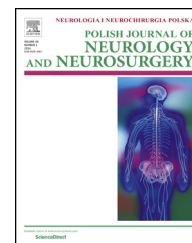


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Early outcomes and perioperative complications of endovascular embolization in patients with aneurysmal SAH

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ABSTRACT

Background: We still lack reliable data on the outcomes of endovascular coiling for ruptured cerebral aneurysms. As this is still an evolving technique, the outcomes of the procedures performed in the past and more recently cannot be directly compared. We present the early outcomes of endovascular coiling in a relatively large group of patients with ruptured intracranial aneurysms.

Method: The study included 190 consecutive patients (a total of 216 aneurysms) subjected to endovascular coiling in 2006–2013 (127 women aged 56 ± 13 years and 63 men aged 50 ± 15 years). Up to 87.5% of the aneurysms were located within anterior circulation. Most patients presented with “mild to moderate” subarachnoid hemorrhages (85% of Hunt & Hess scores 1–3, and 72% of Fisher scores 1–3).

Results: Embolization was feasible in 176 (92.6%) patients. In 14 cases, the embolization was not attainable due to unfavorable anatomy of the aneurysm, intraoperative vasospasm and/or aneurysm rupture, or prolapse of a coil. Early complications related to the procedure were recorded in 23 (13.1%) patients. The most common perioperative complication was aneurysm rupture. All fatal complications occurred in patients with aneurysms located at the anterior circle of Willis. At the time of discharge, 126 patients scored 4 or 5 on the Glasgow Outcome Scale.

Conclusions: Endovascular embolization is an effective and relatively safe method for treatment of ruptured cerebral aneurysms. Complications related to the procedure are significantly less frequent in the case of vertebral-basilar complex aneurysms.

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1. Introduction

Endovascular coiling is increasingly considered worldwide as a therapeutic option in patients with intracranial aneurysms [1–4]. However, despite a number of published studies dealing with the problem in question, we still lack the reliable data on the overall efficiency of this procedure and perioperative complication rates. Multicenter randomized trials comparing the outcomes of the aneurysm coiling and clipping did not provide clear evidence on the superiority of either procedure [2,4,5]. Although ISAT study showed that coiling of ruptured aneurysms is superior to clipping in terms of its general outcomes, it also documented poor permanency of embolization with high recanalization rate in individuals treated with the former technique [4]. Moreover, when the ISAT cohort was re-examined 7 years later, the outcomes of the intravascular technique turned out to be worse than those of the open surgery due to higher re-embolization rate [6].

However, the problem is not straightforward, as endovascular treatment of cerebral aneurysms is a relatively new and still evolving technique. The outcomes of the endovascular procedures performed 15 years ago cannot be directly compared to those performed recently, since a number of factors, e.g. techniques of imaging and embolization, perioperative care and staff expertise have improved considerably in the meantime. This may at least in part explain the significant discrepancies in the reported outcomes of endovascular treatment [4,7–9]. Therefore, we still need actual data on the results of endovascular treatment in individuals with cerebral aneurysms. Surprisingly, although the endovascular technique has been increasingly used in the vast majority of neurosurgical centers for more than 15 years, only one such report, presenting the outcomes of no more than 17 Polish patients with subarachnoid hemorrhage (SAH), has been published to date [7].

The aim of this study was to present the early outcomes in a relatively numerous case series of patients with ruptured intracranial aneurysms, subjected to endovascular treatment at a regional center of neurosurgery in the years 2006–2013, with special emphasis on the perioperative morbidity and mortality.

2. Materials and methods

2.1. Patients

A total of 358 patients after SAH were hospitalized at our center in 2006–2013 and subjected to surgical treatment, endovascular embolization or conservative management (typically in persons with Hunt and Hess [H&H] scores equal to 5). This study includes the data of 190 consecutive patients (presenting with a total of 216 aneurysms); all of them experienced SAH and were subjected to endovascular embolization within 24 h from the insult, after careful consideration of both aneurysms clipping or coiling. A total of 190-ruptured aneurysms have been a subject of embolization during the analyzed period. The choice of a specific embolization technique depended on the aneurysm size and shape. Most aneurysms were coiled with

detachable Guglielmi coils (GDC): initially (in 2006–2008) with bare platinum coils, then gradually replaced by platinum coils with a volume-expanding hydrogel coating (Microvention) in 2009–2013. Some aneurysms were treated with mechanical detachable coils (MDS, Balton). Finally, additional balloon remodeling technique was used in 16 patients. No diverter stents were implanted in any case.

The decision on coiling/clipping was always made on an individual basis, by an experienced vascular neurosurgeon, neurologist and interventional neuroradiologist [10]. The exact indications for endovascular treatment changed over time, along with technical progress and growing experience of neuroradiological staff. Coiling was chosen as a first line treatment in poor-grade patients, especially those presenting with large and surgically inaccessible aneurysms. While coiling was typically preferred in the case of aneurysms located within posterior circulation and anterior cerebral artery (ACA) aneurysms, the choice of treatment modality in subjects with carotid, distant ACA and middle cerebral artery aneurysms depended rather on individual characteristics of the malformation, patient preference and sometimes also logistics (e.g. current access to a given facility).

The analyzed group included 127 (67%) women aged 56 ± 13 years and 63 (33%) men aged 50 ± 15 years. As shown in Table 1, up to 87.5% of the 216 aneurysms were located within anterior circulation (mostly on the anterior communicating artery, ACoA), and the remaining 12.5% within the vertebral-basilar complex, typically on the basilar artery.

The vast majority of patients scored 13–15 on the Glasgow Coma Scale (GCS) and experienced the so-called “mild to moderate” SAH, 85% of individuals scored 1–3 on H&H scale, and 72% scored 1–3 on Fisher scale. Intraventricular or/and intracerebral hemorrhages were found in 54 patients, all of them scoring 4 on the Fisher scale. In 12 (6.3%) cases, intraventricular hemorrhage resulted in hydrocephalus which necessitated external ventricular drainage.

2.2. Perioperative preparation and postoperative care (applied neuro-anesthesia)

All procedures were performed under general anesthesia. It is our routine that each patient qualified to embolization is supervised by a dedicated neuro-anesthesiologist who obtains complete history and performs physical examination with special emphasis on cardiac function, potential hypovolemia and hyponatremia. Premedication, typically a short-acting benzodiazepine, was given solely to good-grade patients. Each patient was subjected to a standard monitoring, including electrocardiography, continuous measurement of intra-arterial pressure, pulse oximetry, capnography, determination of urinary output and body temperature. Poor-grade patients were monitored via a central venous line. Radial artery cannula was always inserted prior to induction of anesthesia. For patient's comfort, this procedure was carried out under local anesthesia, after intravenous administration of low dose fentanyl. Central venous catheter was inserted after induction of anesthesia and achieving neuromuscular block.

Special care was taken to induce the anesthesia as smoothly as possible. Particular attention was paid to prevent any uncontrolled fluctuations in arterial blood pressure.

Table 1 – Clinical characteristics of the study group.

Characteristic	Number of patients
Mean age in years ± SD	54.2±14.0
Gender: male/female	63/127
Male to female ratio	1 : 2
Glasgow Coma Scale	
13-15	143
9-12	18
≤8	29
Hunt and Hess grade	
1	74
2	57
3	30
4	23
5	6
Fisher scale	
1	13
2	87
3	36
4	54
Embolization was feasible	176/190^{\$}
Glasgow Outcome Scale	
5	92/98 ^{\$}
4	34/37 ^{\$}
3	21/26 ^{\$}
≤2	29/29 ^{\$}
Site of all aneurysms/ ruptured aneurysms	216 (100%)
Altogether (ruptured and non- ruptured	
anterior communicating artery	84 (39%)
anterior cerebral artery	7 (2.3%)
internal carotid artery	71 (33%)
middle cerebral artery	27 (12.5%)
basilar artery	9
vertebral artery	5
posterior communicating artery	4
posterior cerebral artery	4
PICA	4
superior cerebellar artery	1
	} 27 (12.5%)

SD – standard deviation, \$ – all group of patients (190 patients).

During the procedure, mean arterial blood pressure (MAP) was maintained at a normal preoperative level for a given patient, and cardiovascular function was monitored carefully in order to prevent hypoperfusion of the brain [11].

After the procedure, each subject was extubated carefully, with special attention paid to avoid coughing and fluctuations in arterial blood pressure. Subsequently, the patient was transferred to a neurosurgical high-dependency unit to provide continued hemodynamic monitoring, adequate oxygenation, optimal fluid and electrolyte management and early control of potential complications. Postoperative pain was alleviated with regular paracetamol and low doses of opiates whenever needed. Color-coded transcranial sonography was performed on a daily basis to detect any cerebral vasospasm [12].

2.3. Statistical analysis

The results were analyzed with SYSTAT 10.0 for Windows software. Student's t-test was used to verify the significance of

intergroup differences in the analyzed parameters. Determinants of the outcome and risk factors of postoperative morbidity were identified on the basis of odds ratios (OR) determined on logistic regression analysis.

3. Results

Effective embolization proved feasible in 176 out of the 190 patients (92.6%). In 14 patients, the embolization was not attainable due to unfavorable anatomy of the aneurysm ($n = 6$), intraoperative vasospasm and/or aneurysm rupture ($n = 6$), or prolapse of a coil through the wall of the aneurysmal sac and resultant need for an open surgery ($n = 2$). In 11 out of these 14 patients, the aneurysms were clipped surgically shortly after the unsuccessful embolization. In the remaining 3 patients, the surgeries needed to be postponed due to severe brain swelling.

Early complications, directly related to the procedure, were recorded in 23 (13.1%) patients. The most common

Table 2 – Serious perioperative complications resulting in death or vegetative state.

Sex/age	Aneurysm location/size	Complications	GOS
M/74	ACoA	ICA vasospasm	2
F/66	ICA	Re-bleeding	1
F/42	MCA	Re-bleeding	2
F/49	ACoA	Re-bleeding, cardio-ventilatory insufficiency	1
F/74	ACoA	MCA embolism, ischemic stroke	1
M/70	MCA	ICA vasospasm	1
F/76	ICA	Re-bleeding, cardio-ventilatory insufficiency	2
F/62	ICA	MCA embolism, ischemic stroke	1
F/50	ACoA	Re-bleeding, cardio-ventilatory insufficiency	1
M/45	ACoA, MCA (non-ruptured)	Re-bleeding, cardio-ventilatory insufficiency	2
F/61	ACoA	Re-bleeding, cardio-ventilatory insufficiency	2

M – male, F – female, ACoA – anterior communicating artery, ICA – internal carotid artery, MCA – middle cerebral artery.

perioperative complications included aneurysm rupture, acute vasospasm, thromboembolism and prolapse of a coil. As many as 11 patients (6.3%), died or remained in a vegetative state (GOS scores 1–2) due to complications related to the embolization procedure. As shown in Table 2, the main reason for such unfavorable outcome was aneurysm rupture during the embolization; early vasospasm and thromboembolism were recorded in 2 patients each. Importantly, all the fatal perioperative complications occurred rather in patients with aneurysms located at the anterior circle of Willis but not in the case of malformations within vertebral/basilar circulation. In another 35 patients complications occurred during the hospitalization in subsequent days after the procedure thus cumulating the rate of post-procedural complications and complications of natural course after the SAH. They included in a decreasing order of frequency: hemiparesis/hemiplegia, dysphasia/aphasia, vasospasm, hydrocephalus and re-bleeding. A total of 18 patients died or remained in a vegetative state due to these complications, making the total rate of “unfavorable outcome” equal to 16.5% (29 patients – Table 1).

Altogether early complications associated with the embolization and the “natural course of SAH” was found in 33% of patients. Hemiparesis/hemiplegia were found in 11.8% of the patients, dysphasia/aphasia in 2.5%, vasospasm in 12.6%, hydrocephalus in 6.3% and re-bleeding from the aneurysm in 3.2% (some patients experienced more than one complication type). Complications related to SAH and embolization were most commonly observed in patients with aneurysms of the

middle cerebral artery, followed by those with the ACoA, basilar artery and internal carotid artery aneurysms. The number of patients with the GOS scores 5, 4 and 3 at the time of discharge was 92 (52%), 34 (19.3%) and 21 (11.9%), respectively (Table 1).

Multivariate logistic regression analysis was conducted to identify predictors of outcome in patients with aneurysmal SAH. Table 3 shows the factors predisposing to low score in GOS (score 1–3) in a descending order of their OR values. The most significant predictors of worse outcome were greater severity of SAH (assessed with H&H and Fisher scales) and presence of intracerebral hemorrhage ($p < 0.001$). Older age (above 60 years) turned out to be weaker, albeit still statistically significant, predictor of worse outcome after SAH and aneurysm embolization with OR 2.9, CI 1.1–7.3, $p < 0.005$. If a dependent variable was restricted to “serious complications” then older age has increased its OR to 4.65 but the confidence interval has expanded to 0.9–25.5, making the result “statistically insignificant”. Another significant predictor of serious postoperative complications was location of the aneurysm within anterior circulation.

4. Discussion

Our study was limited to the analysis of short-term outcomes in patients subjected to endovascular embolization of ruptured cerebral aneurysms. The hereby-documented morbidity

Table 3 – Predictors of poor outcome (*) and complications (†) in patients with SAH subjected to endovascular coiling, identified on a multivariate logistic regression analysis (in descending order of power).

Predictor	OR	p	95% CI
* H&H scale	22.1	0.000	7.8–62.3
* Procedure-related serious complications	15.4	0.000	3.3–73.0
* Intracerebral hemorrhage	6.1	0.001	2.0–18.7
* Fisher scale	5.7	0.000	2.8–11.6
* Age	2.9	0.024	1.1–7.3
* Vasospasm	2.3	0.064	1.0–5.4
† Age	4.65	0.06	0.9–25.5
† Aneurysm location	1.2	0.048	0.7–2.2

OR – odds ratio, CI – confidence interval.

and mortality rates fall well within the limits reported by previous studies dealing with the problem in question [2,4,5,7,9,18].

In many previous studies, the outcomes of aneurysm embolization were typically compared to the results of surgical clipping [4,13-15]. In our study, including a relatively large group of patients, early embolization with coils proved technically feasible in 92.6% of individuals with aneurysmal SAH – the proportion being only 4% lower than the fraction of the ISAT participants who have been subjected to successful aneurysm clipping (96.5%) [13]. High feasibility of the embolization in our series was associated with a relatively low overall mortality of 11.9% – the figure also similar to 10.2% and 9% reported respectively by ISAT and by Natarajan et al. in the case of patients subjected to surgical clipping [4,15]. Altogether, 16.5% of our patients died or remained in a permanent vegetative status, thus fulfilling the criteria of an “unfavorable outcome”. Also this figure is similar to a 13.3% rate reported by ISAT for aneurysm clipping [13].

Clinical and demographic characteristics of our group were similar to those presented in other studies dealing with aneurysm coiling. Most patients included in our clinical material were women (66.8%) with aneurysms located within anterior cerebral circulation (87.9%) – figures which obviously reflect natural distribution of aneurysmal SAH. Similar characteristics of aneurysm patients were previously reported by Park et al. [16] and Dumont et al. [17]: their cohorts included respectively 72.2% and 71% of women while anterior cerebral circulation aneurysms were seen in 74.6% and 92% of patients, respectively. The ISAT study included a smaller proportion of women (63%) and a larger fraction of patients with anterior cerebral circulation aneurysms (up to 97.5%) [4]. Approximately 75% of our patients represented “mild to moderate” SAH, which is also consistent with the results of previous studies [4,16,17]. All this implies that the hereby-presented findings can be directly compared with the results of previous studies dealing with the problem in question.

In 7.4% of our patients embolization was not feasible due to unfavorable anatomy, intraoperative vasospasm, intraoperative rupture of the aneurysm and/or prolapse of a coil to the parental vessel. Also this observation is consistent with the results of previous research: Gallas et al. [18] reported the feasibility of embolization at up to 96.9%, Molyneux et al. [4] at 92.5% and Gizewski et al. [19] at 95.6%. Failure of catheterization and unfavorable anatomy of the aneurysm area were the main predictors of unfavorable outcome of endovascular treatment in the studies mentioned above [4,18,19]. According to Gallas et al. [18], embolization failure may be also associated with unfavorable shape of the aneurysm or instability of a coil on deployment.

Approximately 3/4 of our patients scored 4 or 5 on the GOS at the time of discharge, about 12% of the study participants were discharged home with moderate disability (GOS score 3) and 16.5% satisfied the criteria for unfavorable outcome (GOS scores 1 or 2). Molyneux et al. [4] used modified Rankin scale to show that up to 74% of patients recovered after SAH and embolization. His group included 19% of asymptomatic patients, 29% individuals with minor symptoms and 25.7% with some restrictions in the activities of daily living. Approximately 10% of the ISAT patients were discharged with

a moderate disability and required assistance during the activities of daily living whereas only 7% of them died [4]. In another study [8], the proportions of patients with successful and unsuccessful outcomes of aneurysm coiling were 87% and 13%, respectively. Kaku et al. [10] achieved good recovery in 12 out of 19 patients (63.1%) with SAH [10]. In only Polish series published to date, Birski and colleagues presented results of aneurysm coiling in 17 patients. They documented successful outcomes in 43.8% of their patients, and reported 6% mortality [7]. Interesting data were published by Johansson et al. [20], who followed their patients for up to 6 months, documenting favorable outcomes in 41%, severe disability in 36% and mortality in 22%.

Perioperative complications occurred in 13.1% of intravascular procedures. This rate is similar to the 11% of morbidity reported by Byrne et al. and Johansson et al., who claimed such rate of complications “acceptable” considering the severity of the disease which determines the treatment-related risk [20,21]. Higher rate of periprocedural complication amounting to 19% has been presented by Friedman et al. in *Am J Neuroradiol*. The majority of complications presented by above mentioned authors can be classified as potentially serious and like in our group they included rupture of aneurysm during the embolization; early vasospasm, coil migration and thromboembolism.

It must be again pointed out that a proportion of good-grade to poor-grade patients in our series was similar to one reported in other published clinical series whereas our group is more numerous than most of the groups reported by other authors [4,10,20,22]. Out of the 23 of our patients who experienced periprocedural complications, 11 patients died or remained in vegetative state (GOS 1-2). In Johansson's series consisted of 62 individuals as much as 7 patients suffered a procedural complication which was shown to be a reason of poor outcome in 1 patient, severe disability in another one whereas 5 remained patients enjoyed favorable outcome [20]. In Byrne's series of 75 patients procedure – related complications occurred in 10 patients. Only 3 patients from this group recovered without sequelae, 6 suffered from permanent deficits and one died [21]. Like in our study, the most frequent complications were rupture of aneurysms during coil placement, and thromboembolism. Friedman et al. reported 16 periprocedural complication, which in 14 patients resulted in no or only a minor & temporary neurological deficit. Major complications occurred in two of his patients – resulting in serious neurologic disability in one patient and death in another one [22]. It is worth noticing that in Friedman's series (in contrast to our study) the most frequent reason of both minor and major complication was thromboembolism.

Multivariate logistic regression analysis demonstrated that the most significant predictors of non-optimal outcome were greater severity of SAH (assessed with both H&H and Fisher scales) and presence of intracerebral hemorrhage. The positive association between low Fisher grade on diagnostic CT and a favorable outcome has been found also by Johansson et al. whereas Pegoli et al. found on their multivariable analysis that as much as 4 variables were most strongly associated with excellent outcome: good clinical grade, the absence of ICH on initial CT scan and blood transfusion during hospitalization [20,23]. Predictably, the older age turned out to be a statistically significant predictor of sub-optimal outcome. One interesting

restriction as to this relationship can be pointed out: when “serious complications” was used as a dependent variable then OR increased from 2.9 to 4.65 and in the same time older age becomes “statistically insignificant”. This result point out at the advanced age of a patient as a potential predictor of serious complication but relatively small content of such complication in the studied group apparently prevented the OR to fall into “statistically significant” range of confidence interval.

It was of some surprise to find localization of the aneurysm within anterior circulation a significant predictor of serious postoperative complications. There is a scarce data in the literature on this particular question. Brilstra et al. [1] did not find any difference in the complication rate for patients with SAH from the anterior and posterior circulation aneurysms. Serious complications resulting in permanent neurological deficits occurred in 5.4% and 3% of individuals with anterior and posterior circulation aneurysms, respectively [1].

It is important to conclude that our rather satisfactory results of endovascular embolization of ruptured intracranial aneurysms were achieved thanks to a beneficial effect of a strict cooperation between vascular neurosurgeons, endovascular specialists and neuro-anesthesiologists. This includes smooth and atraumatic induction of anesthesia, followed by careful intraoperative monitoring of patient's cardiovascular function and blood volume to prevent a patient against uncontrolled hemodynamic incidents. Finally, to reduce the rate of serious complications, intravascular procedures must be executed only in such center in which an experienced vascular neurosurgeon is continuously available for a prompt and immediate intervention in cases of coil herniation, migration, thrombo-embolic complications or unsuccessful coiling [24].

Conflict of interest

None declared.

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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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