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Outpatient Day-Care Management of Unruptured Intracranial Aneurysm: A Retrospective Cohort Study

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Objective: This study aimed to assess the outcomes of outpatient day-care management of unruptured intracranial aneurysm (UIA), and to present the risks associated with different management strategies by comparing the outcomes and adverse events between outpatient day-care management and management with longer admission periods.

Materials and Methods: This retrospective cohort study used prospectively registered data and was approved by a local institutional review board. We enrolled 956 UIAs from 811 consecutive patients (mean age ± standard deviation, 57 ± 10.7 years; male:female = 247:564) from 2017 to 2020. We compared the outcomes after embolization among the different admission-length groups (1, 2, and ≥ 3 days). The outcomes included pre- and post-modified Rankin Scale (mRS) scores and rates of adverse events, cure, recurrence, and reprocedure. Events were defined as any cerebrovascular problems, including minor and major stroke, death, or hemorrhage.

Results: The mean admission period was 2 days, and 175 patients (191 aneurysms), 551 patients (664 aneurysms), and 85 patients (101 aneurysms) were discharged on the day of the procedure, day 2, and day 3 or later, respectively. During the mean 17-month follow-up period (range 6–53 months; 2757 patient years), no change in post-mRS was observed compared to pre-mRS in 99.6% of patients. Cure was achieved in 95.6% patients; minimal recurrence that did not require re-procedure occurred in 3.5% patients, and re-procedure was required in 2.3% (22 of 956) patients due to progressive enlargement of the recurrent sac during follow up (mean 17 months, range, 6–53 months). There were eight adverse events (0.8%), including five cerebrovascular (two major stroke, two minor strokes and one transient ischemic stroke), and three non-cerebrovascular events. Statistical comparison between groups with different admission lengths (1, 2, and ≥ 3 days) revealed no difference in the outcomes.

Conclusion: This study revealed no difference in outcomes and adverse events according to the admission period, and suggested that UIA could be managed by outpatient day-care embolization.

Keywords: *Intracranial aneurysm; Coil embolization; Outcome; Neurointervention; Outpatient management*

INTRODUCTION

Many patients with unruptured intracranial aneurysm (UIA), diagnosed with aneurysm upon routine checkup, fear the risk of rupture and describe aneurysm as a "ticking time bomb" although such terms should be avoided [1]. Therefore, the care provider traditionally takes up the responsibility of explaining the actual risk of rupture and taking legal protection against any unexpected risk of adverse events, if surgery is performed, until recovery after the treatment, as the risk of surgical clipping is relatively high [2].

Methods of neurointerventional and endovascular management have rapidly evolved, and the guidelines for the same, have changed significantly since the development of detachable coils in 1990 [3]. This change

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in the management of cerebral aneurysms has dramatically contributed to the improvement of outcomes. The anxiety of patients regarding the risk of treatment can be reduced if UIA can be managed by same day care treatment [4,5]. Therefore, we performed a retrospective single-center cohort study to evaluate the outcome of outpatient day-care management of UIA, and present the risk associated with such management, which may help reduce patients' anxiety and unnecessary fear by understanding recent outcome data.

MATERIALS AND METHODS

Patients

This retrospective cohort study used prospectively collected data and was approved by the Institutional Review Board (IRB No. 2021-1265). The requirement for written informed consent was waived. This study included 956 UIAs in 811 consecutive patients (mean age ± standard deviation, 57 ± 10.7 years; male:female = 247:564) treated between January 2017 and December 2020 at a tertiary referral center (Table 1). Among the enrolled patients, 705 (86.9%) had a single aneurysm and 106 (13.1%) had two or more aneurysms.

When selecting patients, we excluded those with ruptured aneurysms or pre-existing neurological deficits (modified Rankin Scale [mRS] ≥ 2) before treatment. Data on the demographic information and functional independence of the patients at initial hospital visits, which had been prospectively collected from the hospital database, were retrieved for analysis. The functional independence of patients was measured using the mRS [6,7].

We evaluated the age, sex, aneurysm size, multiplicity, and location according to the number of days of admission. The procedures were performed under general anesthesia for 902 aneurysms (94.4%), and sedative anesthesia for 54 aneurysms (5.6%). The procedural details have been described previously [4,5,8-14]. The femoral approach

Table 1. Summary of the Study Participants

Parameter	All	Subgroups according to Admission Period			*P*
		1 Day	2 Days	≥ 3 Days	
Per-patient statistic					
Number of patients	811	175	551	85	
Age, year	57 ± 10.7	57 ± 10.3	57 ± 10.5	57 ± 12.5	0.881
Male:female, female %	247:564 (69.5)	63:112 (64)	156:395 (71.7)	28:57 (67.1)	0.137
Multiplicity					< 0.001
No	705 (86.9)	169 (96.6)	464 (84.2)	72 (84.7)	
Yes*	106 (13.1)	6 (3.4)	87 (15.8)	13 (15.3)	
Per-aneurysm statistic					
Number of aneurysm	956	191	664	101	
Absolute size of aneurysm, mm		3.64 [3.06–4.95]	4.14 [3.26–5.50]	4.80 [3.28–6.46]	< 0.001
Size category of aneurysm, mm					< 0.001
< 10		188 (98.4)	645 (97.1)	86 (85.2)	
10–25		2 (1.1)	19 (2.9)	13 (12.9)	
≥ 25		1 (0.5)	0 (0.0)	2 (2.0)	
Multiplicity					< 0.001
No	716 (74.9)	173 (90.6)	468 (70.5)	75 (74.3)	
Yes†	240 (25.1)	18 (9.4)	196 (29.5)	26 (25.7)	
Aneurysm location					0.004
Anterior circulation	881 (92.2)	179 (93.7)	618 (93.1)	84 (83.2)	
Posterior circulation	75 (7.8)	12 (6.3)	46 (6.9)	17 (16.8)	
Procedure					0.001
Coiling	278 (29.1)	53 (27.7)	190 (28.6)	35 (34.7)	
Stent-assisted	502 (52.5)	83 (43.5)	370 (55.7)	49 (48.5)	
Others	176 (18.4)	55 (28.8)	104 (15.7)	17 (16.8)	

Data are mean ± standard deviation for age, median [interquartile range] for other continuous parameters, and number of patients or aneurysms with % in parenthesis. *Total number of patients with multiple aneurysms, †Total number of aneurysms in 106 patients with multiple aneurysms.

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(n = 954 aneurysms) was routinely used, while the radial approach (n = 2 aneurysms) was used in selected patients. Patients were observed for at least 3 hours after treatment. The decision to discharge was based on the patient's condition, diffusion-weighted magnetic resonance imaging (DWI), time-of-flight (TOF) angiographic findings, patient acceptance, and physician agreement. The length of admission refers to the number of days the patients stayed in the hospital for the procedure, and was counted as 1 day if the patient was discharged on the same day after the procedure. Table 1 shows the patients' basic characteristics according to the admission period.

The procedures were categorized into coiling, stent-assisted coiling, and others, which included balloon-assisted coiling, double microcatheter technique, and flow diverter. The Woven Endobridge device was not used because it was not available in our country [15]. AngioCalc software (available at. http://www.angiocalc.com) was used to calculate the packing density and the fraction of aneurysm space filled by the coil introduced into the aneurysm.

A cure was defined as the absence of a residual neck or sac on TOF magnetic resonance angiography (MRA) during follow-up. Minor recurrence was defined as the presence of neck remnants on follow-up MRA compared with MRA on day 1, which did not require a re-procedure. Major recurrence was defined as progressive enlargement of the residual or recurrent sac, which required a re-procedure (re-embolization).

Adverse events were defined as any cerebrovascular event (major/minor strokes, hemorrhage, or death) and any cerebrovascular or any other medical problem, as previously described [5,16,17]. Minor stroke was defined as a new, non-disabling neurological deficit or an increase in the National Institutes of Health Stroke Scale (NIHSS) score of 3, which was completely resolved within 30 days. Major stroke was defined as a new neurological deficit with an increase in the NIHSS score by 4 that persisted for longer than 30 days [17].

TOF MRA, including DWI, was routinely performed on the same or the day after the procedure; moreover, TOF MRA including T_2-weighted fluid attenuated inversion recovery images was performed as a follow-up imaging. The patients' clinical status after discharge was assessed using the mRS score at 1 or 3 months, 6 or 12 months, and every year thereafter. Recurrence of the treated aneurysm (neck remnant or compaction, or reappearance of the aneurysm sac) was based on follow-up MRA and was reported by neuroradiologists independent of the procedure. The decision to perform re-procedure in the case of recurrence was based on three-dimensional catheter angiographic imaging findings.

Statistical Analysis

The unit of analysis was an aneurysm; therefore, any patient-level parameters in those who had multiple aneurysms were included in the summary statistics multiple times. The outcome analysis included the comparison of pre- and post-mRS, adverse event rate, and re-procedure between subgroups divided by the admission period (1, 2, or ≥ 3 days). All continuous values, except for age, are summarized as the median [1st quartile; 3rd quartile]. Categorical variables were summarized as frequencies (percentages). The Kruskal–Wallis test was used to compare continuous data, and Pearson's chi-square test or Fisher's exact test was used to compare categorical data. All statistical analyses were performed using R version 3.3.3 (R Foundation for Statistical Computing). *p* values smaller than 0.05 were considered statistically significant.

RESULTS

Of the 956 treated UIAs, discharge occurred on the same day of the procedure for 191 aneurysms (20%), on day 2 for 664 aneurysms (69.5%), and after 3 or more days for 101 aneurysms (10.6%) (Table 1). The median admission period was 2 days. Statistical comparisons among the different admission day groups revealed differences in sex, size, multiplicity, location, procedures, packing density, and mean follow-up period (Tables 1, 2). The procedures performed included coiling (n = 278, 29.1%), stent-assisted coiling (n = 502, 52.5%), and others (n = 174, 18.2%). Others included balloon-assisted coiling (n = 76), double microcatheter technique (n = 36), and flow diverter (n = 35).

During the mean 17-month (range 6–53) follow-up period, no change in patient status was observed (mRS 0 → 0, 1 → 1) before and after the procedure in 99.6% of the patients. Cure was achieved in 94.2% patients; minor recurrence not requiring re-procedure occurred in 3.5% patients, and re-embolization due to progressive enlargement of the recurrent sac occurred in 2.3% (22/956) patients. The change in the mRS score was noted only in four patients (mRS 0 → 1 in 3, 0 → 2 in 1), and none of

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Table 2. Summary of Treatment Outcomes

Outcome	All (n = 956)	Subgroups according to Admission Period			*P*
		1 Day (n = 191)	2 Days (n = 664)	≥ 3 Days (n = 101)	
Packing density, %*	39.6	42.8	39.5	33.0	< 0.001
Pre- → post-mRS					
0 → 0	947 (99)	191 (20.1)	660 (69.3)	101 (10.6)	
0 → 1	3	0	3	0	
0 → 2	1	0	1	0	
1 → 1	5	1	1	3	
Follow-up, mean month (range)	17 (6–53)	12 (6–39)	17 (6–53)	24 (6–53)	< 0.001
Cure	901 (94.2)	180 (19.9)	630 (69.9)	91(10.2)	0.328
Recurrence	33 (3.5)	6 (18.2)	20 (60.6)	7 (21.2)	0.149
Re-procedure	22 (2.3)	5 (22.7)	14 (63.6)	3 (13.6)	0.699
Adverse event	8 (0.8)	1	4	3	0.086

Data are number of aneurysms with % in parenthesis, unless specified otherwise. The unit of the analysis was an aneurysm, and, therefore, any patient-level parameters in those who had multiple aneurysms were included in the summary statistics multiple times.
*Packing density, fraction of aneurysm space filled by of introduced coil into the aneurysm. mRS = modified Rankin Scale

the patients experienced any problems in relation to daily and social life.

Eight adverse events (0.8%) occurred during the mean 17-month follow-up, which corresponded to 2757 patient years. The eight events included five cerebrovascular and three non-cerebrovascular events. The five cerebrovascular events comprised two major strokes, two minor strokes, and one transient ischemic attack (TIA). One case of major stroke was related to an occipital hematoma that developed 4 days after the procedure, which was then evacuated leaving the patient with an mRS score of 2. Multifocal infarcts caused another major stroke, followed by focal hemorrhage in the parietal lobe, which was related to a mycotic pseudoaneurysm at the cortical branch of the middle cerebral artery and embolized with an mRS score of 1. A paradoxical embolism of a patent foramen ovale was suspected but not proven by an echocardiogram. A minor stroke was related to a localized basal ganglion infarction two weeks after the procedure, with an mRS score of 0. Another minor stroke was related to a localized internal capsule infarction one year after the procedure, with a final mRS score of 1. A TIA was related to a brief subjective symptoms of weakness, which revealed no acute lesion on the subsequent DWI. Neither subarachnoid hemorrhage nor death was recorded during the follow-up.

Three non-cerebrovascular events were observed: two femoral arteriovenous fistulae at the puncture site that required endovascular occlusion and a biopsy-proven high-grade glioma multiforme, which developed 1 year after aneurysm embolization, with an mRS score of 2.

DISCUSSION

The results of this study showed that the median admission period was 2 days, and 20% of the patients were discharged on the day of the procedure. Adverse events, including cerebrovascular events, occurred in only 1% of cases during the mean 17-months (range 6–53) follow-up period (2757 patient years). Cure was achieved in 95.6% of the patients; minor recurrence not requiring re-procedure occurred in 3.5% patients, and re-embolization due to progressive enlargement of the recurrent sac was performed in 2.3% of patients during follow-up. Although day-care management was initially provided to the study patients, the decision to discharge each patient could be delayed according to variable factors that were not evaluated in this study. Nevertheless, this study may support the possibility of day-care management of UIA, even though aneurysm management is known to carry a high risk and requires consideration of the patients' post-procedural condition, DWI and TOF angiographic findings, patient acceptance, and physician agreement.

Statistical comparison according to the number of admission days (≥ 1 day) revealed no significant differences. Although this study is based on a recent single-referral center experience in Korea, we nevertheless demonstrated that aneurysm embolization could be achieved via outpatient day-care management, and showed the possibility that cases could be managed in an outpatient clinic. To our knowledge, to date, few studies have investigated the issue of possible outpatient

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management for UIA [18]. The criteria to decide the length of the admission period may depend on post-procedural day one DWI and MRA, as well as patient status. The emotional status of the patient after the procedure may also need to be considered before deciding on early or late discharge. This study revealed a 95.6% cure rate, with an adverse event rate of 0.8%, with no difference according to the admission period, which can help reduce the anxiety of patients by recognizing the reality of the recent outcome data.

According to a meta-analysis of 60 studies including 9845 patients undergoing surgical repair for 10845 UIAs, the overall morbidity was 6.7%, with a mortality rate of 1.7% [19,20]. According to the obliteration rates reported for 2180 UIAs (20.1%), 91.8% were occluded, 3.9% had neck remnants, and 4.3% were incompletely occluded [19]. Data on hemorrhage after surgical repair of UIAs were available in nine publications, and 7.9% of all patients. During the average follow-up time of 1.2 years per patient, the hemorrhage incidence was 0.38%.

A meta-analysis of endovascular repair including 5771 UIAs in 5044 patients from 71 studies revealed that the percentage of treatment-related unfavorable outcomes was 4.8%, including death [21]. Acceptable outcomes with complete occlusion or neck remnant occlusion revealed in 86.1% of the UIAs. Recurrences were detected in 24.4% of 1316 patients with aneurysms during a follow-up of 0.4–3.2 years. The annual risk of hemorrhage was 0.2%, but these data were limited to follow-up periods of ≤ 6 months in most patients (76.7%). Furthermore, among patients with UIAs who underwent treatment with additional endovascular devices, unfavorable outcomes were reported in 7.1% of patients who underwent balloon-assisted coiling, 9.3% of patients with stent-assisted coiling, and 11.5% of patients with flow-diverting stents.

Compared with other studies, this study revealed better outcomes in cure, recurrence, re-procedure, and adverse event rate, and the final patient status was almost the same as the pre-treatment level (99.6%). The reason why our study revealed good results seems to be partly due to the constant management process during treatment driven by the same procedure team. If this procedure is generalized or randomized to any operator or team, the outcomes may differ from those of this study.

Aneurysm is a worrisome disease that is likened to a "ticking bomb," as it is associated with high morbidity and mortality rates [20]. Therefore, a variable degree of anxiety is commonly observed after diagnosis, depending on the emotional response of the physician who explains the risk to the patient and recommends treatment to relieve anxiety, especially in women [22]. Recent increases in health checkups in the Korean population has meant that more young people undergo brain MRA, which results in the detection of more aneurysms [2,23]. Once detected, patients often try to seek solutions to relieve their anxiety and fear, and sometimes urge the clinician to perform invasive catheter angiography to treat the aneurysm [22]. However, to the best of our knowledge, only a few studies have focused on the management of anxiety and fear in patients.

This study showed that endovascular treatment outcomes have been much improved since the advent of surgical clipping [24,25]. In this study, the adverse event rate of 1% without any mortality was so low that the UIA could be managed in an outpatient clinic. Furthermore, the finding indicating no change in the patient status (mRS 0 → 0, 1 → 1) before and after the procedure in 99.6% of the treated UIAs can further reduce the excessive anxiety and fear of patients before the management of UIA.

However, this study has several limitations. First, our data cannot be generalized because our study was not a randomized controlled study. Because an unexpected procedural risk of UIA still exists, especially depending on the operator's experience, it might be difficult to design such studies [26]. The recent increase in the rate of endovascular treatment for UIA may further prove the need for better treatment approaches for UIA in the near future. Second, a selection bias was present; this study may have tended to include patients with UIA with a less severe degree of risk, who were discharged early. However, the admission period cannot be determined based only on patient severity. Randomization of the admission period might be difficult as patients themselves tend to choose the treatment modality, and a significant amount of medical information is being provided via social network services. Third, long-term follow-up was not performed in our study. A lifelong follow-up of > 10 years may be necessary to confirm the effectiveness of the procedure. Fourth, we did not measure patient anxiety or satisfaction levels before and after treatment. Further studies may be required to estimate the benefit of outpatient day-care management of UIA regarding patient satisfaction or cost comparison.

In conclusion, our study showed that the management of UIA using an endovascular procedure presents a low risk,

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and suggested that UIA could be managed by outpatient day-care embolization.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Dae Chul Suh. Data curation: Yun Hyeok Choi, Sang Ik Park, Suyoung Yun, So Yeong Jeong, Soo Jeong, Boseong Kwon. Formal analysis: Dae Chul Suh, Yun Hyeok Choi. Funding acquisition: Dae Chul Suh. Investigation: Yunsun Song. Methodology: Dae Chul Suh. Project administration: Yun Hyeok Choi. Resources: Yun Hyeok Choi. Supervision: Dae Chul Suh. Validation: Dae Chul Suh. Visualization: Yun Hyeok Choi. Writing—original draft: Dae Chul Suh. Writing—review & editing: Dae Chul Suh, Yun Hyeok Choi.

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