

Prevalence of ruptured small and very small aneurysms: a retrospective single-centre study

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ABSTRACT

Aim of study. To retrospectively assess the occurrence and consequences of subarachnoid haemorrhages (SAH) caused by ruptured intracranial aneurysms (RIA), particularly focusing on the treatment outcomes of small aneurysms treated with either endovascular embolisation or surgical intervention.

Material and methods. We retrospectively analysed data from 408 patients (144 males and 264 females) who were hospitalised between 2013 and 2022 at the Department of Neurosurgery and Neurology in University Hospital Nr 2 in Bydgoszcz, Poland. Clinical conditions at admission, assessed using the Glasgow Coma Scale, Hunt-Hess scale (H-H), modified Rankin scale (mRS), as well as age and sex, were recorded. Additionally, aneurysm data including size, localisation, and the method and outcome of endovascular or surgical treatment were examined.

Results. Among the 408 patients hospitalised due to SAH, the most common localisation of the 375 RIAs was the anterior communicating artery (AcomA) complex (111 cases, 29.6%), followed by the medial cerebral artery (MCA) (95 cases, 25.3%), internal carotid artery (ICA) (94 cases, 25%), and the vertebrobasilar complex (consisting of the basilar artery (BA) — 25 cases, vertebral artery (VA) — 13 cases, anterior inferior cerebellar artery (AICA) — one case, and posterior inferior cerebellar artery (PICA) — four cases), which accounted for 43 SAH cases (11.46%). In 33 cases, neither RIA nor a haemorrhage source was identified, or arteriography showed no cerebral arteries contrast flow. Among the examined group of 375 RIAs, 45 (12%) were microaneurysms (\leq 3 mm), 35 (9%) were small aneurysms ($3 \leq$ 5 mm), 89 (24%) were medium-sized ($5 \leq$ 7 mm), and 151 (40%) were large aneurysms (> 7 mm), serving as the source of SAH. A better outcome was significantly associated with lower initial H-H grade (p < 0.001), higher GCS (p < 0.001), lower mRS at admission (p < 0.001), younger age (p < 0.001), smaller size (\leq 3 mm) $(p < 0.001)$, and endovascular treatment $(p < 0.001)$.

Conclusions. In this series, over 21% of patients suffered from SAH resulting from ruptured small aneurysms (≤ 5 mm), with 12% specifically attributed to ruptured very small aneurysms (\leq 3 mm), despite large aneurysms ($>$ 7 mm) being the most prevalent source of bleeding in 40% of cases. A worse prognosis was primarily associated with the severity of SAH, reflected in poorer clinical status at admission and older age. Endovascular embolisation was found to be effective and associated with better outcomes compared to surgical treatment.

Keywords: intracranial aneurysm, microaneurysm, subarachnoid haemorrhage, aneurysm embolisation

(*Neurol Neurochir Pol 2024; 58 (4): 445–452*)

Submited: 28.10.2023 Accepted: 29.05.2024 Early publication date: 05.08.2024

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Introduction

In the modern era of widespread high-resolution CT and MR angiographic studies, small (3.1–5 mm) and very small (≤ 3 mm) unruptured intracranial aneurysms (UIAs) are commonly diagnosed. The diagnosis of a UIA raises critical questions about their potential danger and whether intervention is necessary. Previous research suggests that aneurysms smaller than 7 mm generally carry a very low risk of rupture [1]. However, the natural history, risk of rupture, clinical outcomes, and risks associated with surgical or endovascular treatment should all be considered in the decision-making process regarding intervention. Regular follow-up imaging for UIAs is generally recommended [2]Nonetheless, subarachnoid haemorrhages (SAH) resulting from ruptured small aneurysms (RSA) or very small aneurysms (RVSA) are not uncommon and can lead to serious neurological complications[3].

The management of ruptured intracranial aneurysms (RIA) aims to prevent further bleeding and reduce the risk of complications such as vasospasm or secondary brain injury. Endovascular treatment of cerebral aneurysms is globally recognised as best practice according to evidence-based guidelines [4].

Coil embolisation of RSAs, however, is challenging and demands a high level of expertise [5]. Prophylactic coiling of multiple small UIAs has been shown to be more effective than conservative treatment [6]. Over the past 35 years, based on 240 studies, there has been a significant reduction in the size threshold for safely treatable UIAs [7].

Intracranial aneurysms measuring 3.1–5 mm are typically classified as small [8].

The objective of this study was to retrospectively assess the prevalence and outcomes of SAH from RSAs and RVSAs treated mainly with endovascular embolisation or surgical clipping, and to investigate the factors influencing these outcomes.

Material and methods

This retrospective study was conducted at a single institution, involving 408 patients (264 males, 65%; 144 females, 35%; mean age 56, range 21–93), who were admitted for aneurysmal subarachnoid haemorrhage (SAH) at the Department of Neurosurgery and Neurology in University Hospital Nr 2 in Bydgoszcz, Poland, between 2013 and 2022. The clinical data collected at admission included assessments using the Hunt- -Hess scale (H-H)[9], Glasgow Coma Scale (GCS), and modified Rankin Scale (mRS), as well as age and sex. Aneurysm characteristics, such as size and location, were categorised as very small (tiny) (\leq 3 mm), small (\leq 5 mm), medium (5–7 mm), large (7–25 mm), and giant (>25 mm). Patient outcomes were evaluated using the Glasgow Outcome Score (GOS), where a GOS of 1 indicates death. The study was conducted following the ethical guidelines of the Declaration of Helsinki and

received approval from the Bioethics Committee at Nicolaus Copernicus University (approval number 346/2022).

Endovascular embolisation and surgical treatment

All endovascular procedures for patients with SAH due to ruptured intracranial aneurysms (RIAs) were performed under general anaesthesia. The typical procedural approach involved puncturing the right femoral artery, followed by 3D rotational angiography to visualise, measure, and plan the embolisation of the aneurysm. A large-bore 6F guiding catheter was inserted into the cervical portion of the targeted artery. Using angiographic roadmaps, microcatheters, and microguidewires, the aneurysm sac was catheterised and embolised with coils selected based on the aneurysm's size and morphology. For anatomically complex aneurysms, remodelling techniques involving balloons or stents were employed. A loading dose of 5,000 IU of heparin was administered following the safe deployment of the first coil. In cases requiring stent placement, patients received intravenous eptifibatide in weight-adjusted doses for 12 hours, followed by standard oral double antiplatelet therapy comprising ASA and ticagrelor.

Among the 408 patients with SAH, 375 had a known source of bleeding. Of these, 59 (15.7%) underwent surgical clipping primarily between 2013 and 2018 (Tab. 1). A total of 306 endovascular procedures were performed, involving the insertion of coils in 299 patients. Stents were implanted in four cases, comprising two flow diverter (FD) stents and two regular braided stents. In one patient with a distal posterior inferior cerebellar artery (PICA) aneurysm, embolisation was performed using N-butyl cyanoacrylate glue. Two other patients experienced issues with vascular access due to atherosclerosis. Remodelling procedures involving stents were conducted in 38 patients (12.7%), with 26 (9.7%) receiving stents and the remaining 12 (4%) treated using balloon-assisted techniques. In 33 cases (8%), digital subtraction angiography (DSA) did not confirm the presence of an aneurysm; this included six cases showing no arterial flow on arteriography, suggesting brain death (1.2%), and two patients who were disqualified from treatment due to other serious diseases.

Patients undergoing surgical treatment included those with intracranial haematomas resulting from ruptured MCA, ICA, AcomA aneurysms, as well as those whose aneurysm's morphology and widened neck, as visualised on angio-CT, rendered coiling unfeasible. Clipping was usually performed within 48 hours after admission.

Statistical analysis

The statistical framework incorporated four tests. For examining the 'effect of hospitalisation' (a nominal variable with two categories), we employed the Welch test for numerical data and the chi-square test of independence (maximum likelihood method) for categorical data. The Glasgow Outcome Score (GOS), which ranges from 1 to 5, was analysed using the Spearman correlation test for numerical variables.

Table 1. Outcome after surgical and endovascular treatment

Table 2. Characteristics of examined group

Localisation Number AcomA 111(29.6%) ACA 20(5.3%) ICA 94(25.0%) MCA 95(25.3%) PcomA 6(1.6%) PCA 6(1.6%) PICA 4(1.0%) BA 25(6.7%) VA 13(3.5%) AICA 1(0.3%) no RIA 33(8.0%) Total 408 **Size (mm) Number** > 7 151(40.3%) $5 \le 7$ 89(23.7%) $3 \leq 5$ 35(9.3%) ≤ 3 45(12%) n/d 55(14.7%) Total 375 **Gender Number** Female 144(35.3%) Male 264(64.7%)

artery; ICA — internal cerebral artery; MCA — medial cerebral artery; PcomA — posterior communicating artery; PCA — posterior cerebellar artery; PICA — posterior inferior cerebellar artery; BA — basilar artery; VA — vertebral artery; AICA — anterior inferior cerebellar artery, n/d: no data; H-H — Hunt-Hess score at admission; GCS — Glasgow Coma Scale at admission; mRS — modified Rankin Scale; GOS — Glasgow Outcome Scale at discharge

communicating artery (AcomA) complex in 111 cases (29.6%), the middle cerebral artery (MCA) in 95 cases (25.3%), and the internal carotid artery (ICA) in 94 cases (25%). The vertebrobasilar complex accounted for 43 SAH cases (11.46%), including the basilar artery (BA) in 25 cases, the vertebral artery (VA) in 13 cases, the anterior inferior cerebellar artery (AICA) in one case, and the posterior inferior cerebellar artery (PICA) in four cases (Tab. 2). In 33 patients (8%), despite the presence of radiological and clinical evidence of SAH, no RIA was visualised on angiography or angio-CT, no haemorrhage source was identified, or arteriography showed no cerebral arteries contrast flow (Fig. 1).

Distribution comparisons across different GOS groups were conducted using the Mann-Whitney U test for two groups and the Kruskal-Wallis H test for multiple groups. Statistical significance was set at a p-value of < 0.05.

Results

Localisation

Of the 408 patients hospitalised for subarachnoid haemorrhage (SAH), the most common localisations for the 375 identified ruptured intracranial aneurysms (RIAs) were the anterior

Figure 1. Localisation of aneurysms and outcomes of treated aneurysms in different localisations

Size

Among the 375 RIAs, microaneurysms (\leq 3 mm) accounted for 45 cases (12%), small aneurysms (3–5 mm) for 35 cases (9%), medium aneurysms (5–7 mm) for 89 cases (24%), and large aneurysms (> 7 mm) for 151 cases (40%). Additionally, 75 aneurysms (20%) measured between 10.1 mm and 25 mm, and only two aneurysms (> 25 mm) were identified as giant, accounting for 0.5% of the SAHs. The mean size of the ruptured aneurysms was 7.5 ± 4.4 mm, ranging from 1 to 26 mm. In this retrospective study, data regarding aneurysm size was not gathered in 55 cases (14.6%), as set out in Table 2. Among these cases, patients underwent surgical clipping; however, information regarding aneurysm size was unavailable. This limitation stemmed from the lack of reliable data obtained from angio-CT exams conducted at external facilities. The only trustworthy measurements were derived from 3D arteriographies performed in our centre during endovascular procedures.

Outcome

The mean Glasgow Coma Scale (GCS) score at admission was 12 ± 4 , showing a slight improvement to 13 ± 3.3 at discharge. The mean modified Rankin Scale (mRS) at admission was 2.6 ± 1.7 across 408 SAH cases, improving to 1.9 ± 1.8 at discharge for 361 cases. The mean Hunt-Hess (H-H) score was 2, with the distribution at admission as follows: 125 patients in the 2nd grade, 130 in the 1st grade, 57 in the 3rd grade, 63 in the 4th grade, and 29 in the 5th grade (Tab. 1). The average Glasgow Outcome Scale (GOS) at discharge was 4.2 ± 1.7 , indicating moderate disability, with 237 patients in the 5th grade. Epileptic seizures during hospitalisation were observed in 10 patients (2.67%).

The discharge outcomes of surgical treatment were as follows: among five patients (8%), there was a score of 0 (indicating no symptoms); in the subsequent five patients (8%), a score of 1 was recorded (reflecting no significant disability); three patients (5%) were rated at 2 points on the modified Rankin Scale (mRS), indicating slight disability; nine patients (15%) scored 3 points, signifying moderate disability; 14 patients (24%) scored 4 points, indicating moderate disability; 13 patients (22%) scored 5 points, indicating severe disability; and in 10 patients (17%) a score of 6 was recorded, representing death.

Correlations

The study analysed 408 patients, finding that 46 (11.3%) died, including 44 of the 375 (11.7%) patients with confirmed aneurysms. Mortality was significantly associated with older age ($p < 0.001$) but showed no significant correlation with gender ($p = 0.42$), aneurysm location ($p = 0.131$), or aneurysm size category (over 7 mm, 5–7 mm, and 3–5 mm). The death rate was influenced by the clinical state at admission, as assessed by the Glasgow Coma Scale (GCS), Modified Rankin Scale (mRS), and Hunt-Hess (H-H) score, all showing significant correlations with outcomes ($p < 0.001$) (Fig. 2) (Tab. 3). Patients who died had an average admission GCS score of 7, compared to 13 for survivors. Further, the extent of SAH, measured by the H-H scale, was significantly linked to mortality; as the H-H score at admission increased, so did the mortality rate. Among patients with confirmed RIAs, the highest mortality rate (37.9%) was observed in patients graded H-H 5, followed by 31.6% in grade 4 and 12.5% in grade 3 (Tab. 4) The H-H grade was a strong predictor of the Glasgow Outcome Scale (GOS) score ($p < 0.001$). The most common sources of SAH leading to a GOS of 1 (death) were anterior communicating artery (AcomA, 16 cases), middle cerebral artery (MCA, 10 cases), and internal carotid artery (ICA, seven cases). However, the case fatality rate (CFR) was highest (30%) for vertebral artery (VA) aneurysms, although aneurysm location was not a significant predictor of mortality (Fig. 1).

Regarding aneurysm size, a significant correlation was found between microaneurysms (\leq 3 mm) and better outcomes (p < 0.001); 77% of patients with microaneurysms achieved a GOS of 5, compared to 53% of those with larger aneurysms. No deaths occurred in patients with microaneurysms ≤ 3 mm

Table 3. Predictive factors of GOS

Figure 2. Effect of GCS at admission on case fatality rate

(Fig. 3). The median size of aneurysms was 7 mm for those who died, with a mean size of 9.70 mm and a standard deviation (SD) of 6.419, whereas the median size was 6 mm for survivors, with a mean of 7.32 mm and an SD of 4.135 ($p = 0.041$).

Most bleeding microaneurysms were found in the AcomA (16 cases), ICA (14 cases), and MCA (four cases). Among these, a fatal case occurred with an MCA-located microaneurysm. During the diagnosis of SAH, 338 patients had a single ruptured aneurysm, while 37 had multiple aneurysms, and no source was identified in 32 cases.

Complications

There were two cases of acute stent thrombosis, both successfully treated with abciximab and integrilin, resulting in no clinical sequelae. Of the 299 embolisation procedures, four led to haemorrhages (1.34%), three of which were intraprocedural (1.00%) and one unrelated to the procedure (rebleeding occurred during the induction of general anaesthesia). The latter was the only case resulting in clinical consequences (death during hospitalisation). In 13 cases (4.36%), coils dislodged into the parent artery; of these, five (1.67%) required no intervention, while eight (2.68%) necessitated stent implantation. None of these instances resulted in clinical consequences. Overall, the outcomes of endovascular treatment were significantly superior to those of surgical clipping, with 63% of patients achieving good recovery (Glasgow Outcome Scale score of 5) post-coiling, compared to only 21% following surgical treatment ($p = 0.00$) (Tab. 1).

Discussion

The principal finding of our study was that large and medium aneurysms were the most frequent sources of bleeding. However, ruptured small $(\leq 5 \text{ mm})$ and very small (≤ 3 mm) microaneurysms accounted for over 21% of patients with subarachnoid haemorrhage (SAH) in our series ($n = 80$), with tiny aneurysms (\leq 3 mm) causing haemorrhage in more than 12% ($n = 45$) of cases. This aligns with other studies [3, 10–14]. Among 421 Korean patients with SAH, 51 (12.1%) had ruptured saccular aneurysms measuring less than 3 mm, exhibiting a lower average aspect ratio (aneurysm height/neck width) and a predominance of women [10]. Aneurysms with domes larger than 3 mm exhibit lower wall strength compared to adjacent cerebral arteries, thus presenting a higher risk of rupture, a fact well documented by Lombarski et al. [15]. Further insights from Japanese cohort studies reveal even higher instances (20.7%) of ruptured small cerebral aneurysms (< 3.5 mm) [3]. Historical data suggests that c.13% of bleeding incidents in a cohort of 676 patients with SAH involved aneurysms \leq 5 mm [12]. Comparatively, the International Subarachnoid Aneurysm Trial (ISAT) reported that over half of the patients experienced recurrent SAH due to ruptured aneurysms smaller than 5 mm, which were suitable for coiling or clipping [16]. The International Study of Unruptured

Table 4. Correlation between Hunt-Hess score and survival in patients with ruptured aneurysm

Statistical analysis revealed a strong correlation (p<0.001) between clinical severity at admission assessed with Hunt-Hess scale and the number of deaths. The highest was in the 5th grade. Among 29 patients in the 5th grade 11 died (38%), and in the 4th grade among 63 patients 19 died (32%). Fortunately, the highest number of patients were in the 1st grade, 122, of whom two died (1.6%)

Figure 3. Over 75% of patients with microaneurysms ≤ 3 mm achieved good recovery GOS = 5, compared to 53% of patients with aneury $sms > 3 mm$

Intracranial Aneurysms (ISUIA) highlighted a very low annual risk of rupture in asymptomatic aneurysms < 7 mm, at 0.7% per year [17], while data from the Japanese Small Unruptured Intracranial Aneurysm Verification Study (SUAVe) estimated the average annual risk for rupture of single aneurysms < 5 mm to be 0.34% per year [18]. The Unruptured Cerebral Aneurysm Study of Japan (UCAS Japan), for instance, found the rupture rate of 3–4 mm aneurysms on the MCA to be 0.23/year, whereas those arising from the AcomA exhibited a rupture rate of 0.9/year. Annual risk of rupture of an aneurysm < 5 mm in diameter was reported in the UCAS study, which was estimated at 0.36% per year[19].

Our findings diverge, particularly in that the majority of bleeding microaneurysms in our study were located in the anterior circulation, contrasting with previous research indicating higher risks in other regions. The ISUIA study reported no ruptures among aneurysms < 7 mm in diameter in the anterior circulation, yet aneurysms originating in the posterior circulation carried a 5-year risk of rupture estimated at 2.5 [20]. For aneurysms with a diameter of 5–6 mm, the risk of rupture is 0.31% and 0.75% for MCA and AcomA locations, respectively [19]. A study conducted in Korea found that the majority of ruptured aneurysms were smaller than 7 mm, with 71.8% located on the AcomA [21]. The rupture rate of a BA and ICA - PcomA aneurysm < 5 mm in diameter were 0.23% and 0.41% per year respectively in a Japanese population [17]. Except for size > 4 mm, hypertension, predictors of rupture were aneurysm multiplicity and age < 50 [18]. In our observation over nine years, ruptured aneurysms from the vertebrobasilar system (25 on BA, four on PICA, 13 on VA and one on AICA) accounted for 11% of all RIAs (n=375),

with a fourfold increase in bleeding cases in the posterior circulation observed over the last seven years in Lublin [22]. Multiplicity of aneurysms did not increase the risk in Ishibashi et al.'s study [23]. Dolati et al. observed that 37% of patients with aneurysms < 5 mm presented with poorer clinical status as assessed by the Hunt-Hess scale compared to those with larger aneurysms [24]. Furthermore, we noted that over 75% of patients with tiny aneurysms achieved good recovery. The PHASES risk score, which considers factors like P-population, H-hypertension, A-age, S-size, E-earlier SAH, and S-site, helps predict the 5-year risk of aneurysm rupture [25]. According to the PHASES risk score, patients with aneurysms smaller than 7 mm but located on the ACA/PcomA/posterior circulation are at a higher risk of rupture and should be considered for intervention, the risks of which depend on the expertise of the treating centre [26]. Aneurysmal growth, hypertension and smoking are the main evidenced risk factors of rupture [2]. In another Korean study with a total of 484 surgical cases (248 SAH and 236 unruptured aneurysms) in 460 patients, 33 tiny aneurysms were found in 31 operative cases incidentally discovered and operated by wrapping or coiling (6.4% incidence per operation). Most of them (nearly 55%) were located on the MCA, 30% on the ICA, and 13% on the AComA [11]. The authors noted that the number of open surgeries is decreasing compared to endovascular treatment, due to the development of modern techniques [11]. This same phenomenon is observed in our study where almost all ruptured aneurysms were closed with coiling or stenting in recent years. Over subsequent years, advances in endovascular techniques, accompanied by a broader array of coils and stents, have resulted in a shift wherein all RIAs are managed via an

endovascular approach. Our study is also consistent with the findings of Miękisiak et al. who demonstrated a significant reduction of open surgeries in treatment of RIA in 2020 during the COVID-19 pandemic while endovascular procedures were still being performed [27].The outcome treatment of RIAs can range from complete recovery without any long-term deficits to severe neurological impairment or death, depending on the severity of bleeding and injury to the brain. Our analysis revealed that the leading poor prognostic factors are initial clinical state, age of patient, and size of aneurysm. Endovascular treatment of small brain aneurysms is still a controversial issue. Previous studies have documented that endovascular embolisation carries a higher risk of recurrence and rebleeding compared to microsurgical clipping [16, 20]. A meta-analysis of seven studies with a total of 422 patients with tiny aneurysms, including 171 with ruptured aneurysms, showed that intraprocedural aneurysm rupture during intravascular embolisation occurred in 10.7% of ruptured aneurysms vs 5% unruptured aneurysms [28].

The most serious complication of endovascular treatment of microaneurysms is procedure-related rupture of the embolised aneurysm. A study of 668 patients undergoing endovascular treatment of aneurysms, including 60 with ruptured aneurysms less than 3 mm in diameter, showed that the probability of procedure-related aneurysm rupture increases fivefold for aneurysms < 3 mm compared to larger aneurysms [29]. Other literature data indicates that the risk of intraprocedural rupture of microaneurysms during intravascular embolisation ranges from 3.7% to 16.7% [30, 31]. In our study, intraprocedural haemorrhage occurred only in 1% of all bleeding, of which most were over 5 mm. Pierot et al. did not notice an increased rate of rupture of small aneurysms < 3 mm compared to larger ones, although the overall rate of failure on embolisation was higher in microaneurysms < 3 mm [5]. Wang et al. observed embolisation in 11.9% of small aneurysms $(\leq 3$ mm) among all ruptured cases in their study. They discovered that despite a higher utilisation of stents in smaller aneurysms, there was no notable variance in the safety and effectiveness of endovascular treatment compared to larger aneurysms [31]. In a recently published study from several centres in the Netherlands, the rate of intraprocedural complications was 11% and outcomes were not related to the time of embolisation after the rupture [32]. In our series, almost all patients were treated endovascularly within 24 h after diagnosis of SAH.

Limitations

This study was retrospective in design. Not all data was collected, which limits the results obtained. The absence of data affects the findings related to prevalence and correlations. Furthermore, long-term follow-up data is not presented. The comparison groups, consisting of patients treated with open microsurgery and those with endovascular embolisation, are not equivalent, making them not reliably comparable. There was a significant predominance of aneurysms treated endovascularly in our study cohort.

Conclusions

In this series, the most common sources of bleeding were large aneurysms (> 7 mm) and medium aneurysms (5–7 mm). However, over 21% of patients experienced SAH due to ruptured small aneurysms (\leq 5 mm), including 12% due to microaneurysms (\leq 3 mm). A worse prognosis was associated with the severity of SAH, as evidenced by poorer clinical states at admission and older patient age. Ruptured microaneurysms (≤ 3 mm) were associated with more favourable outcomes. Small and very small aneurysms should also be considered for endovascular treatment to prevent the consequences of SAH. Endovascular embolisation has proved effective and yielded better outcomes compared to surgical treatment.

Article information

Acknowledgements: *The authors thank Krzysztof Leki from the Centre for Statistical Analysis of Nicolaus Copernicus University in Toruń for conducting statistical analysis.* **Conflicts of interest:** *None.* **Funding:** *None.*

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