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Predictors for paraclinoid aneurysm recanalisation after endovascular coiling

Czynniki prognostyczne rekanalizacji tętniaków segmentu ocznego po embolizacji z użyciem spiral

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Abstract

Background: Paraclinoid aneurysms (carotid-ophthalmic aneurysms) are surgical challenge, and have been one of the most common indications for endovascular treatment. Nevertheless, coil embolisation continues to be associated with a high rate of residual/recurrent aneurysm. The aim of the study was to find radiological marker for recanalisation in order to facilitate decision process, which would result in fewer treatment-related complications. **Methods:** Fifty-five patients with saccular ruptured and unruptured paraclinoid intracranial aneurysms treated with coil embolisation were analysed retrospectively. Morphometric measurements were performed in CTA 3D aneurysm models before embolisation. The aneurysm size and volume were measured based on digital subtraction angiography images. The effectiveness of the initial endovascular treatment was determined visually using modified Raymond Roy classification after embolisation and during follow-up digital subtraction angiography. Recanalisation was diagnosed when compaction and filling of the aneurysm occurred, compared to the primary embolisation. Statistical analysis was carried out using Statistica 12.5 software. **Results:** Statistical analysis has shown that aneurysm height, neck size, packing density and parent artery diameter are risk factors for recanalisation. In addition, we have demonstrated statistically significant independent predictors of recanalisation volume (aneurysm volume, size ratio, aspect ratio, maximal perpendicular height to neck size ration and also aneurysm depth to neck size ratio), which are not themselves risk factors for recanalisation. **Conclusions:** If the above-mentioned predictors of recanalisation are present preoperatively, microsurgical clipping can be considered.

Keywords: paraclinoid aneurysm, embolisation, recanalisation, risk factors

Streszczenie

Wprowadzenie: Tętniaki segmentu ocznego tętnicy szyjnej wewnętrznej najczęściej leczone są wewnątrznaczyniowo, jednak embolizacja z użyciem spiral wiąże się z wysokim ryzykiem rekanalizacji tętniaka. Celem pracy było znalezienie radiologicznego markera zwiastującego rekanalizację – po to, by ułatwić wybór sposobu leczenia, tak aby ryzyko rekanalizacji było jak najmniejsze. **Metody:** Przeanalizowano retrospektywnie dane kliniczne 55 chorych z pękniętymi i niepękniętymi tętniakami segmentu ocznego tętnicy szyjnej wewnętrznej poddanych embolizacji z użyciem spiral. Pomiarów morfometrycznych wykonano w oparciu o modele 3D tętniaków wygenerowane z badania angio-CT przeprowadzonego przed embolizacją. Wymiary i objętość tętniaka zmierzono na podstawie obrazów uzyskanych w angiografii subtrakcyjnej. Skuteczność początkowego leczenia wewnątrznaczyniowego określono za pomocą zmodyfikowanej klasyfikacji Raymonda Roya bezpośrednio po embolizacji i podczas kontrolnej angiografii subtrakcyjnej. Rekanalizację określono jako ponowne lub większe wypełnienie tętniaka kontrastem, w porównaniu z pierwotną embolizacją. Do analizy statystycznej wykorzystano program Statistica 12.5. **Wyniki:** Z analizy statystycznej wynika, że wysokość tętniaka, wielkość szyi, gęstość upakowania i średnica tętnicy macierzystej są czynnikami ryzyka rekanalizacji. Ponadto wykazano istotne statystycznie predyktory objętości rekanalizacji (objętość tętniaka, wskaźnik SR, *size ratio* – maksymalna wysokość tętniaka podzielona przez średnicę naczynia macierzystego, wskaźnik AR, *aspect ratio* – największa prostopadła odległość od szyi tętniaka do kopuły tętniaka podzielona przez szerokość szyi tętniaka, maksymalna wysokość tętniaka prostopadła do wielkości jego szyi, a także stosunek głębokości tętniaka do wielkości jego szyi), które same w sobie nie są czynnikami ryzyka rekanalizacji. **Wnioski:** Jeżeli przedoperacyjnie stwierdza się wyżej wspomniane czynniki ryzyka rekanalizacji, należy rozważyć inne metody leczenia, w tym leczenie mikrochirurgiczne.

Słowa kluczowe: tętniak paraklinoidalny, embolizacja, rekanalizacja, czynniki ryzyka

INTRODUCTION

Paraclinoid aneurysms (carotid-ophthalmic aneurysms) arise from the internal carotid artery (ICA) between the roof of the cavernous sinus and the origin of the posterior communicating artery (PCoA) (Barami et al., 2003; Kattner et al., 1998; Khan et al., 2005). They are an uncommon cause of aneurysmal subarachnoid haemorrhage (aSAH) and account for approximately 1.4–9.1% of all lesions found in patients with ruptured intracranial aneurysms (Colli et al., 2013; Jeon et al., 2014; Mattingly et al., 2013). Nonetheless, patients may present with symptoms of compression of the optic nerve and the surrounding structures (Kallmes et al., 2015; Orlický et al., 2015).

The annual incidence rate for aSAH is 6–16 per 100,000 patients, with greater values recorded in Finland (15–17/100,000) and Japan (22.7/100,000) (Rinkel et al., 1998; de Rooij et al., 2007). Due to the gradual improvement of microsurgical techniques, its management has changed from reinforcing the aneurysm wall (i.e. wrapping) to direct neck clipping, with outcomes surpassing those of the endovascular therapy in terms of total neck obliteration and long-term recanalisation (Liu et al., 2008; Raco et al., 2008). Patient management should be adjusted accordingly, based on the natural history of aneurysm and long-term outcomes of a particular therapeutic strategy. Therefore, unconditional employment of endovascular techniques in these cases seems debatable, albeit they are considered by many authors as superior to microsurgery (MS) (Johnston et al., 1999; Kassell et al., 1985).

Up-to-date many risk factors of recanalisation have been analysed (age, gender, aneurysm size, primary packing density and coil material), but none was found to be significant. If we had a radiological marker foreseeing recanalisation, we could possibly make more accurate treatment decisions resulting in fewer treatment-related complications. In our study, we assessed potential predictors for ruptured and unruptured paraclinoid aneurysm recanalisation after endovascular treatment.

MATERIALS AND METHODS

Fifty-five patients with ruptured and unruptured paraclinoid aneurysms treated with coil embolisation between 2010 and 2015 in the Department of Neurosurgery and Neurooncology at Norbert Barlicki Memorial Teaching Hospital No. 1 in Łódź were analysed retrospectively. Medical information for each patient was gathered from medical records, which included case notes, radiological imaging, surgical reports, and six-month follow-up data. In the case of suspected aneurysm, we performed computed tomography angiography (CTA) using three-dimensional (3D) models. The patients were qualified for embolisation by multidisciplinary teams consisting of a neurosurgeon, a neuroradiologist and an anaesthetist. Follow-up digital subtraction angiography (DSA) was performed within

6 months. The analysis included only patients with saccular intracranial aneurysms and excluded those with multiple lesions. All aSAH cases were evaluated with the Hunt–Hess scale at admission. SAH was assessed on computed tomography (CT) performed within 24 hours from the onset of symptoms, with the Fisher revised scale (FRS). Demographic and medical data (age, sex, additional diseases) were obtained from medical records. Morphometric measurements were performed on CTA 3D aneurysm models, including aneurysm dome and depth size, neck size, parent artery size, dome to neck ratio, neck to parent artery ratio, aneurysm depth to neck size ratio, aneurysm angle, vessel angle, aspect ratio (AR) defined as maximal perpendicular height (the largest perpendicular distance from the neck of the aneurysm to the dome of the aneurysm) divided by neck width, and size ratio (SR) defined as maximum aneurysm height (between the centre of the aneurysm neck and the greatest distance to the aneurysm dome) divided by vessel diameter (Fig. 1). All 3D CTAs were performed on a GE LightSpeed VCT with slice thickness of 0.625 mm and

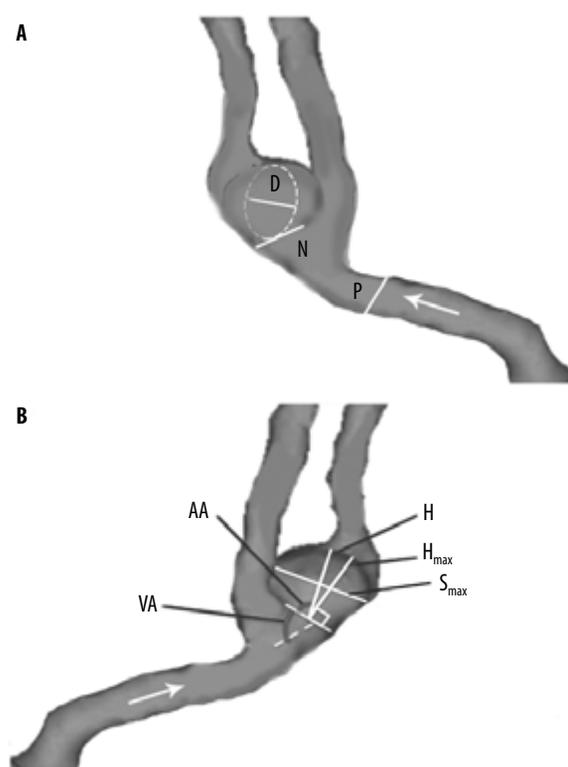


Fig. 1. The variables included in the final model after stepwise logistic regression (ruptured aneurysms group). Morphometric parameters (flow – blood flow direction): A. P – parent artery diameter; D – maximum aneurysm depth; N – neck size; B. S_{max} – maximal aneurysm dome size; H – maximum aneurysm height, measured between the centre of the aneurysm neck and the greatest distance to the aneurysm dome; H_{max} – maximal perpendicular height, the largest perpendicular distance from the neck of the aneurysm to the dome of the aneurysm; AA – aneurysm angle; VA – vessel angle

| | Unruptured | Ruptured | p value |
|--|-----------------------|---------------------|-----------------------|
| Age [years] | 53.97 ± 13.55 | 55.50 ± 17.23 | 0.717 ^a |
| Depth [mm] | 7.00 (5.00–15.00) | 4.00 (3.00–5.70) | <0.001 ^{b,*} |
| Height [mm] | 9.00 (6.00–13.00) | 5.00 (4.00–6.75) | 0.006 ^b |
| Width [mm] | 7.00 (5.00–12.00) | 4.00 (3.00–5.00) | <0.001 ^{b,*} |
| Neck size [mm] | 4.00 (3.20–5.00) | 3.45 (3.00–4.25) | 0.050 ^b |
| Aneurysm volume [mm ³] | 268.08 (78.54–1504.3) | 33.51 (19.90–82.47) | <0.001 ^{b,*} |
| Parent artery diameter [mm] | 4.69 ± 1.09 | 4.20 ± 0.90 | 0.106 ^a |
| Maximum aneurysm size [mm] | 9.00 (6.00–15.00) | 4.90 (4.00–7.00) | 0.003 ^{b,*} |
| SR ratio (maximum aneurysm size/parent artery diameter) | 2.00 (1.32–3.33) | 1.22 (0.98–1.69) | 0.020 ^b |
| Neck size to parent artery ratio | 0.92 (0.74–1.11) | 6.00 (5.48–7.89) | <0.001 ^{b,*} |
| Maximum aneurysm high perpendicular to neck [mm] | 8.00 (5.00–12.50) | 6.35 (4.00–14.35) | 0.192 ^b |
| Aspect ratio (maximum aneurysm high perpendicular to neck/neck size) | 2.00 (1.34–2.94) | 0.22 (0.14–0.45) | <0.001 ^{b,*} |
| Vessel angle [degrees] | 40.00 (30.00–55.80) | 35.50 (31.50–66.80) | 0.909 ^b |
| Aneurysm angle [degrees] | 92.57 ± 20.06 | 102.09 ± 31.00 | 0.173 ^a |
| Aneurysm depth to neck size ratio | 2.00 (1.37–3.33) | 0.14 (0.10–0.18) | <0.001 ^{b,*} |
| Packing density [%] | 28.68 (20.25–35.83) | 30.70 (20.11–40.80) | 0.564 ^b |

^a t-test, ^b Mann–Whitney U test, * Significant after Bonferroni correction.

Tab. 1. Data presented as mean ± SD or median (IQR) depending on variable distribution

increment of 0.5 mm using 3D software, before embolisation. Angiography and embolisation were carried out under general anaesthesia, by two neuroradiologist. All patients received 5,000 international units of heparin intravenously, shortly after placing the introducer into the femoral artery, and additional 2,000 units after one hour. A standard femoral approach was used. A 6F or 5F guiding catheter was placed in the ICA and 5F in the vertebral artery (VA). ICA angiography was performed in four standard projections. In the case of aneurysm diagnosis, optimal projection work was sought, demonstrating aneurysm morphology, sac to neck ratio and anatomic relationship to neighbouring vessels. The aneurysm was accessed with a standard 10 or 14 size microcatheter. The catheter and microcatheter were continuously flushed with a solution of physiologic saline and heparin at the concentration of 2,000 units/L. Two types of spirals were used: bare platinum (Boston Scientific, Fremont, CA; eV3, Irvine, CA; Micrus, San Jose, CA) and augmented coils (Matrix, Boston Scientific; Cerecyte, Micrus), both available in two diameters: 0.010” and 0.018” and two coil forms: a spatial (3D) and helical. The decision to use a stent (Enterprise) was taken individually. The stent was implanted after a thorough assessment of: dome to neck ratio (below 1.5), anatomical relations of aneurysm sac and parent artery, course of parent artery and tortuosity of surrounding vessels. In each case the risk of embolisation was estimated whether it was equal to the conventional or not. Aneurysm size was measured based on DSA images acquired in the anterior-posterior and lateral projection with a 22 cm magnification. All measurements were performed using Siemens Axiom Artis based on the original calibration data. Aneurysm volume and packing density (PD) were calculated using AngioCalc calculator (Hanley, 2006). The effectiveness of the initial endovascular

treatment was determined visually using modified Raymond Roy classification. Recanalisation was diagnosed when compaction and filling of the aneurysm occurred, compared to the primary embolisation during follow-up. We also analysed aneurysm spontaneous occlusion after incomplete treatment.

Statistical analysis

Nominal variables were given as numbers with appropriate percentage, whereas continuous variables were presented as means with standard deviations (SD) or medians with interquartile ranges (IQR). The normality of distribution was verified using the Shapiro–Wilk W test. Chi-square tests, with appropriate corrections, were used to find associations between categorical variables. For pairwise comparisons of continuous variables the Student’s t-test or the Mann–Whitney U test were used. Correlations were assessed using Spearman’s rank correlation coefficient. Multivariate analysis was done with utilisation of stepwise logistic regression model. A p value of <0.05 was considered statistically significant. Bonferroni adjustment for multiple comparisons was used to control the family-wise error rate. The entire statistical analysis was carried out using Statistica 12.5 software (Statsoft, Tulsa, OK, USA).

RESULTS

All aneurysms were located in ophthalmic segment of the ICA. Thirty-five (63.6%) patients were included in the unruptured group (UG) and 20 (36.4%) in the ruptured group (RG) with no differences in the mean age (accordingly: 53.9 ± 13.55 years vs. 55.5 ± 17.23 years; p = 0.717). Gender distribution was as follows: 88.6% (n = 31) female in UG and 85% (n = 17) in RG. Descriptive statistics are

| | <i>r</i> | <i>p</i> |
|---|----------|----------|
| Recanalisation volume [mm³] and aneurysm neck size [mm] | 0.68 | 0.001 |
| Recanalisation volume [mm³] and aneurysm volume [mm³] | 0.69 | 0.001 |
| Recanalisation volume [mm³] and the largest size of the aneurysm [mm] | 0.75 | <0.001 |

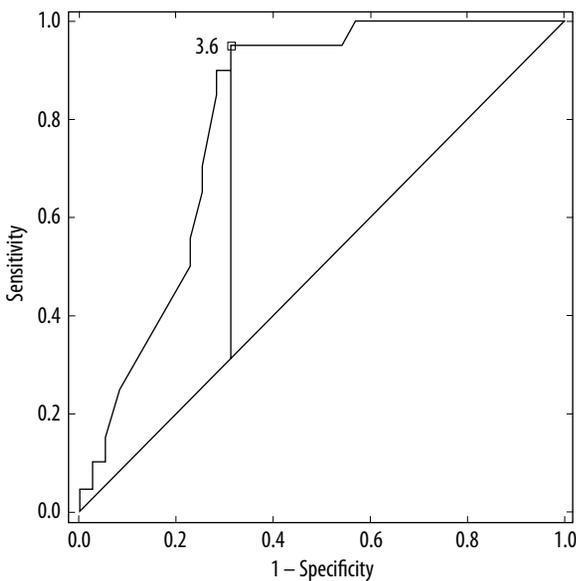
Tab. 2. Spearman analysis of variables for the volume of recanalisation

presented in Tab. 1. The median aneurysm volume was 268.08 mm³ (IQR: 78.54–1504.3 mm³) in UG and 33.51 mm³ (IQR: 19.90–82.47 mm³) in RG (*p* < 0.001). The mean packing density was 28.68% for UG and 30.7% for RG (*p* = 0.571). At the initial intervention, complete occlusion was achieved in 88.57% (*n* = 31) in UG and 70% (*n* = 14) in RG (*p* = 0.144). The overall recanalisation rate was 36.3% [34.3% (*n* = 12) in UG and 40.0% (*n* = 8) in RG, *p* = 0.773], and it occurred mostly at the neck in both groups. The Spearman analysis of variables for the volume of recanalisation turned out to be significant (after exclusion of mutually correlated factors, such as aneurysm height and depth) for 3 factors: aneurysm neck size (*r* = 0.68, *p* = 0.001), aneurysm volume (*r* = 0.69, *p* = 0.001) and the largest size of the aneurysm (*r* = 0.75, *p* < 0.001). The results are presented in Tab. 2.

The multivariate analysis of all aneurysms revealed several factors which had influence on aneurysm recanalisation in our cohort. Aneurysm depth and packing density were found to be protective factors, while incomplete aneurysm occlusion, the largest size of the aneurysm and the neck size of the aneurysm were found to be risk factors of recanalisation. Detailed results of the analysis are presented in Tab. 3. We did not note spontaneous occlusion after incomplete embolisation.

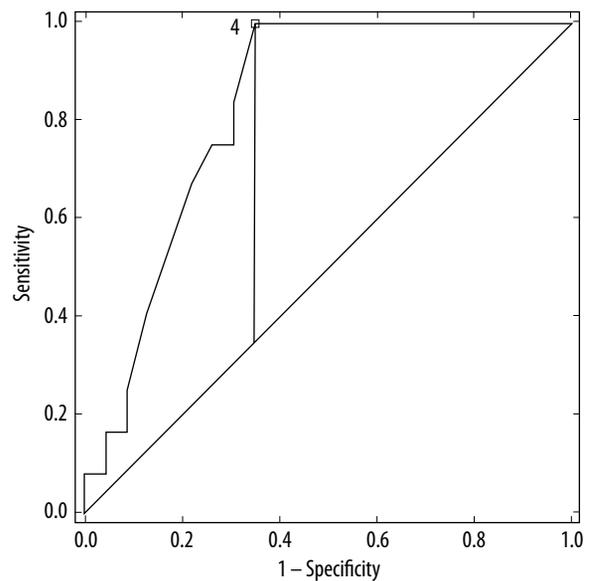
In the next step, we decided to assess the potential quality of our findings. We performed ROC (receiver operating characteristic) analysis to evaluate the sensitivity and specificity of the parameters. Aneurysm neck size was found to be the best one in terms of distinguishing between recanalised and non-recanalised aneurysms (sensitivity = 0.950, *p* < 0.001, Fig. 2).

The influence of the type of coil was not evaluated due too the small sample size (7 bare platinum coils, and 2 augmented). We also performed independent statistical analysis in each group. In the *t*-test and Mann–Whitney *U* test analysis in UG we found that aneurysm height (*p* = 0.025), weight (*p* = 0.045), neck size (*p* = 0.002), maximum size (*p* = 0.031), maximum aneurysm height perpendicular to neck (*p* = 0.031), packing density (*p* = 0.046) and also parent artery diameter (*p* = 0.036) are recanalisation risk factors. The multivariate analysis in the UG showed one factor which had influence on aneurysm recanalisation. Maximum aneurysm height perpendicular to neck (mm) was found to be a risk factor in the terms of recanalisation – OR, odds ratio = 1.28 (95% CI: 1.06–1.56, *p* = 0.012). Detailed results of the analysis are presented in Tab. 4. In the ROC analysis, aneurysm neck size again was found to be the variable with the best diagnostic potential (sensitivity = 1.00, *p* < 0.001, Fig. 3). In the ruptured group, we did not



| Aneurysm neck size [mm] | | | |
|--------------------------------|-------------|-------------|----------|
| AUC (95% CI) | Sensitivity | Specificity | <i>p</i> |
| 0.80 (0.69–0.92) | 0.950 | 0.686 | <0.001 |

Fig. 2. ROC analysis for aneurysm neck size for all aneurysms



| Aneurysm neck size [mm] | | | |
|--------------------------------|-------------|-------------|----------|
| AUC (95% CI) | Sensitivity | Specificity | <i>p</i> |
| 0.83 (0.69–0.96) | 1.000 | 0.652 | <0.001 |

Fig. 3. ROC analysis for aneurysm neck size in UG

| | Parameter | p | OR (95% CI) |
|---------------------------------------|-----------|-------|---------------------|
| Intercept | -1.02 | 0.629 | 0.36 (0.01–22.66) |
| Incomplete aneurysm occlusion | 3.34 | 0.015 | 28.24 (1.92–414.37) |
| Aneurysm depth [mm] | -0.76 | 0.043 | 0.47 (0.22–0.98) |
| The largest size of the aneurysm [mm] | 0.62 | 0.055 | 1.87 (0.98–3.53) |
| Packing density [%] | -16.63 | 0.028 | 0.85 (0.73–0.98) |
| Aneurysm neck size [mm] | 1.08 | 0.036 | 2.95 (1.07–8.13) |

Tab. 3. The variables included in the final model after stepwise logistic regression

| | Parameter | p | OR (95% CI) |
|--|-----------|-------|------------------|
| Intercept | 2.40 | 0.017 | 2.16 (1.50–3.14) |
| Maximum aneurysm height perpendicular to neck [mm] | 0.252 | 0.012 | 1.28 (1.06–1.56) |

Tab. 4. Multivariate analysis of variables for recanalisation in unruptured aneurysms group

| | Parameter | p | OR (95% CI) |
|--|-----------|-------|------------------|
| Intercept | -2.189 | 0.061 | 0.11 (0.01–1.11) |
| Maximum aneurysm height perpendicular to neck [mm] | 0.231 | 0.065 | 1.26 (0.99–1.61) |

Tab. 5. The variables included in the final model after stepwise logistic regression (ruptured aneurysms group)

find significant factors related to aneurysm recanalisation in the multivariate analysis, probably due to the small number of cases. However, maximum aneurysm height perpendicular to neck (mm) was found to be probably disadvantageous – OR = 1.26 (95% CI: 0.99–1.61, $p = 0.065$). Detailed results of the analysis are presented in Tab. 5.

DISCUSSION

Endovascular coil embolisation (ECE) is a minimally invasive technique alternative to surgical clipping (Khan et al., 2005). The main disadvantage of endovascular treatment is pending recanalisation and subsequent formation of recurrent aneurysm, with recurrence rates of 37.5–53% for paraclinoid aneurysm (Boet et al., 2005; Heran et al., 2007). In large and giant aneurysms, recanalisation was observed in 87–90% of patients (Benitez et al., 2004). The outcomes are even more unfavourable in the case of a bleeding aneurysm (Hayakawa et al., 2000). In our opinion, recanalisation is an underestimated clinical problem which carries a potential 1–8% risk of rerupture. This rate can be as high as 17.6% for less than 70% occlusion; consequently, further treatment is required. Although recoiling is safe and efficient, not all recurrent aneurysms can be recoiled due to morphological changes such as a broad neck or mass effect (Wang et al., 2017). Recanalisation occurs as a complication in approximately 30–41% ECE (Pandey et al., 2007), while the risk of incomplete surgical clipping of the aneurysm is estimated to be 4–8% (Pierot et al., 2008). According to CARAT study, the degree of aneurysm occlusion following treatment was strongly associated with the risk of rerupture. Rebleeding tends to occur more often after ECE, particularly during the first year, especially in the first three days, and incomplete occlusion is its main determinant. The risk of rupture after less than 70% embolisation was

24.5% in the first year, whereas the ruptured intracranial aneurysms (RIAs) completely excluded from the circulation have a risk of rebleeding of only 1.1% (Johnston et al., 2008). Furthermore, it is known that the incidence of intraoperative RIA bleed is only 5% for ECE and up to 19% for MS, but the risk of death and disability associated with its occurrence is twice greater in patients treated with endovascular technique, i.e. 63% vs. 31%, respectively (Elijovich et al., 2008). In carotid-ophthalmic aneurysms, complete occlusion was achieved in only 50% of cases (Heran et al., 2007). Our analysis showed that aneurysm volume was a statistically significant risk factor with a cut-off point of 1378.38 mm³ in UG and 69.38 mm³ in RG. When making decision on the treatment of paraclinoid aneurysm higher than 12 mm, it seems appropriate to take into account the greater chance of recanalisation. In contrast, the depth – 1 mm above 13 mm, decreases recanalisation rate by 53%. Ophthalmic artery aneurysms with neck size greater than 3.6 mm are definitely more likely to recanalise. Our analysis demonstrated that a high packing density (>23.48%) protects against recanalisation in paraclinoid aneurysms with volumes smaller than 989.6 mm³. It is worth mentioning that if the parent artery diameter is greater than 4.8 mm, recanalisation will occur more often. It is noteworthy that aneurysm volume, SR ratio, AR ratio, maximal perpendicular height to neck size ratio and also aneurysm depth to neck size ratio affect recanalisation volume. We have demonstrated statistically significant independent predictors of recanalisation volume, which are not risk factors for recanalisation, but strongly correlate with other morphometric parameters. Predicting recanalisation, one could foresee its volume and calculate the risk of long-term complications. In the light of recent research, aneurysms with low AR ratio (less than 1.2) are considered unsuitable for the classic ECE (Brinjikji et al., 2009). According

to the literature, an inflow angle of more than 90 degrees is a significant independent risk factor of recanalisation (Ji et al., 2016); this however, was not confirmed in our analysis.

Flow diverters (FD) are an alternative treatment to microsurgery. FD are endovascular prostheses placed within the parent artery to treat intracranial aneurysms. They utilise altering haemodynamics at the aneurysm/parent vessel interface, resulting in gradual thrombosis of the aneurysm occurring over time. Subsequently, the parent artery lumen is reconstructed and perforators or side branches are preserved, mostly in all cases. They are usually used to treat wide neck and giant aneurysms. There are several risks correlated with flow diverters e.g. in-stent thrombosis, perianeurysmal oedema, distant and delayed haemorrhages, and perforator occlusions.

The efficacy and safety against other therapies (endovascular and microsurgery) are being studied in ongoing trials. The first limitation of our study is relatively small number of patients. Also, the research is limited by its single-centre, retrospective design, thus we cannot exclude the possibility of selection and measurement bias. However, the evaluation was done by the same person to minimise this effect. Furthermore, we excluded patients with flow diverters, which is a common treatment for unruptured paraclinoid aneurysms, since the number of patients who underwent this therapy in our department is still low.

CONCLUSIONS

Different factors seem to influence recanalisation. If the above-mentioned predictors of recanalisation are present preoperatively, microsurgical clipping can be considered. The presented risk factors might influence endovascular and surgical treatment decisions.

Conflict of interest

The authors do not declare any financial or personal links with other persons or organisations that might adversely affect the content of the publication or claim any right to the publication.

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