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Original Article

Subarachnoid Hemorrhage after Resuscitation from Cardiopulmonary Arrest: A Comparison of Survivor and Dead Cases

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Objective: The prognosis of patients with subarachnoid hemorrhage (SAH) who also develop cardiopulmonary arrest (CPA) is highly unfavorable, and hence they are often not aggressively treated. Presently, the therapeutic indications and factors that affect the prognosis of patients who experienced CPA remain unclear. Therefore, we analyzed SAH patients who experienced CPA, comparing the characteristics of the patients who survived with those who did not.

Methods: The 36 patients were divided into the survivor group (n = 4) and the dead group (n = 32). The patient's age, sex, location of the aneurysm, the presence of intracranial hematoma, duration of cardiopulmonary resuscitation (CPR), the presence/absence of bystanders, initial electrocardiogram waveform, recovery of brainstem reflexes with motor response, and administration of vasopressors were compared between the 2 groups.

Results: There were no significant differences in age, sex, location of the aneurysm, and presence of intracranial hematoma between the 2 groups. More than 90% of patients in the dead group had a non-shockable rhythm on the initial electrocardiogram waveform. The duration of CPR in the survivor group tended to be shorter than that in the dead group. Bystander CPR was performed on 14 patients, including all 4 of the survivors. All patients in the survivor group achieved recovery of brainstem reflexes with motor response. In the survivor group, all patients either did not need or only transiently needed the administration of vasopressors after the return of spontaneous circulation (ROSC).

Conclusion: Our analysis suggested the following as favorable prognostic factors in SAH patients with CPA: shockable arrhythmia on the initial electrocardiogram waveform, young age, bystander CPR, a short time from CPA to ROSC, recovery of brainstem reflexes with a motor response, and no or transient use of vasopressors. Our results indicate that aggressive treatment may be indicated in SAH patients with CPA who have stable vitals and show improvements in neurological symptoms.

Keywords ▶ subarachnoid hemorrhage, cardiopulmonary arrest, coil embolization, bystander

Introduction

The initial clinical condition of patients with subarachnoid hemorrhage (SAH) is considered to affect the final outcome.[1] In particular, the prognosis of SAH patients with cardiopulmonary arrest (CPA) is considered to be highly unfavorable, and even when the return of spontaneous circulation (ROSC) is achieved, aggressive treatment is not indicated in most cases. Among such patients, there are a few who can be effectively treated and achieve a favorable outcome. Konczalla et al.[2] demonstrated that the treatment rate of endovascular therapy for SAH categorized as World Federation of Neurosurgical Societies (WFNS) grade V

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increased from 22% (1980–1995) to 67% (2005–2014) and the rates of survival of the untreated and treated groups (2005–2014) were approximately 15% and 68%, respectively, and the rate of favorable outcomes were 8% and 30%, respectively. Therefore, clarifying the role of endovascular treatment in patients with poor WFNS grades is expected to become more important in the future. On the other hand, the criteria and efficacy of treatment of patients who have SAH with CPA have remained controversial, and treatment interventions have often been determined at the discretion of the doctor. There have been some case reports on SAH patients with CPA who underwent surgical treatment and achieved favorable outcomes.[3–10] However, because these reports were all on a small study population, further studies are needed. Here, we analyzed SAH patients who experienced CPA, focusing on their clinical information and condition at the time of admission, and compared the characteristics of the patients who survived with those who did not.

Materials and Methods

Patient selection

A retrospective review was performed on a total of 435 consecutive patients with a history of SAH who were treated at our hospital from January 2010 to December 2019. Patients with traumatic SAH or infectious endocarditis were excluded from this study. Of the 46 patients with a history of CPA caused by SAH, the 36 patients in whom almost all items were measured were compared in 2 groups, that is, the survivor group (n = 4) and the dead group (n = 32). All imaging evaluations were performed using brain computed tomography (CT). The patient's age, sex, location of the aneurysm, the presence of intracerebral, intraventricular, or subdural hematoma, duration of cardiopulmonary resuscitation (CPR), the presence/absence of a bystander, and initial electrocardiogram waveform were compared between the survivor group and the dead group. Post-resuscitation neurologic restorative assessment (PRNRA) was classified into grade I (recovery of brainstem reflexes, and motor response demonstrating flexion to pain) and grade II (recovery of spontaneous respiration only or no recovery),[3] and compared between the survivor group and the dead group. In the present report, a distinction was not made between out-of-hospital and in-hospital CPA. The use of vasopressor agents after ROSC was also investigated. The categories included patients who did not require the administration of vasopressors after ROSC, and patients who required the transient administration of vasopressors, which eventually became unnecessary, and their vitals became stable. Approval for this retrospective study was obtained from the relevant institutional research ethics boards of Tokyo Medical University (approval No. T2022-0105). Representative patients (Case 1 and Case 2) were informed about the study and provided written consent to participate.

Statistical analysis

Data analyses were performed using SPSS software (version 28.0; SPSS Inc., Chicago, IL, USA). Qualitative variables were presented as frequencies and percentages, and quantitative variables were presented as medians and interquartile ranges. Qualitative and quantitative variables were analyzed using the chi-square test and Mann–Whitney *U*-test, respectively. A 2-sided p-value of less than 0.05 was considered to indicate a statistically significant difference between groups for all analyses.

Results

Baseline characteristics and outcomes

At the authors' institution, SAH patients with poor WFNS grades were considered for surgery if they had stable hemodynamics (heart rate and blood pressure), specific neurological findings, such as the presence of brainstem reflexes without pupil dilation and motor response of flexion to pain, and if the family desired treatment. Therefore, all surviving patients fulfilled these conditions and underwent surgical treatment. Patients in whom CPR was initially successful, but who did not meet these conditions ultimately died after conservative treatment.

Table 1 shows the characteristics of the patients in the survivor group and the dead group. There were no significant differences in age, sex, location of the aneurysm, and presence of intracranial, intraventricular, or subdural hematoma between the 2 groups. More than 90% of patients in the dead group had a non-shockable rhythm, such as pulseless electrical activity (PEA) or asystole on the initial electrocardiogram waveform. The duration of CPR in the survivor group tended to be shorter than in the dead group. Bystander CPR had been performed on 14 patients, including all 4 of the survivors, and showed a significant difference between the 2 groups. All patients in the survivor group were PRNRA grade I and those in the dead group tended to be PRNRA grade II. In the survivor group, all patients achieved hemodynamic stability

Table 1 Characteristics of patients in the survivor group and the dead group

Variable	Survivor (n = 4)	Dead (n = 32)	p-Value
Age (years), median (IQR)	64 (48–73)	64 (56–72)	0.75
Sex			0.46
Male	2	11	
Female	2	21	
Aneurysm location			0.41
Anterior circulation	2 (50%)	18 (56%)	
Posterior circulation	2 (50%)	8 (25%)	
No data	0	6	
Intracerebral, intraventricular or subdural hematoma	2 (50%)	24 (75%)	0.31
Duration of CPR (minutes) Median (IQR)	5 (3–6)	34 (19–47)	0.02
Bystander CPR	4 (100%)	10 (32%)	<0.01
No data	0	1	
Initial waveform			0.06
PEA + Asystole	1 (25%)	30 (94%)	
VT	1 (25%)	0 (0%)	
No data	2	2	
PRNRA grade			<0.01
Grade I	4	1	
Grade II	0	29	
No data	0	2	

"No data" was not included in the statistical analysis.
CPR, cardiopulmonary resuscitation; IQR, interquartile range; PEA, pulseless electrical activity; PRNRA, post-resuscitation neurologic restorative assessment; VT, ventricular tachycardia

after ROSC. Three of the 4 patients did not need vasopressors after ROSC, and only 1 of the 4 patients required vasopressors, which then became unnecessary after 36 hours of administration. Two patients in the dead group who had brainstem reflexes were transiently administered vasopressors, but their families did not desire surgical treatment. These 2 patients had the longest survival time among the patients in the dead group, which was 11 days from hospitalization. Other patients in the dead group used vasopressors until death or stopped using the agents once but restarted within 48 hours. The median time to death for the dead group was 3 days (interquartile range: 2–5 days).

Of the survivors, 3 were eventually discharged home, as shown in **Table 2**, and 2 representative cases are presented below.

Case presentations

Case 1

A 46-year-old man received bystander CPR after swooning owing to ventricular fibrillation (VF) and was given an electric shock using an automated external defibrillator. The time of ROSC from CPA was 6 minutes. When the patient arrived at our hospital, his clinical findings after ROSC were as follows: heart rate, 72 beats/min (sinus rhythm); systolic blood pressure, about 150 mmHg (initial dopamine dose was 60 mg/h); consciousness level, Glasgow Coma Scale (GCS) E1V1M5; respiratory condition, mandibular breathing before intubation; and pupils, 2 mm on the right and 4 mm on the left. A CT scan displayed SAH owing to a ruptured anterior communicating artery aneurysm (**Fig. 1A** and **1B**). Coil embolization for the SAH, which was categorized as WFNS grade IV, was performed on the day of onset (**Fig. 1C**). The patient was transferred to a rehabilitation hospital, with a modified Rankin Scale (mRS) of 1 on postoperative day 48. At the follow-up 10 years after the surgery, his mRS was 2 and the patient had no recurrence of the aneurysm. Follow-up magnetic resonance imaging displayed brain atrophy, and ventriculomegaly of the lateral and third ventricles (**Fig. 1D**), but the patient has been under observation without additional treatment because of no gait disturbance.

Case 2

A 73-year-old woman developed PEA in the ambulance after swooning, and CPR was started by a paramedic. The

Table 2 Characteristics of the patients in our case series

Age, sex	Location of the hemorrhage and pathology	GCS E/V/M	Diameter of pupil right/ left (mm) on admission	Treatment	Initial electrocardiogram waveforms	Bystander	Time of ROSC from CPA (minutes)	mRS (180 days after the treatment)	mRS (at last follow-up)
46-year-old man (Case 1)	Anterior communicating artery aneurysm	1/1/5	2/4	Coil embolization	VF	Yes	6	1	2 (10 years)
73-year-old woman (Case 2)	Right vertebral artery dissection	1/1/1	6/6	Coil embolization including parent artery occlusion	PEA	Yes	2	2	3 (3 years 4 months)
73-year-old woman	Left internal carotid artery aneurysm	1/1/4	2.5/2.5	Coil embolization combined with stent	Unknown	Yes	4	3	3 (4 years 7 months)

CPA, cardiopulmonary arrest; GCS, Glasgow Coma Scale; mRS, modified Rankin Scale; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation

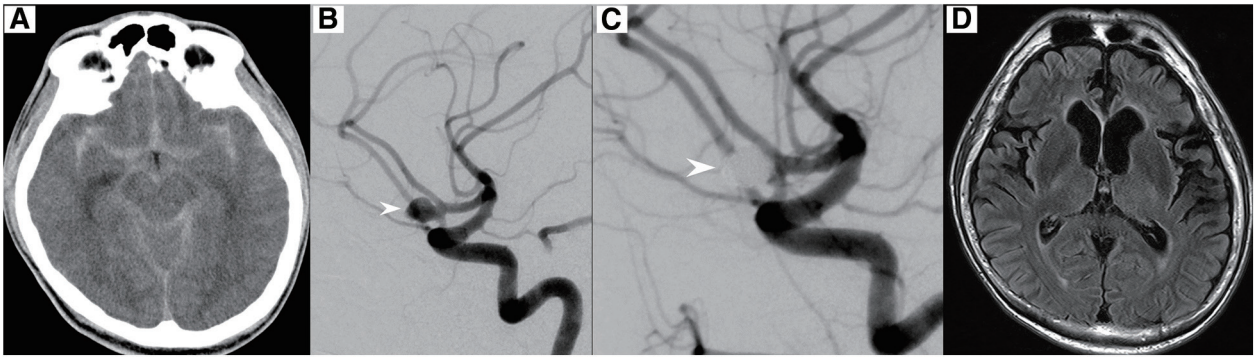

Fig. 1 Intracranial imaging from admission to the last follow-up in the patient of Case 1. (**A**) A CT image of the patient taken on the first day of admission displays a diffuse subarachnoid hemorrhage. (**B**) DSA displays an aneurysm of the anterior communicating artery (arrowhead). (**C**) A magnified image of (**B**), in which the coil embolization performed on the aneurysm is shown (arrowhead). (**D**) Magnetic resonance fluid-attenuated inversion recovery image displaying brain atrophy in the frontal and temporal lobe, and ventriculomegaly of the lateral ventricles at the follow-up 10 years after the coil embolization

time of ROSC from CPA was approximately 2 minutes. When the ambulance arrived at the hospital, her GCS was E1V1M1, her respiratory condition was mandibular breathing, and her pupils were 6 mm on both the right and left, without the light reflex. Her clinical findings after ROSC were as follows: heart rate, 100 beats/min (sinus rhythm); blood pressure, 152/121 mmHg; SpO_2, 100% with 100% fraction of inspired oxygen during oropharyngeal intubation; and consciousness level, GCS E1VTM1. A CT scan displayed SAH, but because her WFNS was grade V and her pupils were dilated, she was treated conservatively. Vasopressors were not used after ROSC, but propofol and fentanyl were used, and the patient's circulation was stable. Her blood pressure trend and anesthetics administered up to treatment (the third day of hospitalization) are shown in **Fig. 2**. A CT scan displayed SAH with severe hematoma in the prepontine cistern (**Fig. 3A**), and the diagnosis was vertebral artery dissection on digital subtraction angiography. Although the initial CT displayed ventricular enlargement, ventricular drainage was not performed, and conservative intensive care was performed instead. On the third day, spontaneous eye opening and body motion were observed, and her pupil dilation improved, so coil embolization was performed (**Fig. 3B** and **3C**). As she developed hydrocephalus during the chronic postoperative period, a ventriculoperitoneal shunt was placed. On postoperative day 56, the patient was transferred to a rehabilitation hospital, with mRS 2. At the follow-up 3 years after the

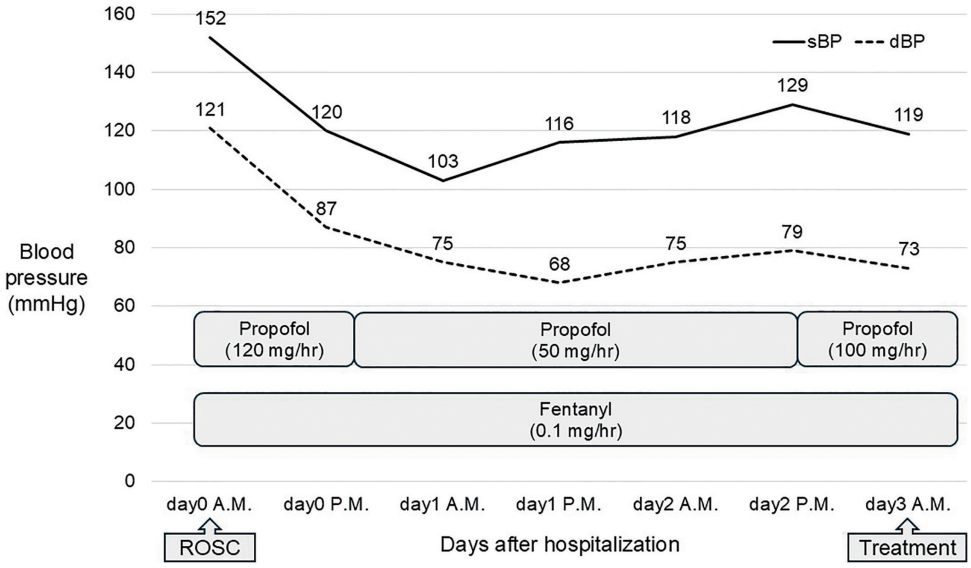

Fig. 2 Blood pressure changes in patients from the time of hospitalization to treatment. Average blood pressures of patients in the morning and the afternoon, from the day of hospitalization to the day of treatment are shown. dBP, diastolic blood pressure; ROSC, return of spontaneous circulation; sBP, systolic blood pressure

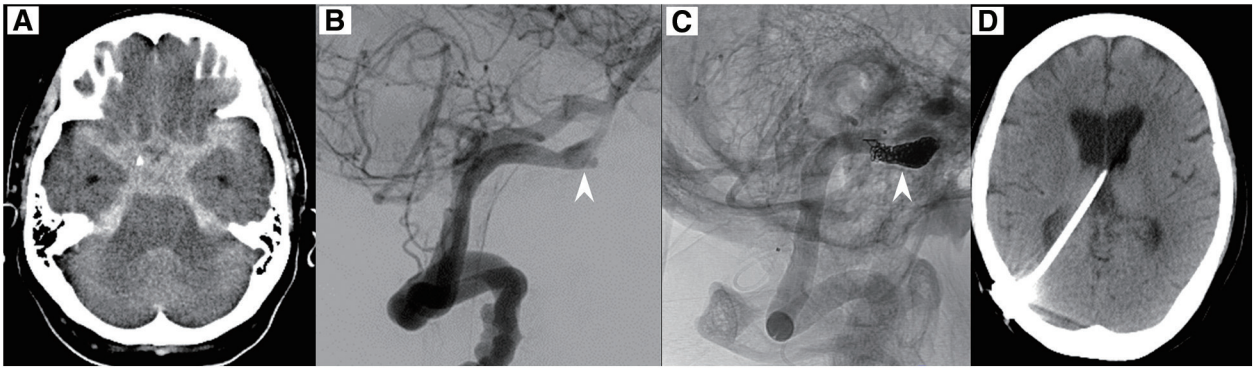

Fig. 3 Intracranial imaging from admission to the last follow-up in the patient of Case 2. (**A**) A CT image of the patient taken on the first day of admission displays a diffuse subarachnoid hemorrhage. (**B**) DSA displaying right vertebral artery dissection (arrowhead). (**C**) DSA displaying an occluded parent artery, and coil embolization performed to the vertebral artery dissection (arrowhead). (**D**) CT displaying the ventriculoperitoneal shunt tube at the follow-up 3 years after the coil embolization

surgery, her mRS was 3 and the patient had no recurrence of the aneurysm (**Fig. 3D**).

Discussion

The prognosis of SAH patients with CPA, even when ROSC is achieved, has been highly unfavorable. Feldstein et al. reported that the survival rate of 5415 patients with SAH who experienced CPA was 18%. Although information regarding the treatment that the survivors underwent was not available, only 3.4% of the patients with SAH who experienced CPA were discharged home.[11] On the other hand, Suzuki et al.[4] reported that among the 66 patients with SAH who experienced CPA, the survival rate was only 9.1%, and all patients were in a critical or vegetative state. Similarly, in our present study, the survival rate was very low, with only 4 patients (8.7%) surviving. Even when ROSC was achieved in patients, they were considered to be unsuitable for surgical treatment if they demonstrated pupil dilation and unstable circulatory dynamics, and in our institution, such patients are usually treated by conservative therapy. In patients with CPA-associated SAH, early intracranial damage, such as brainstem compression and brain edema owing to increased intracranial pressure, may prevent the patient from being indicated for surgical treatment and, consequently, result in an unfavorable

Table 3 Reviews of favorable outcomes in cases of patients with SAH after cardiopulmonary arrest resuscitation

Author, year	Age, sex	Location of aneurysm	Comorbidity	Time of ROSC from CPA (minutes)	Initial rhythm	Bystander	Treatment	CPC
Kürkciyan (2001)[5]	43-year-old man	Basilar artery	None	1	VF	Unknown	Surgical treatment	2
Toussaint (2005)[6]	58-year-old man	A-com	N/A	1	Asystole	Yes	Clipping	1
Toussaint (2005)[6]	51-year-old man	Middle cerebral artery and A-com	N/A	0.5	VF	Yes	Clipping	1
Hess (2005)[7]	40-year-old man	A-com	None	2	VF	Yes	Coiling	1
Fukushima (2009)[8]	50-year-old woman	IC-PC	None	5	VF	Unknown	Clipping	1
Suzuki (2010)[9]	63-year-old woman	A-com	Hypertension and liver cirrhosis	9	VF	Unknown	Coiling	1
Miyata (2014)[3]	45-year-old woman	IC-PC	None	14	Asystole	Yes	Coiling	1
Kano (2021)[10]	50-year-old woman	IC-PC	None	14 + 2 + 5 + 11*	VF	Yes	Coiling	1

*The patient's heartbeat resumed owing to cardiopulmonary resuscitation but was again followed by cardiac arrest.
A-com, anterior communicating artery; CPA, cardiopulmonary arrest; CPC, cerebral performance category; IC-PC, internal carotid artery-posterior communicating artery; N/A, not available; ROSC, return of spontaneous circulation; SAH, subarachnoid hemorrhage; VF, ventricular fibrillation

prognosis. Therefore, we extracted and analyzed cases of SAH patients who experienced CPA and had a favorable disease course, from previous reports in the literature. **Table 3** shows the data of 8 patients with CPA-associated SAH who had favorable outcomes, which correspond to cerebral performance category 1 to 2, that is, an mRS of 3 or less.[3–10]

Reports of cases of CPA-associated SAH describing the patients' initial electrocardiogram waveforms have demonstrated that PEA and asystole are the most common, comprising 92% to 98% of the initial waveforms, with survival rates ranging from 0% to 3%.[3,5,12] In patients with SAH, CPA may not only be caused by respiratory arrest attributed to intracranial hypertension or brainstem compression but may also be caused by lethal arrhythmias, such as VF and ventricular tachycardia.[13,14] Lethal catecholaminergic arrhythmias are induced by sympathetic hypertonia, that is, catecholamine storm, caused by SAH. PEA and asystole were the most common electrocardiogram waveforms observed in the dead patients of the present case series, suggesting that patients with PEA/asystole tended to have a more unfavorable prognosis. One patient in the present case series and 6 out of the 8 patients shown in **Table 3** had VF, suggesting that SAH with CPA owing to lethal catecholaminergic arrhythmia may be considered to be a favorable prognostic factor.

The mean time from the start of CPR to ROSC was 7.7 minutes,[5] 28.2 minutes,[12] and 32.7 minutes[3] in previous reports of patients with CPA-associated SAH, in which the outcome was death. On the other hand, **Table 3** shows that the mean time from the start of CPR to ROSC in these 8 patients was 4.6 minutes, excluding the report in which percutaneous cardiopulmonary support was introduced.[10] The mean time from the start of CPR to ROSC in our present patients was 4 minutes, which may be why the patients were able to undergo surgical treatment and achieve a favorable prognosis. A shorter time from CPA to ROSC is expected to contribute to improved patient outcomes.

According to Fukuda et al., younger age, witnesses, and arrhythmia that can be treated by defibrillation were associated with improved outcomes in stroke-associated out-of-hospital CPA patients.[15] However, note that the report by Fukuda et al. included patients with stroke, hemorrhage, and ischemia, and was not limited to SAH.[15] As the median age of experiencing SAH caused by ruptured cerebral aneurysms is 63 years,[16,17] the age reported in **Table 3** can be considered relatively young. Because 5 of the 8 patients had no comorbidities, young age and the absence of comorbidities may have affected the outcome of these CPA-associated SAH patients. In addition, CPR by a witness or bystander may have played a role in the prognosis. In the present case series, bystanders were present in all cases, and more than half of the cases in **Table 3** had bystanders. Suzuki et al. reported that of the 66 patients with CPA-associated SAH, 6 (14.6%) with a witness survived and were discharged, 5 of whom had bystanders. By contrast, all patients without a witness died.[4] Namely, the presence of a witness or bystander can be considered

a favorable prognostic factor in CPA-associated SAH. Maintaining effective cerebral blood flow in CPA patients by bystander CPR as early as possible may help improve neurological findings after ROSC, which is the only extrinsic factor that appears to be associated with a favorable prognosis, in addition to the intrinsic factors of age, underlying disease, and initial electrocardiogram waveform.

Cases of intracranial aneurysms registered in Unruptured Cerebral Aneurysm Study (UCAS) Japan are mostly patients with anterior circulation aneurysms, accounting for about 86% of all aneurysms.[18] In fact, as shown in **Table 3**, aneurysms in the anterior circulation tend to be more common, but the causal association between the posterior and anterior circulation and the occurrence of CPA or prognosis after ROSC remains unclear, and there appears to be no association among these factors in the present study. Schievink et al.[19] reported that posterior circulation aneurysm rupture increased the risk of sudden death from SAH.

Hematoma leads to secondary hydrocephalus and a mass effect, followed by increased intracranial pressure. Such a condition is ultimately thought to result in a loss of brainstem reflexes or the presence of spontaneous respiration only, defined as PRNRA grade II. In this study, we did not detect a significant difference in the occurrence of hematoma between the survivor group and the dead group, and hence the effect of hematoma on prognosis remains unclear. In the present report, ventricular drainage was not performed preoperatively or in patients receiving conservative treatment, but spinal drainage was performed after interventional radiology. The prognostic relevance of hydrocephalus in SAH patients with CPA also remains unclear. On the other hand, previous reports have shown that only patients with PRNRA grade I can survive,[3] which was the same result as observed in the present patient series. A short time to CPR and the presence of bystanders may be factors leading to a patient being PRNRA grade I.[3] Regardless of the location of the cerebral aneurysm or the hematoma of patients with SAH, those who experience CPA onset and subsequently achieve early ROSC are expected to have favorable outcomes.

PRNRA grade I may be an indication of surgical treatment for SAH patients who experience CPA onset. Patients with PRNRA grade I were reported to administer lower adrenaline doses.[3] Our results indicated that SAH patients who require no or transient use of vasopressor agents after ROSC are generally able to undergo surgical treatment, followed by favorable outcomes.

As shown in **Table 3**, the treatment strategy has increasingly tended to be coil embolization in recent years. Further studies are needed to compare endovascular treatment with craniotomy in patients with SAH experiencing CPA.

Conclusion

Our analysis of SAH patients who experienced CPA, comparing patients who survived with those who did not, suggests the following as favorable prognostic factors: lethal catecholaminergic arrhythmia on the initial electrocardiogram waveform, younger age, bystander CPR, shorter time from CPA to ROSC, PRNRA grade I, and no or transient use of vasopressors. Our results indicate that aggressive treatment may be an option for SAH patients with CPA, whose vitals are stable and are showing improvements in their neurological symptoms.

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Disclosure Statement

The authors declare that they have no conflicts of interest.

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