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Should Cerebral Angiography Be Avoided within Three Hours after Subarachnoid Hemorrhage?

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Objective : While the risk of aneurysmal rebleeding induced by catheter cerebral angiography is a serious concern and can delay angiography for a few hours after a subarachnoid hemorrhage (SAH), current angiographic technology and techniques have been much improved. Therefore, this study investigated the risk of aneurysmal rebleeding when using a recent angiographic technique immediately after SAH.

Methods : Patients with acute SAH underwent immediate catheter angiography on admission. A four-vessel examination was conducted using a biplane digital subtraction angiography (DSA) system that applied a low injection rate and small volume of a diluted contrast, along with appropriate control of hypertension. Intra-angiographic aneurysmal rebleeding was diagnosed in cases of extravasation of the contrast medium during angiography or increased intracranial bleeding evident in flat-panel detector computed tomography scans.

Results : In-hospital recurrent hemorrhages before definitive treatment to obliterate the ruptured aneurysm occurred in 11 of 266 patients (4.1%). Following a univariate analysis, a multivariate analysis using a logistic regression analysis revealed that modified Fisher grade 4 was a statistically significant risk factor for an in-hospital recurrent hemorrhage (p=0.032). Cerebral angiography after SAH was performed on 88 patients ≤3 hours, 74 patients between 3–6 hours, and 104 patients >6 hours. None of the time intervals showed any cases of intra-angiographic rebleeding. Moreover, even though the DSA ≤3 hours group included more patients with a poor clinical grade and modified Fisher grade 4, no case of aneurysmal rebleeding occurred during erebral angiography.

Conclusion : Despite the high risk of aneurysmal rebleeding within a few hours after SAH, emergency cerebral angiography after SAH can be acceptable without increasing the risk of intra-angiographic rebleeding when using current angiographic techniques and equipment.

Key Words : Aneurysm, Ruptured · Angiography · Intracranial aneurysm · Subarachnoid hemorrhage.

INTRODUCTION

Rebleeding can occur anytime after subarachnoid hemorrhage (SAH), with the highest incidence within the first 24 hours[5,10-14]. Thus, emergency or ultra-early treatment has been adopted as a goal at many institutions. In the case of the cur-

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rent authors, this emergency treatment strategy includes emergency catheter angiography right after admission, followed by immediate surgical clipping or endovascular coiling to minimize the time during which the ruptured aneurysm remains unsecured[20].

However, early cerebral angiography immediately after SAH has been reported as a risk factor of intra-angiographic rebleeding, leading to hesitation or delay in performing emergency angiography[2,3,15-17,23,30]. In particular, previous studies by Aoyagi and Hayakawa[3] and Kusumi et al.[17] recommended waiting at least 3 hours after SAH before performing cerebral angiography.

Yet, due to recent improvements in angiographic technology and techniques, digital subtraction angiography (DSA) using a biplane angiographic system now minimizes the rate and volume of the contrast injection, thereby decreasing the risk of intra-angiographic rebleeding. Accordingly, the present study investigated the risk of aneurysmal rebleeding when using a current angiographic technique immediately after SAH.

MATERIALS AND METHODS

Patient population

This study was approved by the Institutional Review Board of Kyungpook National University Hospital (KNUH IRB No. 2017-06-015). As a tertiary referral center, the authors' institution applied a strict emergency treatment protocol for all patients with acute SAH to minimize the time during which a ruptured aneurysm remains unsecured[20]. When a patient presented with a sudden headache or mental deterioration, an SAH diagnosis was primarily obtained based on an immediate computed tomography (CT) scan. Emergency catheter cerebral angiography was then performed within 1 hour of the SAH diagnosis, immediately followed by surgical clipping or endovascular coiling. This emergency treatment strategy was applied 24 hours a day, 7 days a week.

The patients eligible for this prospective study underwent cerebral catheter angiography for an aneurysmal SAH at the authors' institution between April 2015 and December 2018, and the inclusion criteria were as follows : 1) age >20 years; 2) diagnosis of SAH based on CT scan or spinal tap; and 3) diagnosis of a ruptured aneurysm based on cerebral catheter angiography. The exclusion criterion was a non-aneurysmal SAH (e.g., head injury, arteriovenous malformation, moyamoya disease, angiogram-negative SAH).

In the case of patients with the World Federation of Neurosurgical Societies grades 2 to 5, a flat-panel XperCT (Allura FD20/20; Philips Healthcare, Best, The Netherlands) scan, where a flat detector C-arm volume acquisition functionality is integrated with the angiography equipment to allow instant access to CT-like brain imaging in the angiography room, was performed routinely immediately before and immediately after the cerebral angiography[6,25]. These pre- and post-angiographic flat-panel detector CT images were then compared to detect any recurrent hemorrhages during emergency biplane DSA. Meanwhile, for those patients with WFNS grade 1, a post-angiographic flat-panel XperCT scan was performed if the patient demonstrated an aggravated headache, mental change, or neurological deficit suggesting the possibility of a recurrent hemorrhage.

Intra-angiographic aneurysmal rebleeding was diagnosed based on the following findings : 1) extravasation of the contrast medium from the ruptured aneurysm during catheter angiography or 2) increased intracranial hemorrhage in the post-angiographic XperCT scan when compared with the pre-angiographic XperCT scan.

The reviewed radiological data included the first CT scan from the referring hospital, initial CT scan at admission to the authors' institution, angiography, and XperCT scans, along with other information including age, sex, time of SAH, clinical grade at admission, medical history, and current medications.

Pre-hospital aneurysmal rebleeding was identified 1) when the CT scan at admission showed an increased SAH when compared with the CT image taken at the referring hospital and/or 2) when the patient's history revealed a sudden mental deterioration after the first SAH ictus, including a sudden bursting headache or mental change. In addition, intra-hospital aneurysmal rebleeding before angiography was monitored and verified by comparing the initial CT scan at admission and the pre-angiographic XperCT scan. This study was reviewed and approved by the ethics committee at the authors' institution. Informed consent for an angiographic procedure and scientific presentation under anonymity was obtained from all the patients.

Pre-angiographic management

In the case of SAH confirmed by a CT image or spinal tap,

the emergency treatment protocol was strictly applied. Initial attention was focused on ensuring an adequate airway and ventilation, thereby preventing hypoxia, achieving normovolemia and hemodynamic stability, and controlling and/or preventing any seizure activity. In addition, a 1-g dose of tranexamic acid was immediately administered intravenously for antifibrinolytic therapy[9]. Any acute hypertension after SAH was controlled using titratable intravenous antihypertensive medications. Analgesic medication was administered to all patients and sedation given as required.

Following a diagnosis of SAH, cerebral angiography was performed as soon as possible (<1 hour) to determine the cause and treatment modality, endovascular coiling or surgical clipping.

Careful cerebral angiography and flat-panel CT scan

After preparing the patient for cerebral angiography, the first flat-panel detector CT (XperCT) scan was taken under local anesthesia in the angiography suite right before the femoral arterial puncture. Cerebral DSA was then performed, including rotational angiography for 3-dimensional (3D) reconstruction imaging using a biplane angiographic system (Allura FD20/20; Philips Healthcare).

In this study, the cerebral angiography started with Seldinger catheterization of the femoral artery, followed by a four-vessel examination, including both the common or internal carotid artery (ICA) and the vertebral artery. Five French Headhunter or Simmons angiographic catheters (Cook, Bloomington, IN, USA) were primarily used, with iodixanol (Visipaque, 320 mg iodine/mL; Nycomed, Oslo, Norway) as the contrast medium that was diluted half and half with saline in the contrast syringe. While manual injection was used for the conventional 2D-DSA, an automatic power injector (Liebel flarsheim; Philips Healthcare) was used for the 3D rotational angiography. For the manual injection, the volume and injection rate of the contrast medium were 8–10 mL and 3–4 mL/sec, respectively, for the common carotid artery, 6–8 mL and 3 mL/sec, respectively, for the internal carotid angiography, and 6–8 mL and 3–4 mL/sec, respectively, for the vertebral angiography. Meanwhile, for the automatic power injector, the volume and injection rate were 12–15 mL and 4 mL/sec, respectively, for the common carotid artery, 10–12 mL and 3 mL/sec, respectively, for the ICA, and 8–10 mL and 3 mL/sec, respectively, for the vertebral artery. Particular caution with the minimum injection rate and volume was used on the ipsilateral side of the lesions.

Immediately after the angiography, the second XperCT scan was routinely performed to detect any intra-angiographic aneurysmal rebleeding. The patient's blood pressure was monitored throughout the angiographic examination and any hypertensive episode aggressively managed using intravenous hypertensive medication. Appropriate sedation and pain medication were administered to control agitation and headaches.

Statistical analysis

The statistical analyses were performed with the aid of commercially available statistics software (SPSS version 19.0; SPSS, Inc., Chicago, IL, USA). Univariate and multivariate analyses were both performed. The following variables were investigated as potential risk factors for an in-hospital recurrent hemorrhage : age, sex, WFNS clinical grade, modified Fisher grade, occurrence of prehospital recurrent hemorrhage, time interval between SAH and admission, hypertension, and antiplatelet medication at admission. A Mann-Whitney U test was used for the quantitative variables (age, time interval between SAH and admission), whereas a Fisher's exact test was used for the categorical variables. The multivariate analysis was performed using a binary logistic regression analysis. The results were considered significant for probability values <0.05.

RESULTS

Patient characteristics

The clinical and radiological characteristics of the 266 patients who underwent cerebral angiography after acute SAH are summarized in Table 1. The patient age ranged from 21 to 84 years (mean±standard deviation [SD], 57.0±13.8 years), and 174 patients (65.4%) were female. Twenty-one patients (7.9%) were on anticoagulants or antiplatelet drugs. According to the clinical grading system proposed by WFNS, grade 1 was assigned to 65 patients (24.4%), grade 2 to 140 patients (52.6%), grade 3 to seven patients (2.6%), grade 4 to 28 patients (10.5%), and grade 5 to 26 patients (9.8%).

Based on the initial CT scans, the modified Fisher grading scale was used to assess the SAH severity, where grade 1 was

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assigned to 94 patients (35.3%), grade 2 to 22 patients (8.3%), grade 3 to 83 patients (31.2%), and grade 4 to 67 patients (25.2%). Based on the angiographic examinations, the ruptured aneurysms were located in the ICA (n=81, 30.5%), anterior cerebral artery (n=102, 38.3%), middle cerebral artery (n=57, 21.4%), and vertebrobasilar artery (n=26, 9.8%).

Table 1. Clinical and radiological characteristics of 266 patients with aneurysmal SAH

Characteristic	Value
Mean age (years)	57.0±13.8
Female sex	174 (65.4)
Antiplatelet or anticoagulant medication	21 (7.9)
WFNS grade	
1	65 (24.4)
2	140 (52.6)
3	7 (2.6)
4	28 (10.5)
5	26 (9.8)
Modified Fisher grade	
1	94 (35.3)
2	22 (8.3)
3	83 (31.2)
4	67 (25.2)
Location of ruptured aneurysm	
ICA	81 (30.5)
ACA	102 (38.3)
MCA	57 (21.4)
VB	26 (9.8)

Values are presented as mean±standard deviation or number (%). SAH : subarachnoid hemorrhage, WFNS : World Federation of Neurosurgical Societies, ICA : internal carotid artery, ACA : anterior cerebral artery, MCA : middle cerebral artery, VB : vertebrobasilar

Pre-hospital aneurysmal rebleeding

Pre-hospital rebleeding of a ruptured aneurysm was identified in 6 of the 266 patients (2.3%), as presented in Table 2. Among these six patients, four experienced rebleeding within 3 hours of the first hemorrhagic ictus, four were assessed as WFNS grade 5 upon admission to the emergency room, and three were assessed as modified Fisher grade 4. The treatment procedures included surgical clipping (n=2) or endovascular coiling (n=4), which resulted in modified Rankin Scale (mRS) scores of 1 (n=2), 3 (n=2), 4 (n=1), and 5 (n=1) at 1 month after admission.

In-hospital recurrent hemorrhage

An in-hospital recurrent hemorrhage before definitive treatment to obliterate the ruptured aneurysm occurred in 11 of the 266 patients (4.1%). Their clinical and radiological characteristics are presented in Table 3. Moreover, among these 11 patients, the in-hospital aneurysmal rebleeding occurred before cerebral angiography in seven patients (2.6% of 266 patients) and after cerebral angiography while waiting for surgical clipping or endovascular coiling in four patients (1.5% of 266 patients). The time interval from the initial SAH to in-hospital rebleeding was short at <6 hours in all 11 patients. In particular, the time interval was very short at ≤3 hours in eight of the 11 patients (72.7%).

While three patients with in-hospital rebleeding showed poor clinical grades (WFNS grade 4–5), the other eight patients showed good grades (WFNS grade 1–3). For the WFNS grade 5 patient, the family refused all treatment for the ruptured aneurysm, which resulted in fatality. The remaining

Table 2. Clinical characteristics of patients with pre-hospital recurrent hemorrhage

Case No.	Sex	Age (years)	WFNS grade at admission	Modified Fisher grade at admission	Location of ruptured aneurysm	Time from SAH to rebleed (hours)	Treatment	mRS score at 1 month
1	F	73	5	3	ACoA	4.2	Coiling	4
2	M	42	5	4	ACoA	1.2	Coiling	1
3	M	48	5	4	ACoA	2.8	Coiling	3
4	M	53	5	4	MCA	2.0	Clipping	3
5	F	63	2	3	MCA	24.0	Clipping	1
6	F	46	4	2	VB	1.0	Coiling	5

WFNS : World Federation of Neurosurgical Societies, SAH : subarachnoid hemorrhage, mRS : modified Rankin Scale, F : female, ACoA : anterior communicating artery, M : male, MCA : middle cerebral artery, VB : vertebrobasilar

four patients underwent surgical clipping (n=4) or endovascular coiling (n=6), resulting in mRS scores of 0 (n=2), 1 (n=3), 2 (n=2), 4 (n=1), and 5 (n=2) at 1 month after admission.

Risk factors for in-hospital recurrent hemorrhage

The clinical characteristics of the patient groups with and without in-hospital rebleeding are compared in Table 4. In the univariate analysis, modified Fisher grade 4 was significantly associated with the occurrence of in-hospital rebleeding when compared with modified Fisher grades 1–3 (54.5% vs. 45.5%, p=0.032). In contrast, age, sex, WFNS clinical grade, pre-hospital rebleeding, hypertension history, and antiplatelet or anticoagulant medication showed no between-group differences.

Furthermore, the multivariate analysis using a logistic regression analysis revealed that the modified Fisher grade 4 was a statistically significant risk factor for an in-hospital recur-

Table 3. Clinical characteristics of patients with in-hospital recurrent hemorrhage

Case No.	Sex	Age (years)	WFNS grade at admission	Modified Fisher grade at admission	Location of ruptured aneurysm	Time from SAH to rebleed (hours)	Pre or post-angiography	Treatment	mRS score at 1 month
1	M	53	5	3	ACoA	2.6	Pre-angiography	No	6
2	F	21	2	1	PCoA	2.5	Pre-angiography	Coiling	1
3	M	36	1	1	MCA	2.5	Pre-angiography	Clipping	1
4	M	49	2	2	PICA	2.0	Pre-angiography	Coiling	2
5	F	75	4	3	MCA	2.6	Pre-angiography	Clipping	5
6	M	43	5	4	ACoA	1.0	Pre-angiography	Coiling	4
7	F	62	2	4	ACoA	2.0	Pre-angiography	Coiling	2
8	F	76	2	4	ACoA	4.5	Post-angiography	Coiling	5
9	F	65	2	2	ACoA	3.5	Post-angiography	Clipping	0
10	F	62	2	4	ICA	3.0	Post-angiography	Coiling	1
11	F	61	2	4	ICA	4.0	Post-angiography	Clipping	0

WFNS : World Federation of Neurosurgical Societies, SAH : subarachnoid hemorrhage, mRS : modified Rankin Scale, M : male, ACoA : anterior communicating artery, F : female, PCoA : posterior communicating artery, MCA : middle cerebral artery, PICA : posterior inferior cerebellar artery

Table 4. Clinical characteristics of patients with and without in-hospital recurrent hemorrhage

Variable	Patients without in-hospital rebleeding (n=255)	Patients with in-hospital rebleeding (n=11)	p-value
Age (years)	57.1±13.7 (19–84)	54.8±16.7 (21–76)	0.854*
Male sex	88 (34.5)	4 (36.4)	1.000†
WFNS grade			1.000†
Good grade : grade 1–3	203 (79.6)	9 (81.8)	
Poor grade : grade 4–5	52 (20.4)	2 (18.2)	
Modified Fisher grade			0.032†‡
1–3	194 (76.1)	5 (45.5)	
4	61 (23.9)	6 (54.5)	
Pre-hospital rebleeding	6 (2.4)	0 (0.0)	1.000†
Hypertension history	68 (26.7)	2 (18.2)	0.733†
Antiplatelet medication	21 (8.2)	0 (0.0)	1.000†

Values are presented as mean±standard deviation (range) or number (%). *Mann-Whitney U test. †Fisher's exact test. ‡Denotes statistically significant p-value. WFNS : World Federation of Neurosurgical Societies

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rent hemorrhage (p=0.032) (Table 5).

Occurrence of intra-angiographic rebleeding within 3 hours after SAH

Table 6 compares the clinical and radiological characteristics of the patient groups that experienced cerebral angiography within and beyond 3 hours after SAH. A total of 88 patients (33.1%) underwent DSA ≤3 hours after SAH, while 178 patients (66.9%) underwent DSA >3 hours after SAH. In the case of DSA ≤3 hours, the catheter angiography ranged from 0.4 hours to 3.0 hours after the last SAH (mean±SD, 2.3±0.6 hours). Seven of these 88 patients experienced pre-angiographic in-hospital aneurysmal rebleeding and underwent immediate angiography within 1 hour.

The DSA ≤3 hours group included more patients with a poor clinical grade, represented by significantly higher incidences of a poor WFNS grade (31.8% vs. 14.6%, p=0.001) and modified Fisher grade 4 (37.5% vs. 19.1%, p<0.001). In addition, the incidence of pre-hospital and in-hospital pre-angiographic rebleeding was significantly higher (12.5% vs. 1.1%, p<0.001). No between-group differences were identified for sex, aneurysm location, hypertension history, and antiplatelet medication. However, even though the DSA ≤3 hours group exhibited more risk factors for a recurrent hemorrhage than the DSA >3 hours group, neither patient group experienced any cases of aneurysmal rebleeding during angiography.

Table 5. Results of logistic regression analysis for in-hospital recurrent hemorrhage after aneurysm rupture

Variable	OR	95% CI	*p*-value
Modified Fisher grade 4	3.816	1.125–12.942	0.032*

*Denotes statistically significant *p*-value. OR : odds ratio, CI : confidence interval

Table 6. Clinical characteristics and occurrence of recurrent hemorrhage in patients who underwent cerebral angiography within and beyond 3 hours after SAH

Variable	DSA ≤3 hours after SAH (n=88)	DSA >3 hours after SAH (n=178)	*p*-value
Interval between SAH and DSA (hours)	2.3±0.6 (0.4–3.0)	36.7±61.9 (3.2–365.0)	<0.001*†
Age (years)	54.6±12.9 (21–84)	58.2±14.1 (19–84)	0.034†
Male sex	30 (34.1)	62 (34.8)	0.905‡
Aneurysm location			0.555‡
ICA	23 (26.1)	58 (32.6)	
ACA	36 (40.9)	66 (37.1)	
MCA	18 (20.5)	39 (21.9)	
VB	11 (12.5)	15 (8.4)	
WFNS grade			0.001*‡
Good grade : grade 1–3	60 (68.2)	152 (85.4)	
Poor grade : grade 4–5	28 (31.8)	26 (14.6)	
Modified Fisher grade			<0.001*‡
1	15 (17.0)	79 (44.4)	
2	7 (8.0)	15 (8.4)	
3	33 (37.5)	50 (28.1)	
4	33 (37.5)	34 (19.1)	
Pre-hospital and in-hospital pre-angiographic rebleed	11 (12.5)	2 (1.1)	<0.001*
Hypertension history	19 (21.6)	51 (28.7)	0.219‡
Antiplatelet medication	4 (4.5)	17 (9.6)	0.154‡
Intra-angiographic rebleed	0	0	-

Values are presented as mean±standard deviation (range) or number (%). *Denotes statistically significant *p*-value. †Mann-Whitney U test. ‡χ^2 test or Fisher's exact test. SAH : subarachnoid hemorrhage, DSA : digital subtraction angiography, ICA : internal carotid artery, ACA : anterior cerebral artery, MCA : middle cerebral artery, VB : vertebrobasilar, WFNS : World Federation of Neurosurgical Societies

Table 7. Time interval from SAH to cerebral angiography and occurrence of recurrent hemorrhage during angiography

Time interval (hours)	No. of patients	No. of patients with modified Fisher grade 4	No. of rebleeding cases
0<t≤3	88 (33.1)	33 (37.5)	0
3<t≤6	74 (27.8)	20 (27.0)	0
6<t≤12	28 (10.5)	5 (17.9)	0
12<t≤24	25 (9.4)	4 (16.0)	0
t>24	51 (19.2)	5 (9.8)	0

Values are presented as number (%). SAH : subarachnoid hemorrhage

The numbers of patients according to the time interval from SAH to DSA are summarized in Table 7. A total of 162 patients (60.9%) underwent DSA ≤6 hours after SAH, while 88 patients (33.1%) underwent DSA ≤3 hours after SAH. Yet, neither time interval showed any cases of intra-angiographic rebleeding.

DISCUSSION

Aneurysmal rebleeding

While rebleeding can occur anytime following an aneurysmal rupture, it usually occurs within 24 hours, and most often within 6 hours after SAH[5,10-14]. Ruptured aneurysms are most fragile and unstable during the early stage. In the present case series, in-hospital aneurysmal rebleeding was detected in 11 of the 266 patients (4.1%) ≤4.5 hours after SAH. Fortunately, these occurrence were before and after DSA, however, aneurysmal rebleeding also can occur coincidentally during cerebral angiography early after SAH.

The risk factors for a recurrent aneurysmal rupture, as suggested by previous studies, include rebleeding before admission, an intracerebral or intraventricular hematoma, poor neurological condition on admission, advanced age, and aneurysm diameter >10 mm[4,7,8,18,19]. In the present study, modified Fisher grade 4 (thick SAH with intraventricular hemorrhage) was identified as a risk factor.

Intra-angiographic aneurysmal rebleeding

Waiting at least 3 hours after SAH before performing cerebral angiography has been recommended in the previous studies by Aoyagi and Hayakawa[3] and Kusumi et al.[17]. However, no intra-angiographic aneurysmal rebleeding occurred in this study when using a current angiographic technique, which included DSA using a biplane angiographic system with a low volume and injection rate of a diluted contrast medium, appropriate hypertension management, and adequate sedation. Thus, the present study results demonstrated the safety of early cerebral angiography ≤3 hours after SAH, while also avoiding possible medicolegal issues.

Recognizing intra-angiographic aneurysmal rebleeding in angiographic images is easy in the case of substantial contrast extravasation from the re-ruptured aneurysm[21]. However, aneurysmal rebleeding can be difficult to find when the degree of extravasation is minimal and the angiography is performed on the contralateral side. Moreover, neurological deterioration due to aneurysmal rebleeding can be difficult to recognize in patients with a poor clinical grade. Therefore, in this study, for those patients with a WFNS grade ≥2, the flat-panel CT scans were performed in the angiographic suite.

Previously reported rates of intra-angiographic aneurysmal rebleeding range from 0.04% to 3.3% and are seemingly affected by the angiographic timing after SAH, angiography system and technique, patient risk factors for rebleeding, diagnostic methods of intra-angiographic aneurysmal rebleeding, and study design[1,2,16,24,27]. The patient risk factors include a poor clinical grade after SAH and hypertension[3,15,24,29].

The pressure from a contrast medium injection can be transmitted along the carotid artery and aneurysms at the circle of Willis[28]. A contrast medium injection can also increase the intra-aneurysmal pressure, where a considerable increase can lead to dislodgement of the fibrin plug and clot covering the ruptured dome of an aneurysm. Sorimachi et al.[26] measured the intra-aneurysmal pressure using a microcatheter and needle inserted into an aneurysm, and found that 8 mL of a contrast medium injected at a rate of 6 mL/sec using a mechanical injector increased the intra-aneurysmal systolic pressure by 5–23 mmHg for 1–3 seconds immediately following

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the contrast medium injection. Thus, decreasing the injection rate to 3 mL/sec, as in the current angiographic technique, may reduce and minimize any change in the intra-aneurysmal systolic pressure.

When within 3–6 hours after SAH, a high volume and high injection rate of the contrast medium can create a high risk of aneurysmal rebleeding. Conventional angiography requires a high injection rate to achieve adequate imaging, usually three times higher than the injection rate applied by the biplane DSA used in this study. In the study by Komiyama et al.[16], injecting the contrast medium into the common carotid artery at a rate of 8–10 mL/sec (volume 8–12 mL) using a power injector resulted in a 3.3% (14 of 418 patients) incidence of intra-angiographic aneurysmal rebleeding, where 13 patients developed rebleeding ≤4 hours after SAH. Furthermore, when using the same patient cohort and data from literature to investigate the time interval between SAH and intra-angiographic aneurysmal rebleeding, among 108 patients with detailed time information after SAH, 67 patients (62%) developed rebleeding within 3 hours, 29 (27%) within 6 hours, six (6%) within 9 hours, three (3%) within 12 hours, two (2%) within 18 hours, and one (1%) within 24 hours. Thus, 96 patients (89%) developed intra-angiographic aneurysmal rebleeding within 6 hours after SAH.

Aoyagi and Hayakawa analyzed 70 patients (six of their own cases and 64 from literature) with intra-angiographic aneurysmal rebleeding and found that these cases were clinically distinguished by a high WFNS grade, higher incidence of aneurysms arising at the ICA, less operability and poorer outcome, and concentration of aneurysmal re-ruptures within 3 hours after SAH[3]. Thus, they recommended waiting at least 3 hours after SAH before performing cerebral angiography. In their own case series, a conventional angiography technique was used with an injection rate of 10 mL/sec for the ICA. As a result, five of their six cases experienced aneurysmal rebleeding ≤7 hours after SAH. Thus, the overall aneurysmal re-rupture rate was as high as 25% during early angiography after SAH.

When Saitoh et al.[23] investigated the re-rupture rate of cerebral aneurysms during angiography, they used a contrast medium injection rate of 4.5–8 mL/sec for the ICA, which is roughly twice the injection rate used in the current study. As a result, their overall incidence of aneurysmal rebleeding during angiography was 1.4% (two of 144 patients). Furthermore, the incidence of rebleeding within 6 hours after SAH was 4.8% (two of 42 patients).

In addition to the injection rate and volume, the viscosity of the contrast medium can also affect the intra-arterial pressure[22]. However, the improved performance of image intensifiers used in DSA enables a cautious angiographic technique with a diluted contrast medium and lower injection rate of 3 mL/sec and volume of 6–8 mL for internal carotid angiography.

Management strategy for patients with acute SAH

For emergency treatment of ruptured aneurysms ≤3 hours after SAH, the safety of emergency angiography is of critical concern. Several past studies have reported an increased risk of angiography-induced rebleeding until 3 hours after SAH[3,17]. However, such studies investigated angiography-induced rebleeding in patients who underwent cerebral angiography using a conventional single-plane angiography system.

In contrast, when using more recent angiographic equipment, the current study found that early angiography after SAH did not increase the risk of intra-angiographic rebleeding. Notwithstanding, patients at risk of intra-angiographic rebleeding also remain at risk of aneurysmal re-rupture. Thus, emergency treatment to obliterate the ruptured aneurysm, via surgical clipping or endovascular coiling, is the only definitive treatment to prevent a recurrent hemorrhage.

According to the authors' previous study including 865 patients with an aneurysmal SAH, the change of the management strategy from early (<3 days of SAH) treatment to the immediate emergency treatment achieved a 5% absolute risk reduction of in-hospital rebleeding[20]. In particular, an absolute risk reduction of 2% was achieved for recurrent hemorrhages within 24 hours after admission.

The incidence of contrast-induced nephropathy can be reduced by using a small volume of a diluted contrast. However, the effect of the angiographic contrast on the renal function could not be ascertained in the current study as the angiography was performed as part of a practical sequence that included mannitol administration during the craniotomy, an additional contrast injection during the endovascular treatment, and postoperative CT angiography.

The current study has several important limitations. First, this study is limited based on a small case series from a single

institution. Nonetheless, the current series of 162 patients who underwent early angiography ≤6 hours after SAH is comparable with the patient numbers in previous studies of intra-angiographic rebleeding, including 82 patients in the study by Amagasa et al.[2], 96 patients in the study by Komiyama et al.[16], 42 patients in the study by Saitoh et al.[23], and 149 patients in the study by Kusumi et al.[17]. Thus, to our knowledge, the current study is the largest showing the safety of early cerebral angiography. Second, the current study includes comparative data from previous studies. In their long-term experience, the current authors also occasionally encountered recurrent hemorrhages early after SAH when using conventional angiography prior biplane DSA. However, unfortunately, due to the absence of a current electronic picture-archiving and communication system, no data is available for a comparative study.

CONCLUSION

Despite the high risk of aneurysmal rebleeding within a few hours after SAH, emergency cerebral angiography after SAH can be acceptable without increasing the risk of intra-angiographic rebleeding when using biplane DSA with a low injection rate and small volume of a diluted contrast medium, along with appropriate hypertension management.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in this study.

AUTHOR CONTRIBUTIONS

Conceptualization : JP
Data curation : HA, DHK, WS, YSL, YK
Formal analysis : BO
Methodology : JP
Project administration : JP
Writing - original draft : HA
Writing - review & editing : JP

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