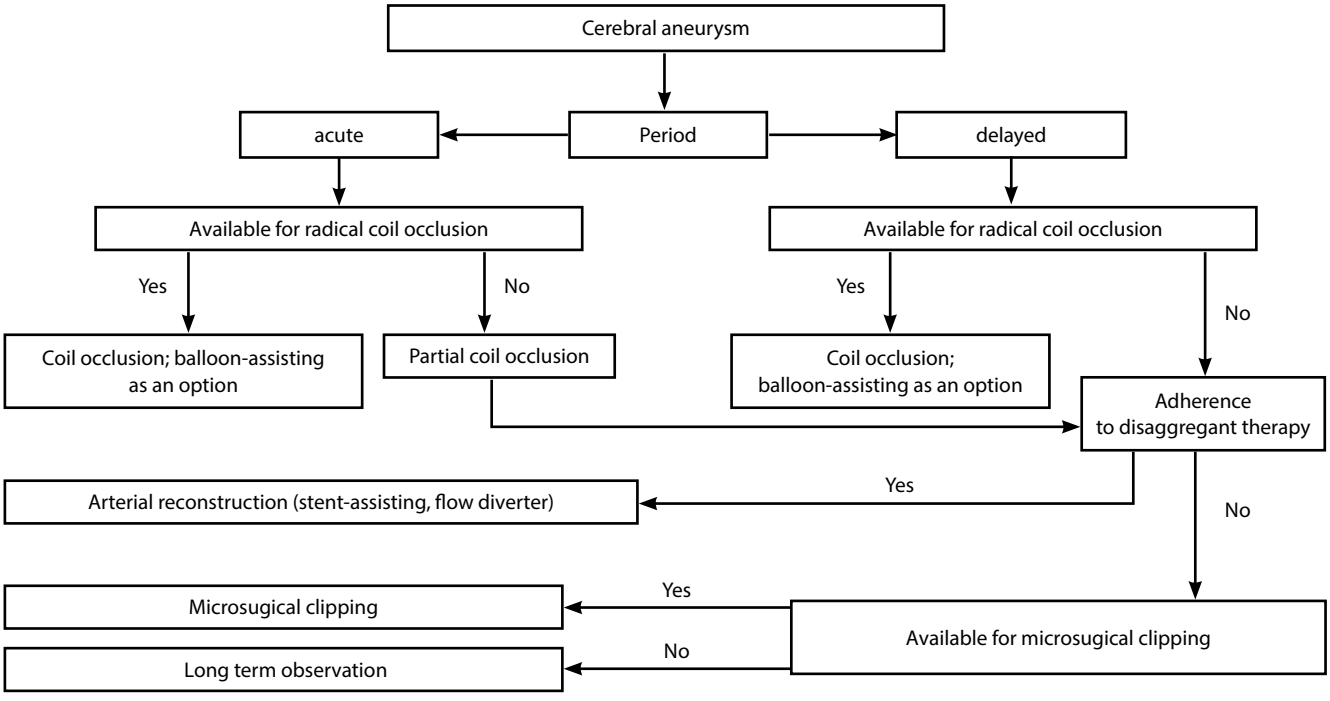

Fig. 5. *Algorithm of differential selection of patients for endovascular treatment*

range from 3 to 6 mm and usual (4–15 mm) dimensions ($p < 0.005$).

According to results of study of effectiveness of balloon assistance in occlusion of cerebral aneurysms, this technique allows achieving a primary radical shutdown of the aneurysm from bloodstream in 69.4% of cases [22]. According to our data on use of the balloon-assist technique, the total shutdown from the bloodstream was achieved in 24 (58.5%) cases out of 41, the subtotal one – in 15 (36.6%) cases and partial – in 2 (4.9%) cases. The results obtained showed a lower effectiveness of the technique when compared with the data published in literature that may be explained by peculiarities of selection of patients for treatment since this group also included patients with contraindications for combined use of double disaggregant therapy and stenting techniques which did not always allow to achieve total aneurysm occlusion.

According to our data, the unfavorable factors preventing achievement of aneurysm total occlusion by detachable spirals with balloon assistance include its neck size of more than 6 mm and large (15–25 mm) aneurysm size ($p < 0.005$); also, the favorable ones are the neck sizes in the range of 3–6 mm and usual size (4–15 mm) of aneurysm ($p < 0.005$). M.M. Balaguruswamy et al. came to similar conclusions in 2021 pointing out low efficiency of using the balloon for large and giant aneurysms with wide neck [23].

Modern publications have noted high efficacy of using stent assistance for occlusion of cerebral aneurysms. So, according data by B.J. Daou et al. [24] and H. Luecking et al. [25], the use of this technique made it possible to achieve primary total aneurysm occlusion in 51.9–81.8% of cases. In our series of operations, stent assistance made it possible to achieve total shutdown of the aneurysm from bloodstream in 44 (68.8%) cases out of 64, subtotal – in 10 (15.6%) cases and partial – in 10 (15.6%) cases, the outcomes were comparable with the results of previous studies.

It should be noted an increase in primary radicality of surgical treatment aimed at turning off the aneurysm from bloodstream using assisting techniques (OR = 1.726; 95% CI 0.917–3.251; $p < 0.05$). At the same time, stent-assistance has higher rates of radicality as compared with the group without assisting techniques (68.8 and 51.6%, respectively; OR = 2.067; 95% CI 1.005–4.250; $p < 0.05$). The best radicality of occlusion when using stent assistance was demonstrated by aneurysms with a neck size of 3–6 mm (77.8%) ($p = 0.048$), that is better that the results obtained when only spirals (61.1%) and balloon assistance (65.5%) were used. The unfavorable result on radicality was also confirmed by us in the group of aneurysms with a wide neck – the partial occlusion of aneurysms in this group reached 31.2% ($p = 0.048$).

A complete reconstruction of the vessel carrying the aneurysm can be achieved by using a flow diverter stent. According to publication by W.A. Florez et al., this technique makes it possible to remodel an parent artery in 80.4% of cases, however, complete shutdown of the aneurysm from bloodstream occurs delayed due to slowing of blood flow in the aneurysm sac and its gradual thrombosis [26]. In our series, the 26 patients underwent installation of flow diverter stent. In all cases of using this technique, the blood flow in the aneurysm sac was slowed down with artery remodeling (class IVA according to CSC), the outcome that is fully matching the published data on the use of this category of stents.

The need for postoperative monitoring after surgical treatment of aneurysm was first reported in 1965 by McKissok, who revealed a recurrence of an aneurysm of the middle cerebral artery in a patient who died from repeated intracranial hemorrhage. Also, the need for angiographic control was reported in the monograph of A.N. Konovalov "Surgical treatment of arterial aneurysms of the brain" [27].

Studying long-term angiographic results of endovascular occlusion of aneurysms by detachable spirals during the international randomized trial Barrow Ruptured Aneurysm Trial (BRAT), R.F. Spetzler et al. came to disappointing conclusion that 10 years after surgery, only 22% of aneurysms retained a stable radical occlusion result [28]. Our series of 64 cases of aneurysms operated using isolated occlusion with detachable spirals demonstrated stable angiographic results in 49.9% of cases, which significantly exceeds the published results, but assumes necessity to continue the angiographic control.

According to K. Aydin et al., the use of balloon assistance contributes not only to increase in primary radicality of occlusion but also to preservation of stable angiographic result in the long-term postoperative period [29]. Our data demonstrate stable angiographic result of occlusion of 41 cerebral aneurysms in 54.1% of cases, the portion is slightly higher than that obtained with isolated occlusion by detachable spirals.

According to J. Kim et al., stent assistance have demonstrated the best stability of the angiographic result among the aneurysm occluding techniques [30]. According to G. Xue et al., in patients operated with stent assistance, the long-term angiographic result may differ significantly from the postoperative one: it was noted that with initially total occlusion of 21.7% of aneurysms, in the long-term period total occlusion was already demonstrated by 87% [31] ones. According to our data, the use of this technique shows a stable angiographic result in 65.9% of observations, which is consistent with information from similar studies.

The data from our study have demonstrated that the result of aneurysm occlusion may be unstable, while the radicality of occlusion may both increase due to thrombosis of aneurysms with initially incomplete occlusion and decrease due to formation of recurrence. According to our data, in the long-term postoperative period an increase in radiality of occlusion due to delayed thrombosis of sac of an initially non-radially switched-off aneurysm was noted in 24.8% cases when using isolated occlusion with detachable spirals, in 19.8% cases with balloon assistance and in 18.1% cases with stent assistance.

The recurrence (or unstable occlusion) of aneurysm is define by J.V. Byrne et al. as increase in amount of contrast agent filling the aneurysm relative to angiographic type of aneurysm at the end of treatment. They also have suggested that aneurysm recurrence may occur as a result of subtotal occlusion of aneurysm or compaction of spiral complex that raises concerns about ability of this technique to protect against continued aneurysm growth and repeated hemorrhage [32].

The analysis of literary sources have allowed us to compare our own results with the data of other researchers. So, in 1998, C. Cognard et al. have reported about 19% of recurrences after isolated occlusion of aneurysms by detachable spirals [8], R.A. Willinsky et al. in 2009 – about 20.3% [33] and J.R. Vanzin et al. in 2012 – about 26.8% [11]. According to our data, the probability of aneurysm recurrence after its isolated spiral occlusion can reach 13.1% as early as 6 months after surgical treatment, 31.7% – after 12 months and 22.3% – after 36 months, which is an average of 22.5% ($p < 0.05$).

When aneurysm is occluded by spirals using the balloon-assisted technique, aneurysm recurrence may occur in 16.2% of cases 6 months after surgical treatment, in 31.3% after 12 months and 30.8% after 36 months, this is an average of 26.1%. The higher frequency of recurrence formation in this group may be explained by the peculiarities of selection of patients for this type of intervention, complex anatomico-topographic and morphometric features of the aneurysm, as well as the inability to reconstruct the vessel carrying the aneurysm (lack of adherence to regular use of disaggregant therapy, presence of contraindications to its reception).

The use of stent assistance is accompanied by a lower percentage of recurrence – 12.5% after 6 months, 12.2% – after 12 months, 7.7% – after 36 months, which is an average of 10.8%. When using flow diverter stents, there is the lowest risk of recurrence, while monitoring the degree of aneurysm occlusion is required to assess the effectiveness of the treatment after cancellation of double disaggregant therapy. The delayed mechanism of occlusion with this method is achieved by diverting the blood flow from the aneurysm sac followed by formation of blood clot in it. In addition, the implanted stent is serves as a matrix for further endothelization which eventually leads to complete remodeling of the artery lumen.

When analyzing the anatomo-topographic and morphometric characteristics of aneurysms, it was the large (15–25 mm) size of the aneurysm that turned out to be a statistically significant risk factor for recurrence increasing it by 1.75 times ($p = 0.043$) as compared with smaller aneurysms. At the same time, it was found that the height of the aneurysm less than 6 mm significantly reduces the risk of recurrence by 1.85 times ($p = 0.024$).

Our analysis of long-term angiographic results, depending on the method of endovascular treatment used, showed that risk of aneurysm recurrence is 1.83 times higher when using detachable spirals without the use of assisting techniques ($p = 0.028$), which is supported by the information from the world literature [19, 34], and also 2.03 times higher ($p = 0.011$) if the radicality that has been achieved corresponded to Class II according to RROC at the end of operation. According to J. Raymond et al., gender, age and localization of the aneurysm are not significant for the aneurysm recurrence; while during the aneurysm treatment in acute phase of hemorrhage, its large size and wide neck as well as initially incomplete shutdown of the aneurysm from bloodstream may be associated with recurrence. In their work, the authors also identified 2 main types of recurrence – large and small, based on the size of the aneurysm part that was filled with contrast [18].

The classification of recurrent cerebral aneurysms developed and proposed by us after endovascular interventions includes the previously proposed by J. Raymond et al. the degrees of recurrence and also specifies timing of formation, type, cause and nature of the clinical course of recurrence. Based on the predictors of recurrence formation identified by us, namely – use of isolated aneurysm occlusion with detachable spirals ($p = 0.028$), subtotal aneurysm occlusion of class II according to RROC ($p = 0.011$), large (15–25 mm) aneurysm size ($p = 0.043$), – the 2 algorithms were formulated: 1) the choice of optimal method of endovascular treatment of patients with cerebral aneurysms and 2) the differentiated approach to choice of method for surgical intervention in case of cerebral aneurysm recurrence.

In spite of development of endovascular neuroradiology, today none of the available methods of endovascular intervention can reliably guarantee a complete stable cure of a particular patient due to possibility of aneurysm recurrence [35, 36]. Therefore, such topical issues as optimal primary choice of the endovascular intervention type as well as need to optimize or even develop a new personalized approach to endovascular treatment of cerebral aneurysms come to the fore [37, 38].

CONCLUSION

The use of the algorithms developed and proposed by us will contribute to optimization of endovascular treatment of patients with cerebral aneurysms, minimizing risks of their recurrence, reducing risks of recurrent subarachnoid hemorrhage in the long-term postoperative period, as well as the need for repeated surgical intervention.

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