Acta Neurochirurgica (2022) 164:781–793
https://doi.org/10.1007/s00701-022-05112-1

ORIGINAL ARTICLE - VASCULAR NEUROSURGERY - ANEURYSM

The role of microsurgery for poor-grade aneurysmal subarachnoid hemorrhages in the endovascular era

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Received: 3 November 2021 / Accepted: 31 December 2021

Abstract

Background Poor-grade aneurysmal subarachnoid hemorrhage (PGASAH) is associated with high mortality and morbidity regardless of treatment. Herein, we re-evaluate the safety and efficacy of microsurgical treatment for managing PGASAH patients in the current endovascular era.

Methods We retrospectively reviewed 141 consecutive patient records in a single institution who underwent microsurgical ($n=80$) or endovascular ($n=61$) treatment for PGASAH.

Results Baseline characteristics were similar, except for more intracerebral hematomas (46.3% vs 24.6%, $p=0.009$), fewer intraventricular hemorrhages (26.3% vs 59%, $p<0.001$), and fewer posterior circulation aneurysms (5.1% vs 44.3%, $p<0.001$) in the microsurgery group. Decompressive craniectomy (58.5% vs 24.6%, $p<0.001$) and shunt-dependent hydrocephalus (63.7% vs 41%, $p=0.01$) were more common for microsurgery, while procedural ischemic complications were less common (5% vs 24.6%, $p=0.001$). Both early (12.5% vs 32.8%, $p=0.006$) and late mortality rates (22.5% vs 39.3%, $p=0.041$) were lower for microsurgery, and favorable 12-month outcomes (modified Rankin scale = 0–2) were better (62.5% vs 42.6%, $p=0.026$). Multivariate analysis revealed that advanced age, neurological grade, modified Fisher grade, larger aneurysm size, rebleeding, and cerebral infarctions were independent predictors of poor outcome. Microsurgery fared marginally better than endovascular treatment (OR: 2.630, 95% CI: [0.991–6.981], $p=0.052$).

Conclusions Timely and efficient treatment, either via open microsurgery or endovascular surgery, provided favorable outcomes for over half of PGASAH patients in this series. Therefore, early treatment should be offered to all PGASAH patients regardless of clinical and/or radiological factors. Microsurgery remains an effective treatment modality for selected PGASAH patients in the endovascular era.

Keywords Poor grade · Aneurysm · Subarachnoid hemorrhage · Surgery · Clipping · Endovascular

Abbreviations

ACA	Anterior cerebral artery
AcomA	Anterior communicating artery
aSAH	Aneurysmal subarachnoid aneurysmal hemorrhage
BA	Basilar artery
BBA	Blood blister–like aneurysm
CSF	Cerebrospinal fluid
CT	Computed tomography
CTA	Computed tomography angiography
CVS	Cardiovascular system
DSA	Digital subtraction angiography
DVT	Deep venous thrombosis
HH	Hunt and Hess
ICA	Internal carotid artery
ICH	Intracerebral hemorrhage
ICU	Intensive care unit
ISAT	International subarachnoid aneurysm trial
ISAT	International subarachnoid aneurysm trial
IVH	Intraventricular hemorrhage
MCA	Middle cerebral artery
mRS	Modified Rankin scale
PcomA	Posterior communicating artery

This article is part of the Topical Collection on Vascular Neurosurgery – Aneurysm

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PE	Pulmonary embolism
PGASAH	Poor-grade aneurysmal subarachnoid hemorrhage
PICA	Posterior inferior cerebellar artery
RA	Ruptured aneurysm
RR	Raymond-Roy
SAFIRE	Size of the aneurysm, Age, FIsher grade, REsuscitation
VPS	Ventriculo-peritoneal shunt
WFNS	World Federation of Neurological Surgeons

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating disease associated with poor outcomes and enormous socioeconomic burden [5, 6, 11, 24, 29, 32]. The neurological grade at admission is the most important determinant for outcomes for aSAH. Poor-grade aneurysmal subarachnoid hemorrhage (PGASAH), defined as Hunt and Hess (HH) or World Federation of Neurological Surgeons (WFNS) grades IV and V aSAH, accounts for 20–30% of all aSAH, and is associated with high mortality rates and poor outcomes [15, 19, 21]. Without definitive treatment, virtually all PGASAH patients will die from aSAH. Because of this devastating natural history, neurosurgeons have historically avoided definitive treatment of PGASAH patients unless they improved to better grades [9, 31, 47], which led to conservative or delayed treatment, with surgical treatment only occurring in selected cases [9, 12]. However, several recent studies have demonstrated significantly improved outcomes by early securing of the ruptured aneurysm (RA) coupled with aggressive critical care, in comparison to delayed or conservative treatment [9, 10, 15, 21, 36, 45].

Following the International Subarachnoid Aneurysm Trial (ISAT) comparing neurosurgical clipping to endovascular coiling, microsurgery gradually lost its wide use for the management of RAs [22, 23]. However, PGASAH patients comprised less than 5% of the ISAT cohort; thus, any advantage for endovascular treatment may not have been adequately evaluated for these patients. Furthermore, recent meta-analyses have reported comparable outcomes for clipping and coiling in PGASAH treatment [16, 20, 35, 43]. Our study objective was to describe the outcomes for PGASAH patients who were treated with microsurgery or endovascular surgery, in a contemporary single-center clinical series.

Methods and materials

Study population

This study was approved by our Institutional Review Board. Patient consent was not sought due to the retrospective nature of the study.

The patient population for surgically treated PGASAH patients ($n = 80$) was obtained from a record review of all consecutively treated patients with RAs operated on by the senior author from 2006 to 2019. These were compared to patients derived from a record review of all consecutive endovascularly treated PGASAH patients ($n = 61$) in the same institution, where approximately 100 aSAH patients are treated annually by 3 neurovascular and 3 endovascular surgeons. All PGASAH patients (and their families) were counseled on surgical and endovascular treatment options by the admitting physician. Patients who met the criteria for brain dead at admission, or whose families declined treatment, were excluded (16 patients). Subarachnoid hemorrhage was confirmed in all patients by computed tomography (CT) at admission and was graded according to both Fisher and modified Fisher scales. Aneurysm characteristics were identified and assessed with digital subtraction angiography (DSA) and/or CT angiography (CTA) in all patients. All clinical and radiological data were independently assessed blind by three neurosurgeons who were not involved with treatment.

Surgery and clinical management

All patients were managed according to a standardized protocol of immediate admission to the neurosurgical intensive care unit (ICU), aggressive resuscitation, early CTA and/or DSA, ventriculostomy placement, and intracranial pressure management with decompressive craniectomy performed, if necessary. This was followed by rapid definitive treatment of the RA via microsurgical clipping or endovascular coiling within 24 h of aSAH, whenever possible. Patients were monitored for delayed cerebral ischemia by frequent clinical examination, transcranial Doppler, and CT perfusion. Cerebral vasospasm prophylaxis consisted of oral nimodipine administration and active maintenance of central venous pressure > 5 mmHg. Those developing clinical vasospasm were treated with intra-arterial verapamil injection with/without angioplasty, and triple-H therapy (induced hypertension, hypervolemia, and hemodilution). Patients with persistent hydrocephalus underwent ventriculo-peritoneal shunt (VPS) insertion.

For the microsurgery group, maximally safe and minimally disruptive surgical techniques included wide arachnoid dissection with cleaning of subarachnoid blood, minimal or no brain retraction, the use of skull base approaches where excessive brain retraction was anticipated, and evacuation of intracerebral and/or intraventricular hemorrhages (ICH and IVH) by ventricular opening. For the endovascular group, primary or balloon-assisted coiling was the standard strategy, unless there were compelling reasons for other treatments such as flow diverter placement, stent-assisted coiling, or parent vessel occlusion.

Data collection

Patient history was obtained from electronic data records for microsurgical and endovascular-treated patients (Table 1). This also included radiological characteristics quantified using Hunt-Hess (HH), World Federation of Neurological Societies (WFNS), Fisher and modified Fisher grading, and the presence of intracerebral hemorrhage (ICH) and/or intraventricular hemorrhage (IVH), categorized as all (any IVH including sediment in occipital horns) and extensive (considerable blood in ventricles). Table 2 provides aneurysm features including location (anterior or posterior circulation), which artery, aneurysm size, and numbers of multiple aneurysms. Table 3 summarizes surgical management, including timing, treatment, aSAH procedural and medical complications, outcomes, and follow-up duration. Figure 1 shows neurological outcomes using the modified Rankin scale (mRS).

Table 1 Baseline demographic, clinical, and radiological characteristics of the patients with poor-grade aneurysmal subarachnoid hemorrhage: number (%), if not otherwise indicated

	Microsurgery	Endovascular	Total	*P* value
Number of patients	80 (56.7)	61 (43.3)	141 (100)	
Age				
Mean ± SD	54.9 ± 14.1	56.3 ± 11.3	55.5 ± 12.9	0.509
Median (range)	57 (10–84)	57 (21–78)	57 (10–84)	
Sex				
Male	25 (31.3)	20 (32.8)	45 (31.9)	0.857
Female	55 (68.8)	41 (67.2)	96 (68.1)	
Comorbidities				
Smoking	43 (53.8)	31 (50.8)	74 (52.5)	0.737
Hypertension	36 (45)	33 (54.1)	69 (48.9)	0.311
Diabetes	7 (8.8)	6 (9.8)	13 (9.2)	1.00
Hyperlipidemia	20 (25)	10 (16.4)	30 (21.3)	0.299
Other CVS diseases	11 (13.8)	6 (9.8)	17 (12.1)	0.605
Pulmonary diseases	13 (16.3)	2 (3.3)	15 (10.6)	0.014
Hunt-Hess grade				
Grade IV	54 (67.5)	35 (57.4)	89 (63.1)	0.224
Grade V	26 (32.5)	26 (42.6)	52 (36.9)	
WFNS grade				
Grade IV*	44 (55)	31 (50.8)	75 (53.2)	0.504
Grade V	36 (45)	30 (49.2)	66 (46.8)	
Fisher grade				
Grade 2	1 (1.3)	0 (0)	1 (0.7)	0.338
Grade 3	35 (43.8)	21 (34.4)	56 (39.7)	
Grade 4	44 (55)	40 (65.6)	84 (59.6)	
Modified Fisher grade				
Grade 1	1 (1.3)	1 (1.6)	2 (1.4)	
Grade 2	3 (3.8)	2 (3.3)	5 (3.5)	
Grade 3	56 (70)	24 (39.3)	80 (56.7)	0.002
Grade 4	20 (25)	34 (55.7)	54 (38.3)	
Intraventricular hemorrhage (IVH)**				
All	51 (63.7)	52 (85.2)	103 (73)	0.007
Extensive	21 (26.3)	36 (59)	57 (40.4)	< 0.001
Intracerebral hemorrhage (ICH)	37 (46.3)	15 (24.6)	52 (36.9)	0.009

*One patient from each group had WFNS grade lower than 4

**IVH “All” indicates any IVH including sediment in occipital horns. “Extensive” indicates considerable blood in ventricles

CVS cardiovascular system, *ICH* intracerebral hematoma, *IVH* intraventricular hemorrhage

Table 2 Aneurysm features of the patients with aneurysmal subarachnoid hemorrhage: number (%)

	Microsurgery ($n=80$)	Endovascular ($n=61$)	Total ($n=141$)	*P* value
Aneurysm location				
Anterior circulation	75 (94.9)	34 (55.7)	109 (77.9)	< 0.001
Posterior circulation	4 (5.1)	27 (44.3)	31 (22.1)	
AcomA	27 (33.8)	14 (23)	41 (29.1)	< 0.001
MCA	23 (28.8)	4 (6.6)	27 (19.1)	
PcomA	11 (13.8)	4 (6.6)	15 (10.6)	
ICA*	12 (15)	10 (16.4)	22 (15.6)	
ACA	3 (3.8)	3 (4.9)	6 (4.3)	
BA	1 (1.3)	12 (19.7)	13 (9.2)	
PICA	2 (2.5)	6 (9.8)	8 (5.7)	
Other post circulation	1 (1.3)	8 (13.1)	9 (6.4)	
Aneurysm size				
< 7 mm	47 (58.8)	33 (54.1)	80 (56.7)	0.583
7–12 mm	19 (23.8)	19 (31.1)	38 (27)	
13–24 mm	10 (12.5)	8 (13.1)	18 (12.8)	
≥ 25 mm	4 (5)	1 (1.6)	5 (3.5)	
Blood blister–like aneurysms	9 (11.3)	5 (8.2)	14 (9.9)	0.548
Multiple aneurysms	13 (16.3)	12 (19.7)	25 (17.7)	0.659

*Excluding PcomA aneurysms

ACA anterior cerebral artery, *AcomA* anterior communicating artery, *ICA* internal carotid artery, *MCA* middle cerebral artery, *PcomA* posterior communicating artery, *BA* basilar artery, *PICA* posterior inferior cerebellar artery

Chi-square tests were used to test differences in categorical variables

Outcome measures

Functional outcomes were evaluated with the mRS (scores from 0 to 6) at discharge, at 3, 6, and 12 months, and at the last follow-up visit, by two independent neurosurgeons who were not involved in the care of these patients using electronic health records. The outcome was then dichotomized into good, defined as functionally independent (mRS 0–2), and poor, defined as disabled or dead (mRS 3–6). Early mortality was assessed as death within 30 days of the aSAH.

Statistical analysis

Statistical analyses were performed using SPSS, version 22.0 (IBM, New York). Data are presented as mean ± standard deviation for parametric, median (range) for non-parametric continuous, and percentage for categorical variables. Kaplan–Meier survival analysis was performed for mortality assessment. Student's *t*-test was used for continuous, and chi-square and Fisher's exact tests were used for categorical variables, to compare between two groups. Logistic regression was performed to test the effect of potential predictors of outcome. All factors with *p* value < 0.1 in the univariate analysis, but omitting those with a high degree of inter-correlation, were incorporated into the multivariate model. A *p* value < 0.05 was considered statistically significant.

Results

Demographic and clinical characteristics

Baseline demographic, clinical, and radiological characteristics of the patients are summarized in Table 1. The mean age was 55.5 ± 12.9 years (range 10–84 years) in the overall study cohort, with no difference between the two treatment groups ($p=0.509$). The female-to-male ratio of 2.1 was also similar between the two groups ($p=0.857$). Smoking, hypertension, and other medical comorbidities were all similar between the two groups (Table 1), except for pulmonary diseases (e.g., COPD, asthma) being more frequent in the surgical group.

Neurologic grading at admission

At admission, 36.9% of patients were HH grade V, whereas WFNS grading showed slightly more grade V (46.8%). There were no statistically significant differences between the surgical and endovascular treatment group's

Table 3 Details of surgical management, complications, and hospital course: number (%), mean ± SD

	Microsurgery (*n* = 80)	Endovascular (*n* = 61)	Total (*n* = 141)	*P* value
Timing of surgery				
< 24 h	61 (76.3)	51 (83.6)	112 (79.4)	0.303
24–72 h	6 (7.5)	7 (11.5)	13 (9.2)	
> 72 h	13 (16.3)	3 (4.9)	16 (11.3)	
Bypass & trapping	10 (12.5)	N/A	10 (7.1)	N/A
Decompressive craniectomy	47 (58.8)	15 (24.6)	62 (44)	< 0.001
SAH complications				
Rebleeding	8 (10)	8 (13.1)	16 (11.3)	0.600
Shunt-dependent hydrocephalus	51 (63.7)	25 (41)	76 (53.9)	0.010
Vasospasm	47 (58.8)	45 (73.8)	92 (65.2)	0.075
All infarcts*	43 (53.8)	26 (42.6)	69 (48.9)	0.234
New ischemic infarcts**	26 (32.5)	23 (37.7)	49 (34.8)	0.593
Procedural complications	14 (17.5)	20 (32.8)	34 (24.1)	0.047
Hemorrhagic	9 (11.3)	5 (8.2)	14 (9.9)	0.586
Ischemic	4 (5)	15 (24.6)	19 (13.5)	0.001
Other	1 (1.2)	0 (0)	1 (0)	N/A
Medical complications	29 (36.3)	15 (24.6)	44 (31.2)	0.148
Infection†	18 (22.5)	12 (19.7)	30 (21.3)	0.836
DVT/PE	11 (13.8)	3 (4.9)	14 (9.9)	0.096
Early mortality (≤ 30 days)	10 (12.5)	20 (32.8)	30 (21.3)	0.006
Mortality at 12 months	18 (22.5)	24 (39.3)	42 (29.8)	0.041
Good outcome at 12 months	50 (62.5)	26 (42.6)	76 (53.9)	0.026
Follow-up duration (months)	93.9 ± 52.3	73.3 ± 47.3	86.1 ± 51.8	0.045

*Including baseline hemorrhagic or ischemic infarcts

**Any ischemic infarcts (i.e., CT hypodensity) that occurred after admission, due to surgery, vasospasm, or thromboembolism

†Pneumonia, sepsis, meningitis/ventriculitis, etc.

CSF cerebrospinal fluid, *DVT* deep venous thrombosis, *PE* pulmonary embolism

T-tests for independent samples were performed to test differences in means. Chi-square tests were used to test differences in categorical variables

neurological grading at admission, measured using either HH grade V ($p = 0.22$) or WFNS grade V ($p = 0.504$) (Table 1). Ten patients (7.1%) neurologically improved (downgraded) after ventriculostomy, while five patients (3.5%) upgraded to grade V due to multiple bleeds in the preoperative period.

Radiological grading at admission

Intraventricular (all 73%, extensive 40.4%) and intracerebral (36.9%) hemorrhage were frequent (Table 1). All patients but one (99.3%) had either Fisher grade 3 hemorrhage (39.7%) or grade 4 (59.6%) hemorrhage with no difference in grades between the groups (Table 1). However, modified Fisher grade showed a different distribution between two groups: the microsurgery group had more modified Fisher grade 3 (70% vs 39.3%), while the endovascular group had more modified Fisher grade 4 (55.7% vs 25%) hemorrhages on admission CT scans ($p = 0.002$). In line with the modified Fisher scale, ICH (46.3% vs 24.6%, $p = 0.009$) and IVH (all IVH: 85.2% vs 63.7%, extensive IVH: 59% vs 26.3%, $p < 0.001$) were more frequent in the microsurgery and endovascular groups, respectively.

Aneurysm characteristics

Aneurysm characteristics are summarized in Table 2. The distribution of aneurysm locations differed significantly between the groups ($p < 0.001$). Most posterior circulation aneurysms underwent endovascular treatment whereas the microsurgery group mainly consisted of anterior circulation aneurysms. Small aneurysms (< 7 mm) comprised 56.7% of all RAs. No differences in aneurysm size were detected between the groups. Blood blister–like aneurysms (BBAs) were noted in 9.9% of the cases, with no significant differences between the groups. The presence of multiple aneurysms was also similar between the two groups ($p = 0.659$).

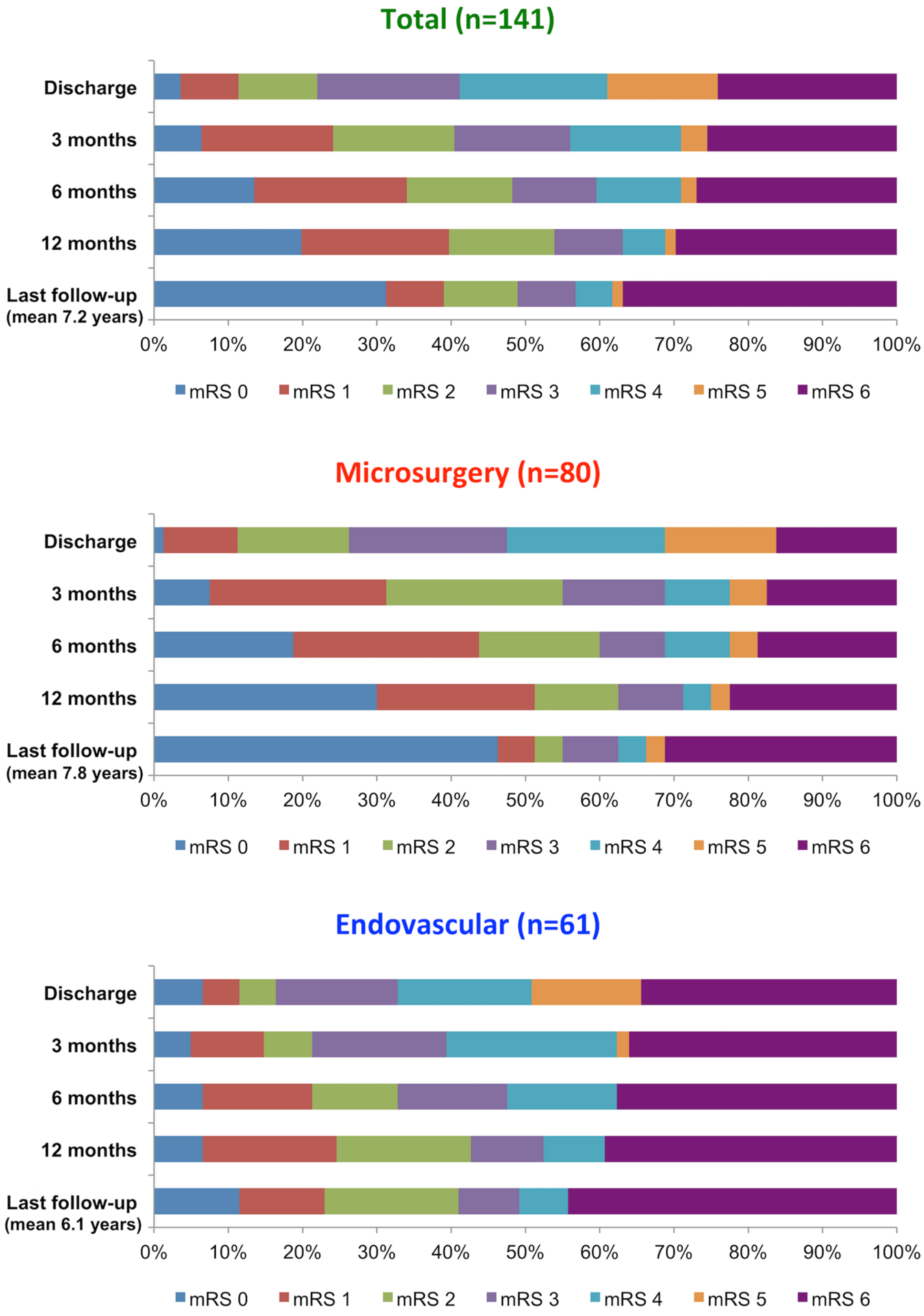

Fig. 1 Poor outcome aneurysmal subarachnoid hemorrhage patient outcomes: modified Rankin scale (mRS) at discharge, and at 3, 6, 12 months, and last follow-up. mRS 0 = no symptoms, mRS 1 = no disability but symptoms, mRS 2 = slight disability, mRS 3 = moderate disability, mRS 4 = moderate severe disability, mRS 5 = severe disability, mRS 6 = death

Surgical and endovascular management

Most aneurysms (79.4%) were treated within 24 h after aSAH onset, with no significant difference between treatment modalities ($p = 0.303$) (Table 3). Patients prepared for bypass surgery, and those clinically unstable at early periods (11.3% overall; 16.9% in microsurgery, 4.9% in endovascular), underwent treatment delayed by 72 h or more post-SAH (median: 15 days). Bypass surgery was performed in 10 patients (12.5%) for aneurysms that were not amenable to clipping or coiling, comprising five BBA, four giant/complex, and one mycotic aneurysm. Endovascular treatments included 43 treated with primary coiling, nine with balloon- or stent-assisted coiling, two with pipeline embolization, and seven with parent vessel occlusion.

There were more crossovers to surgery than the other way around (7 to surgery, 2 to endovascular). Three underwent microsurgery for complete aneurysm obliteration after initial coiling attempts were unsuccessful or when coil packing density was deemed insufficient. In another patient, the ruptured aneurysm was first coiled, but then re-ruptured and was subsequently clipped. Three other patients had bypass and trapping following unsuccessful endovascular treatment attempts. In contrast, one patient had a failed microsurgical attempt and subsequently underwent endovascular treatment, while another microsurgical patient who received aneurysm clipping in the acute period later underwent coiling for early recurrence two weeks later.

A high angiographic complete obliteration rate of 97.5% was achieved with microsurgery. With endovascular treatments, the Raymond-Roy (RR) obliteration rates were as follows: RR class I: 49.2%; RR class II: 21.3%; RR class III: 29.5%.

Decompressive craniectomy with or without hematoma evacuation was carried out in 64 patients (44%), with significantly more of these microsurgical patients ($p < 0.001$) (Table 3). Patients who survived after craniectomy (59.7%) had cranioplasty 0.5–10 months (median 1.5) after their initial surgery.

Complications

Subarachnoid hemorrhage complications

Complications due to aSAH are summarized in Table 3. The most common complication was vasospasm, followed by shunt-dependent hydrocephalus, infarcts, and rebleeding (Table 3). There were no significant differences between groups for vasospasm, infarcts, and shunt-dependent hydrocephalus complications, although more microsurgery-treated patients underwent VPS insertion ($p = 0.01$). Rebleeding occurred in 11.3% of the study cohort, mostly before treatment, with no significant difference between the groups. One patient with a BBA initially had his ruptured aneurysm coiled with stenting, which then rebled a few hours later and treated with bypass surgery. For all cases, rebleeding was associated with neurological deterioration and/or mortality.

Surgical complications

Surgical or procedural-related complications were observed in 24.1% of the patients and were more common in the endovascular group ($p = 0.047$) (Table 3). Ischemic complications were significantly more common in the endovascular group ($p = 0.001$), with more than one-third of ischemic complications in this group resulting in major strokes. Hemorrhagic complications were similar between the groups, with most being either subdural or epidural hematomas in the surgery group. Three patients (two microsurgery, one endovascular) had surgical complications following cranioplasty procedures, of the 37 patients (26.2%) that underwent cranioplasty.

Medical complications

Many PGASAH patients (31.2%) had medical complications during hospitalization, although the rates of medical complications were similar for the two groups (Table 3). These included pneumonia and sepsis infections, followed by deep vein thrombosis and pulmonary embolism.

Clinical outcomes

Hospital stay and early mortality

On average, PGASAH patients spent nearly 1 month in the hospital, with a mean stay slightly but not significantly longer for microsurgery patients ($p = 0.06$). Overall, the early (30-day) mortality rate was 21.3%, which was significantly greater for endovascular-treated patients ($p = 0.006$) (Table 3). Hunt-Hess grade IV patients had a significantly lower early mortality rate than HH grade V patients in the overall cohort (10.1% vs 40.4%, $p < 0.001$), as well as in the separate microsurgical (7.4% vs 23.1%, $p = 0.047$) and endovascular (14.3% vs 57.7%, $p = 0.001$) groups.

Neurological outcome

No patients were lost to follow-up. At discharge, 24.1% of patients had died, with endovascularly treated patients having a greater death rate than those surgically treated at < 30 days ($p = 0.017$). Only 22% of all patients had good neurological outcomes (mRS 0–2) at discharge, with no difference between groups (Table 3). However, while 12-month mortality slightly increased in comparison to mortality at discharge, good outcomes dramatically increased to 53.9% overall, with surgically treated patients having significantly better outcomes ($p = 0.026$) (Table 3, Fig. 1). At the last follow-up (mean 7.2 ± 4.3 years), 48.9% of patients were functionally independent (defined here as mRS 0–2), 14.2% had moderate to severe disability (mRS 3–5), and 36.9% had died (mRS 6) (Fig. 1). Hunt-Hess grade IV patients had significantly better 12-month functional independence rates than HH grade V patients in the overall cohort (68.5% vs 28.8%, $p < 0.001$), as well as in both the microsurgical (75.9% vs 34.6%, $p < 0.001$) and endovascular (57.1% vs 23.1%, $p = 0.008$) groups. Kaplan–Meier survival curves for HH admission grades and treatment modalities are shown in Fig. 2.

Predictors of outcome

Using logistic regression ($p < 0.05$), determinants of early mortality included age > 65 years, HH grade V, modified Fisher

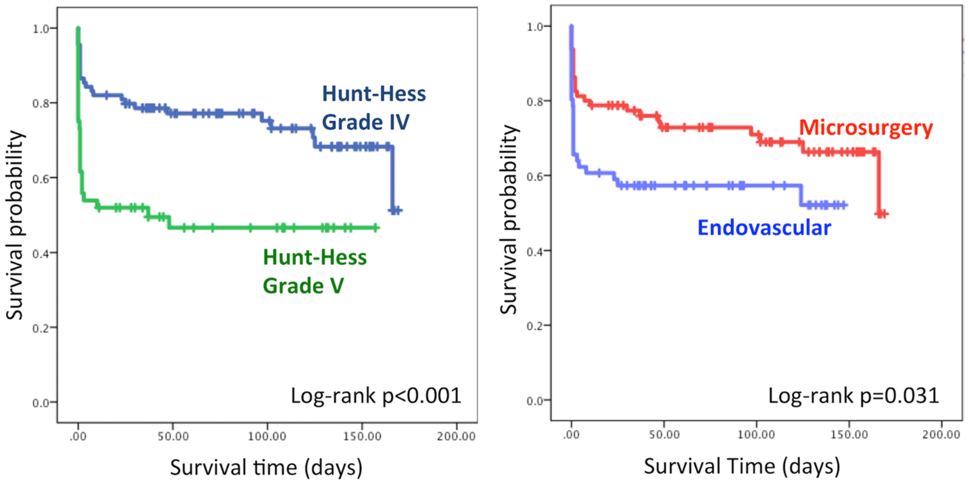

Fig. 2 Comparative Kaplan–Meier survival times (days) for poor outcome aneurysmal subarachnoid hemorrhage patients. **a** Survival compared for neurological grades for combined surgical and endovascular groups. **b** Survival compared for microsurgical versus endovascular treatment

grade IV, presence of IVH, rebleeding, treatment modality (endovascular vs microsurgery), procedural complications, and new ischemic cerebral infarctions (Table 4). Independent predictors of early mortality in multiple linear regression included age > 65 years ($p = 0.012$), HH grade V ($p = 0.018$), modified Fisher grade IV ($p = 0.029$), rebleeding ($p = 0.004$), and procedural complications ($p = 0.002$). Outcome predictors at 12 months were age, neurological grade, radiological grade (both Fisher and modified Fisher grades), presence of IVH, aneurysm size, rebleeding, treatment modality, procedural ischemic complications, and vasospasm; all and new ischemic cerebral infarctions were predictive ($p < 0.05$), as determined with univariate logistic regression. Within the microsurgery group, bypass surgery was associated with a heightened risk of preoperative rebleeding compared to the non-bypass (i.e., only clipping) subgroup (30% vs 7.1%, $p = 0.024$); however, bypass surgery was not linked to significantly worse clinical outcomes at any assessed time points (e.g., good outcomes at 12 months: 50% vs 64%, $p = 0.489$). Multivariate analysis also showed that advanced age, HH and modified Fisher grade, larger aneurysm size (> 7 mm), rebleeding, and cerebral infarction (at any time point) were independent predictors of poor outcome at 12 months. Although only marginally significant, microsurgically treated patients fared better than endovascular treatment in this multivariate analysis (OR: 2.630, 95% CI: [0.991–6.981], $p = 0.052$) (Table 4).

Discussion

In this single-center retrospective cohort study, we have shown that early microsurgical or endovascular treatment yields good neurological outcomes in more than half of the patients with PGASAH. Baseline differences in aneurysm characteristics and radiological findings precluded a direct comparison between these two surgical modalities. After controlling all the possible confounders, microsurgery was at least comparable, if not superior, to endovascular treatment in the current series. Multivariate analysis demonstrated that advanced age, neurological grade, modified Fisher grade, larger aneurysm size (> 7 mm), rebleeding, and cerebral infarction (at any time point) were independent predictors of poor outcome at 12 months after PGASAH.

Early treatment of ruptured aneurysm

In the present study, we show that early microsurgical treatment coupled with aggressive ICU management led to functional independence for up to 62.5% of PGASAH patients (vs 42.6% in the endovascular group), representing one of the highest proportions in the contemporary literature examining both surgical and endovascular treatment [43]. The present study confirms these previous findings, while also raising expectations for surgical PGASAH treatment.

While, historically, delaying surgery until the patient improves to better grades was the general strategy for PGASAH [9, 44], selective early surgery was adopted in the 1990s due to higher rebleeding rates in the early post-aSAH period. Various authors have reported improved outcomes with early surgery of selected PGASAH patients since then [14, 19, 27, 33, 42]. In recent decades, outcome improvements to 30–50% favorable have been reported after early securing of the RA with either clipping or coiling, combined with aggressive ICU management in all PGASAH patients [13, 15, 19, 21, 33, 37, 38, 43, 45].

Our institutional management strategy for PGASAH was similar to those authors; early surgery or endovascular treatment combined with aggressive medical treatment, but without a selective strategy. Almost 80% of patients in our series underwent aneurysm treatment within 24 h of aSAH. Delayed surgery primarily occurred in our series with patients requiring bypasses. Early closure of ruptured aneurysms not only prevented rebleeding, but also

Table 4 Univariate and multivariate analyses of potential predictors for poor outcomes at 12 months in poor-grade aneurysmal subarachnoid hemorrhage patients

	Univariate			Multivariate		
Variable	OR	95% CI	P-value	OR	95% CI	P-value
Preoperative factors						
Demographics						
Sex	0.762	0.373-1.556	0.455			
Age (continuous)	1.036	1.007-1.065	**0.014**	1.063	1.022-1.107	**0.003**
Age (>65 years)	1.867	0.867-4.020	0.111			
Medical history						
Smoking	0.739	0.381-1.437	0.373			
Hypertension	1.527	0.785-2.971	0.212			
Hyperlipidemia	1.394	0.621-3.131	0.421			
CVD	1.011	0.366-2.793	0.982			
DM	0.473	0.139-1.615	0.232			
Pulmonary disease	0.533	0.172-1.648	0.274			
Clinical grading						
Hunt Hess grade (V vs IV)	5.913	2.769-12.628	**<0.001**	4.030	1.485-10.940	**0.006**
WFNS (V vs IV)	4.176	2.088-8.354	**<0.001**			
Radiological grading						
Fisher grade	2.266	1.148-4.473	**0.018**			
Modified Fisher grade	2.041	1.156-3.605	**0.014**	2.105	1.003-4.415	**0.049**
IVH (all)	2.388	1.088-5.239	**0.030**			
IVH (large)	2.720	1.360-5.441	**0.005**			
ICH	1.084	0.546-2.151	0.818			
Aneurysm characteristics						
Location	1.120	0.965-1.299	0.136			
Location (anterior vs. posterior circulation)	1.512	0.678-3.368	0.312			
Multiplicity	0.714	0.297-1.721	0.453			
Size (>7 mm)	2.884	1.449-5.740	**0.003**	3.742	1.446-9.685	**0.007**
Blood-blister like	1.586	0.520-4.835	0.417			
Rebleeding	21.765	2.787-169.986	**0.003**	38.219	3.917-372.901	**0.002**
Operative factors						
Modality (endovascular vs microsurgery)	2.400	1.213-4.747	**0.012**	2.630	0.991-6.981	0.052
Ultra-early treatment	1.106	0.487-2.511	0.810			
Early treatment	1.538	0.527-4.491	0.431			
Bypass surgery	0.677	0.245-1.866	0.450			
Craniectomy	1.586	0.812-3.100	0.177			
Procedural complications (all)	1.617	0.743-3.518	0.226			
Procedural complications (hemorrhagic)	0.838	0.275-2.552	0.755			

Table 4 (continued)

Variable	Univariate OR	Univariate 95% CI	Univariate P-value	Multivariate OR	Multivariate 95% CI	Multivariate P-value
Procedural complications (ischemic)	2.821	1.006-7.913	**0.049**			
Postoperative factors						
VP Shunt	0.663	0.340-1.291	0.227			
Vasospasm	2.455	1.190-5.067	**0.015**			
All infarcts*	2.966	1.492-5.896	**0.002**	8.164	2.870-23.229	**<0.001**
New ischemic infarcts**	2.774	1.364-5.641	**0.005**			
Medical complications	1.205	0.590-2.459	0.609			
DVT/PE	1.586	0.520-4.835	0.417			
Infection	0.993	0.442-2.228	0.986			
Hospital stay	0.998	0.980-1.106	0.813			

DVT deep venous thrombosis, *ICH* intracerebral hematoma, *IVH* intraventricular hemorrhage, *PE* pulmonary embolism, *WFNS* World Federation of Neurological Surgeons

*Including baseline hemorrhagic or ischemic infarcts

**Any ischemic infarcts (i.e., CT hypodensity) that occurred after admission, due to surgery, vasospasm, or thromboembolism. The following factors were included in the multivariate analysis: age (continuous), Hunt-Hess grade, modified Fisher grade, size, rebleeding, modality (endo vs surgery), procedural complications (ischemic), and all infarcts

Bold text indicates statistically significance with a *p*-value less than 0.05

allowed aggressive management of vasospasm and other complications.

Microsurgery vs endovascular treatment

The ISAT marked the beginning of the endovascular era for the management of RAs [22, 23]. Since then, treatment trends for RAs have moved significantly towards endovascular coiling [1, 28]. However, overall survival with endovascular treatment cannot be extrapolated to PGASAH patients, who comprised less than 5% of the ISAT cohort. Indeed, two meta-analyses [20, 43] and the adjusted results of a multicenter, prospective, non-randomized study [45] showed that treatment modality was not a significant prognostic factor among PGASAH patients. Indeed, the present single-center cohort outcome data shows that surgery is certainly not inferior; in fact, it appears to be at least as effective as an endovascular treatment of PGASAH. This observation remained marginally significant even after controlling for other confounders in the multivariate model. Thus, we believe that microsurgery and endovascular treatments should not be seen as alternative or competing techniques, but rather as complementary and cooperative. Therefore, surgery should be offered as an effective and viable strategy, either standalone or in combination with endovascular management for PGASAH treatment, particularly in high-volume, experienced centers that have the necessary surgical capabilities.

In a surgical versus endovascular study similar to ours, Chua et al. [3] reported that the outcomes for PGASAH significantly improved from 25.6 to 46.8% for surgical treatment, and from 18.8 to 42.5% for endovascular treatment, in a single center from 1998–2003 to 2007–2013. These authors argued that progress in ICU care, aggressive management of complications, and better patient selection for surgery versus endovascular therapy may underlie this improvement [3]. Our findings lend support to these arguments. In addition, we believe that advances in surgical techniques and technologies, as well as rigorous surgical training and experience through specialization, are also important factors contributing to the incremental improvements observed in several recently published surgical series [33, 38, 45, 46].

Justification of aggressive treatment

Whether an aggressive approach for PGASAH patients is justified has been debated for decades. Many suggest that this would increase the risk of surgical complications, lead to many survivors in poor condition, and consume an inordinate level of resources. However, Le Roux et al. [18] showed that PGASAH patients demonstrate a similar risk of surgical complications such as intraoperative aneurysm rupture and failure to secure the aneurysm or cerebral contusion, in comparison to good-grade patients; and that the proportion of chronically disabled patients was comparable for aggressive and less-aggressive management. Finally, although the average treatment costs for grade IV were the greatest for grades I–IV, the treatment cost for grade V patients was actually comparable to grade II, perhaps due to premature mortality. Indeed, a significant subset of PGASAH patients benefited from aggressive treatment, and although this management is expensive, it was reported to be cost-effective overall [40]. In the present report, we found that the rates of both functional independence and death increased with time, while the proportion of patients with significant disability decreased simultaneously (Fig. 1). Most patients with mRS 3–5 either improve, or they die in the long run, as suggested previously [41].

Predictors of clinical outcomes

Clinical outcome predictors for aSAH have been extensively explored, although there is still a debate on methods to assess outcomes [25]. Advanced age and neurological grade (HH or WFNS grade V) have been consistently shown to independently predict poor outcome after PGASAH [10, 19, 21, 34, 39, 47]. Additional predictors of worse outcomes also have been demonstrated, including brain herniation, IVH [47], hyperglycemia, aneurysm size [21], and cerebral infarction associated with vasospasm [34]. In the present study, multivariate analysis confirmed advanced age, Hunt-Hess and modified Fisher grade, larger aneurysm size (>7 mm), rebleeding, and cerebral infarction (including baseline, procedural and delayed ischemia) as independent determinants of poor outcome, similarly to prior reports [5, 21, 30]. Recently, a novel grading scale (SAFIRE) has been introduced and validated in independent cohorts as an accurate and easily applicable early predictor of clinical outcomes after aSAH [2, 7]. The SAFIRE scale includes the size of the aneurysm, age, Fisher grade, and WFNS grade after resuscitation [2]. The present study confirms these baseline factors, while showing that the modified Fisher grade is a more powerful predictor than Fisher grade, in addition to other important determinants such as rebleeding and cerebral infarctions occurring during the hospital course.

Differences of the present study from previous reports

The present series differs from prior reports in several aspects. First, we had a higher proportion of ruptured BBAs (10%) than other reports, where this was typically 1–2% [8]. These are classically known to exhibit more aggressive behavior in comparison to saccular aneurysms, and that might be reflected in the higher incidences we observed. These also were more often associated with intraoperative complications [8], although we did not encounter any serious complications, and our observations of long-term outcomes were similar to saccular counterparts. Second, bypass surgery was performed in 12.5% of the surgery group, which is greater than other studies [15, 19, 21, 34, 46]. The percentage of good outcomes for bypass patients was slightly lower than for clipped patients, but still high enough to justify its use in challenging cases. Third, shunt-dependent hydrocephalus was more frequent than in most other published series [26]. In addition to relatively higher rates of IVH in our series, we believe that excessive drainage of CSF in the early period of aSAH might also have played a role in shunt-dependency.

Treatment decisions should be made on the basis of aneurysm characteristics, patient's status, and the surgeon's experience. Additionally, a thorough discussion with the family before surgery is critical, as demonstrated in our series where two families decided to withdraw support for grade IV patients, even though they were improving neurologically. Once the decision is made, surgery should not be delayed unless clearly necessary, since rebleeding rates are considerably higher for PGASAH patients (11.3%), as we observed (Table 3). Based on these observations, we have recently changed our policy towards early surgery even for patients requiring bypass/trapping. Due to this complexity, neurovascular surgeons dealing with PGASAH should have mastery in multiple surgical techniques, including bypass, so they are prepared for worst-case scenarios [4, 17].

Strengths and limitations

The present study provides a contemporary clinical series of surgically and endovascularly treated consecutive PGASAH patients at a single institution. All patients were offered both treatment options at the earliest time possible, which was within 24 h for most. The selection of the treatment modality was based on discussion with both the surgical and endovascular teams. Data completeness was satisfactory at $>95\%$. Outcomes were assessed at multiple time points from discharge through late follow-up. Besides these strengths, this study also has certain limitations. It is a retrospective study from a single-institutional series. As anticipated, an inherent selection bias was evident between treatment modalities, although multivariate analysis allowed us to control all potential confounders and hence provide a valid comparison. The sample size was insufficient for subgroup analyses. Multicenter, prospective randomized controlled trials are needed to clarify treatment-related issues such as clipping versus coiling, or timing of surgery.

Conclusions

The present study suggests that early microsurgical or endovascular treatments lead to favorable outcomes for a considerable proportion of poor-grade aSAH patients, when coupled with aggressive critical care and functional rehabilitation. It thus seems rational to offer this life-saving surgery to all PGASAH patients, although advanced age, larger aneurysm size, higher neurological and radiological grades, rebleeding, and cerebral infarctions predict worse outcomes. Microsurgery appears as effective as endovascular treatment when performed in a high-volume experienced neurosurgical center; therefore, microsurgery should be considered for managing PGASAH, especially in the anterior circulation that may cause ICH and/or require bypass surgery.

Previous publications Portions of this work were presented in poster form at the 16th WFNS World Congress of Neurosurgery, Istanbul, Turkey, August 20–25, 2017.

Acknowledgements The authors thank Steven L. Goodman, PhD for his editing assistance.

Declarations

Ethics approval and informed consent This study was approved by our Institutional Review Board. Patient consent was not sought due to the retrospective nature of this study.

Conflict of interest The authors declare no competing interests.

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