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Clinical paper

Clinical and cardiac features of patients with subarachnoid haemorrhage presenting with out-of-hospital cardiac arrest☆

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ABSTRACT

Background: Subarachnoid haemorrhage (SAH) is known as one of the aetiologies of out-of-hospital cardiac arrest (OHCA). However, the mechanisms of circulatory collapse in these patients have remained unclear.

Methods and results: We examined 244 consecutive OHCA patients transferred to our emergency department. Head computed tomography was performed on all patients and revealed the existence of SAH in 14 patients (5.9%, 10 females). Among these, sudden collapse was witnessed in 7 patients (50%). On their initial cardiac rhythm, all 14 patients showed asystole or pulseless electrical activity, but no ventricular fibrillation (VF). Return of spontaneous circulation (ROSC) was obtained in 10 of the 14 patients (14.9% of all ROSC patients) although all resuscitated patients died later. The ROSC rate in patients with SAH (71%) was significantly higher than that of patients with either other types of intracranial haemorrhage (25%, $n = 2/8$) or presumed cardiovascular aetiologies (22%, $n = 23/101$) ($p < 0.01$). On electrocardiograms, ST-T abnormalities and/or QT prolongation were found in all 10 resuscitated patients. Despite their electrocardiographic abnormalities, only 3 patients showed echocardiographic abnormalities.

Conclusions: The frequency of SAH in patients with all causes of OHCA was about 6%, and in resuscitated patients was about 15%. The initial cardiac rhythm revealed no VF even though half had a witnessed arrest. A high ROSC rate was observed in patients with SAH, although none survived to hospital discharge.

1. Introduction

Stroke is a cause of cardiac arrest (CA). American Heart Association (AHA)/American Stroke Association guidelines emphasize that stroke is an impending condition leading to CA.[1,2] Death from subarachnoid haemorrhage (SAH) is often sudden and different from that of ischemic stroke and other types of intracranial haemorrhage (ICH).[3–5] SAH is known to be one of the causes of out-of-hospital cardiac arrest (OHCA).[5,6] Some reports showed that SAH accounts for 4–10% of all OHCA.[6–8] On the other hand, SAH is often accompanied with abnormal cardiac findings, such as electrocardiographic and echocardiographic abnormalities and increased cardiac enzymes.[9] The mechanisms leading to CA after SAH have remained unclear, and cardiac findings of resuscitated patients have hardly been discussed before. In this study, we examined clinical and cardiac features of patients with OHCA after SAH.

2. Methods

2.1. Study population

The study protocol was reviewed and accepted by the local ethics committee of Niigata University Department of Medicine. We investigated patients with OHCA who arrived at the emergency department of Niigata University Medical and Dental Hospital, a tertiary referral center covering a local population of approximately 800,000, from April 2007 to June 2009. Cardiopulmonary resuscitation (CPR) for OHCA victims is performed in accordance with the Basic/Advanced Cardiac Life Support guidelines of 2005.[10,11] Data was recorded according to the Utsutein style which includes such factors as sex, age, initial cardiac rhythm, time course of

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Table 1
Clinical features of OHCA patients.

	SAH ($n=14$)	Other types of ICH ($n=8$)	Presumed cardiovascular aetiology ($n=101$)	p
Age (years)	67 ± 15	65 ± 14	72 ± 18	0.3
Female	10	5	41	0.05
Initial cardiac rhythm				
VF	0	0	14	
Non VF (asystole/PEA)	14 (8/6)	8 (6/2)	84 (59/25)	0.11
Witness	7	2	40	0.29
Bystander CPR	5	1	42	0.25
ROSC	10	2	23	<0.01
1-Week survival	2	0	11	
1-Month survival	1	0	11	

CPR, cardiopulmonary resuscitation; ICH, intracranial haemorrhage; OHCA, out-of-hospital cardiac arrest; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; SAH, subarachnoid haemorrhage; VF, ventricular fibrillation.

resuscitation, bystander-initiated CPR, and return of spontaneous circulation (ROSC).[12] CA was defined as the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation, according to the criteria of the AHA.[10] Head computed tomography (CT) of all patients was performed after ROSC or death for the diagnosis of hemorrhagic stroke. Traumatic ICH was excluded from this study. Hemorrhagic stroke was divided into SAH and other types of ICH.

2.2. Classification of SAH

The CT grading scale of SAH was determined according to the data from Claassen et al.[13]: grade1, minimal or diffuse thin SAH without bilateral intraventricular haemorrhage (IVH); grade 2, minimal or thin SAH with bilateral IVH; grade 3, cisternal clot without bilateral IVH; and grade 4, cisternal clot with bilateral IVH. The CT of patients with OHCA were grouped and graded by 2 experienced neurologists blinded to the patients' clinical data. The severity of the clinical presentation after ROSC was quantified by the guideline of the World Federation of Neurological Surgeons[14]: grade 1, 15 points of Glasgow Coma Scale (GCS) without motor deficit; grade 2, 13 or 14 points of GCS without motor deficit; grade 3, 13 or 14 points of GCS with motor deficit; grade 4, 7–12 points of GCS with or without motor deficit; and grade 5, 3–6 points of GCS with or without motor deficit.

2.3. Cardiac examinations

In SAH patients after ROSC, a standard 12-leads electrocardiogram (ECG), chest X-ray and echocardiogram were obtained. ECG was recorded at a paper speed of 25 mm/s and amplification of 10 mm/mV. ST segment elevation or depression, T-wave inversion, and QT interval were analyzed by 2 experienced cardiologists blinded to the patients' clinical data, as previously described.[15] The corrected QT interval (QTc) was calculated according to Bazet's formula. Two-dimensional echocardiography was performed within 6 h after ROSC to evaluate the LV wall motion abnormality and ejection fraction was measured by a modified Simpson's method.[16]

2.4. Statistical analysis

Values are expressed as mean ± standard deviation (SD). Comparisons among the 3 groups were performed using one-way ANOVA with Tukey's post hoc test. Comparisons of proportions were performed by the Chi-square test. A two-sided p-value <0.05 was considered to be statistically significant. All statistical analyses were performed with SPSS (SPSS Inc., Chicago, Illinois) for Windows (Microsoft Corp., Redmond, Washington) version 17.

3. Results

3.1. The clinical features of SAH in OHCA

During this study period, 244 patients with OHCA were transferred to our emergency department, and 67 patients (27%) achieved ROSC. Spontaneous SAH, other types of ICH, and presumed cardiovascular aetiology were identified as the cause of CA in 14, 8, and 101 patients, respectively. SAH was found in 5.7% of all OHCA. Clinical characteristics of SAH patients with OHCA are shown in

Table 2
Clinical features of patients with OHCA after SAH.

No.	Age/sex	Initial cardiac rhythm	ROSC	Witness	Bystander CPR	Initial symptoms	WFNS grade	CT grade	Outcome
1	32/F	PEA	+	+	–	Collapse after moaning	5	4	Death, 8 days
2	40/M	Asystole	+	+	–	Sudden collapse	5	4	Death, 5 days
3	62/M	PEA	+	+	–	Sudden unresposiveness	5	3	Death, 2 months
4	69/M	PEA	+	+	+	Collapse after moaning	5	4	Death, 18 h
5	71/F	PEA	+	+	+	Sudden collapse	5	3	Death, 2 days
6	71/F	Asystole	+	–	–	Vomiting	5	4	Death, 3 h
7	72/F	Asystole	+	+	–	Collapse after headache	5	4	Death, 6 h
8	78/F	Asystole	+	–	+	Unknown	5	4	Death, 40 min
9	78/F	PEA	+	+	+	Unresposiveness after vomiting	5	3	Death 16 h
10	79/F	PEA	+	–	–	Unknown	5	3	Death, 4 days
11	57/F	Asystole	–	–	–	Unknown	–	3	Not resuscitated
12	74/F	Asystole	–	–	–	Vomiting	–	4	Not resuscitated
13	81/M	Asystole	–	–	–	Unknown	–	4	Not resuscitated
14	84/F	Asystole	–	–	+	Unknown	–	4	Not resuscitated

CPR, cardiopulmonary resuscitation; CT, computed tomography; ICH, intracranial haemorrhage; OHCA, out-of-hospital cardiac arrest; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; SAH, subarachnoid haemorrhage; WFNS, World Federation of Neurological Surgeons.

Tables 1 and 2. The mean age was 67 years (aged 32–84). A tendency of female dominance in SAH was observed in comparison with other aetiologies ($p = 0.05$). All 14 SAH patients showed asystole or pulseless electrical activity (PEA), but not ventricular fibrillation (VF), though sudden collapse was witnessed in 7 patients (50%). ROSC was obtained in 10 of 14 SAH patients (71%), and SAH was found in 14.9% of all ROSC patients. The ROSC rate was significantly higher in SAH patients than in OHCA patients with other types of ICH and presumed cardiovascular aetiology ($p < 0.01$). Head CT of all 14 SAH patients showed grade 3 or 4, and clinical presentation after ROSC showed deep coma without motor deficit (Table 2). However, all resuscitated SAH patients finally died later. Of those with other types of ICH, 4 had a brainstem haemorrhage, 2 had a thalamus haemorrhage, and 2 had a subcortical haemorrhage (frontal and occipital). Although 2 patients with brainstem haemorrhage achieved ROSC, all 8 patients eventually died.

3.2. Clinical and cardiac features of resuscitated SAH patients

Clinical characteristics of resuscitated SAH patients are shown in Table 2 (No. 1–10). Of the 10 patients, the mean age was 65 years (ranging from 32 to 79) and 7 were female. CA of 7 patients (70%) was witnessed, and 5 patients (No. 1, 2, 4, 5, and 7) collapsed suddenly after the onset of SAH. Although 6 patients had bilateral IVH, diffuse and thick SAH was found on the head CT scan in all resuscitated patients. The initial ECG monitor recorded by emergency medical service showed asystole in 4 and PEA in 6 patients, while VF was not present. Table 3 shows cardiac features of resuscitated SAH patients. ECG after ROSC showed sinus rhythm in 7 and atrial fibrillation in 3 patients. The median heart rate was 115 beats/min (ranging from 86 to 157), and wide QRS was found in 3 patients. All 10 patients had ST segment deviations. Eight patients had ST elevation in aVR with ST depression in widespread leads (such as that of severe myocardial ischaemia). Three of these patients showed ST elevation $\geq$2 mV in aVR (No. 6, 9 and 10). ST depression was found in 9 patients, and large (>5 mV) depression in 3 patients (No. 2, 6, and 9). ST segment was frequently depressed in leads V4 and V5. Echocardiograms were obtained in 9 of 10 patients. LV contraction was impaired in 3 patients; akinesis of LV apical and mid ventricular segments with normal wall motion in basal segment (apical ballooning) was found in 2 (No. 1 and 7), and akinesis of mid ventricular segments with normal wall motion in both apical and basal segments (mid ventricular ballooning) was found in 1 patient (No. 3). Serial echocardiograms of 2 patients showed that these ventricular contraction abnormalities were transient and improved 7 and 14 days later. Serum creatine kinase levels on admission were normal in 9 and slightly elevated in 1 patient with normal LV contraction. Chest X-ray film was obtained in 6 patients. Pulmonary edema was present in 3 patients. Although 2 of 3 had pulmonary edema with LV contraction abnormalities, 1 patient (No. 9) had pulmonary edema without LV contraction abnormalities.

4. Discussion

In this study, we found 4 major findings: (1) in patients with OHCA after SAH, the initial cardiac rhythm recorded by emergency medical service revealed no VF even though half had a witnessed arrest, (2) the frequency of SAH in all ROSC patients was about 15%, (3) there was a high ROSC rate in SAH patients although their survival rate and neurological outcome were poor, and (4) various cardiac findings were documented in SAH patients after ROSC.

Previously, some reports suggested that SAH is one of the causes of OHCA. From earlier reports, SAH was found to be present in 4–10% of all OHCA, and about 4% of SAH patients experience CA

Table 3
Cardiac features of 10 patients with SAH after ROSC.

No.	EGG						Echocardiogram		Creatine kinase/MB fraction (IU/l)	Pulmonary edema on chest X-ray
	Rhythm	Heart rate (min)	QRS	ST elevation	ST depression	QTc (ms)	Left ventricular contraction	Ejection fraction (%)		
1	Sinus	135	Normal	I, aVR, aVL	II, III, aVF, V3, 4, 5	454	Apical ballooning	19	71/29	+
2	Atrial fibrillation	100	Normal	aVR	I, II, III, aVF, V3, 4, 5, 6	527	Normal	56	104/35	Not performed
3	Sinus	96	Normal	V2, 3, 4	None	400	Mid ventricular ballooning	29	79/44	+
4	Sinus	111	Normal	III, aVR, V1	I, II, aVL, V3, 4, 5, 6	575	Normal	70	46/22	–
5	Sinus	119	Normal	aVR, V1, 2	I, II, aVF, V4, 5, 6	497	Normal	66	135/36	–
6	Atrial fibrillation	86	Wide (RBBB)	aVR	I, II, aVF, V2, 3, 4, 5, 6	656	Normal	74	427/54	Not performed
7	Sinus	157	Normal	aVR	V2, 3, 4, 5, 6	491	Apical ballooning	38	83	Not performed
8	Sinus	115	Wide (LBBB)	[a]	III	481	Not performed	–	73/44	Not performed
9	Atrial fibrillation	132	Normal	aVR	I, II, aVF, V2, 3, 4, 5, 6	474	Normal	75	94/–	+
10	Sinus	100	Wide (RBBB)	aVR	I, II, V2, 3, 4, 5, 6	538	Normal	70	126/39	–

LBBB, left bundle branch block; RBBB, right bundle branch block.
[a] Could not be evaluated due to CLBBB creatine kinase normal value <170 IU/l.

after the onset of symptoms.[5–7,17] VF was not common in their studies. Kürkciyan et al. and Inamasu et al. reported that only 2 of 27 (7%) and 1 of 23 (4%) patients showed VF on their initial ECG, respectively.[5,7] In the present study, 50% of patients with SAH had a witnessed CA, but no VF was recorded whereas CA was witnessed in 39% and VF was recorded in 13% when the cause was cardiac in origin. There are 2 possible mechanisms of CA after SAH: CA following respiratory arrest and direct CA.[7,17,18] Respiratory suppression by a sudden increase in intracranial pressure with brainstem herniation can lead to CA in some patients. In this setting, however, patients would not show sudden collapse. In our SAH patients who had a witnessed arrest and had a high ROSC rate, CA was assumed to be cardiac in origin although VF was not documented. Thus, further examination will be needed about a hypothesis concerning the mechanisms of direct CA after SAH without VF. We also found the frequency of SAH in all ROSC patients was about 15%. Although several studies found the frequency of SAH in OHCA patients, this is the first report showing the frequency of SAH in all ROSC patients using head CT.

Several cardiac findings were observed in our resuscitated SAH patients. Abnormalities of ECG, echocardiograms, and cardiac biomarkers are well-known findings after the onset of SAH without CA.[9,19] ECG findings, such as ST-T elevation/depression, T wave inversion, QT prolongation and supraventricular/ventricular arrhythmias, have been found in more than 50% of SAH patients (58–100%).[9,20] Global or segmental LV dysfunction has been observed on left ventriculography and/or echocardiography.[9,21] These ECG and echocardiographic findings were more likely to occur with increased neurological deficits, and 58% and 52% of patients with severe neurological deficits had ECG and echocardiographic abnormalities, respectively.[9] Echocardiographic abnormalities do not always accompany ECG findings.[9] In recent reports, Takotsubo-like wall motion abnormalities (apical ballooning) were observed after SAH.[18,22] These cardiac findings were transient phenomena and irrelevant to the coronary artery disease.[21,23,24] In the present study, we first demonstrated that the frequency of cardiac abnormalities in SAH patients who experienced CA was similar to previous reports of SAH without CA, and wall motion abnormalities of all 3 patients revealed Takotsubo-like regional LV dysfunction. Although the pathophysiology of cardiac abnormalities after SAH remains uncertain, catecholamine surge following brainstem damage has been considered to produce neurogenic myocardial stunning and ECG abnormalities, the same as CA after SAH.[18,19]

There was another clinical implication. Resuscitated patients with SAH often mimic acute coronary syndrome upon cardiac examination as in our study. Thus, clinicians should carefully monitor the existence of SAH in CA because the therapy for acute coronary syndrome is completely different from that for SAH.

We had some limitations. Further large and multicenter studies are needed because our study was small and a single center one. We could not perform angiographical evaluation of the cerebral aneurysm. Thus, the relationship between the aneurysm site and CA could not be investigated, as was undertaken in previous studies.[17] Coronary angiographical evaluation was also not performed for the exclusion of ischemic heart disease.

5. Conclusions

In conclusion, the frequency of SAH in patients with all causes of OHCA was about 6%, and in resuscitated patients was about 15%. The initial cardiac rhythm revealed no VF despite the high incidence of witnessed collapse. A high ROSC rate was observed but their outcomes were poor in patients with SAH.

Conflict of interest statement

None.

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