Case Report

The prognostic value of agonal respiration in refractory cardiac arrest: a case series of non-shockable cardiac arrest successfully resuscitated through extracorporeal cardiopulmonary resuscitation

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Background: Agonal respiration following out-of-hospital cardiac arrest is associated with favorable neurological outcomes. Resuscitation using extracorporeal membrane oxygenation could contribute to achieving favorable neurological outcomes in patients with refractory cardiac arrest.

Case presentation: We report two cases of refractory cardiac arrest with non-shockable rhythms and agonal respiration; both patients were successfully resuscitated through extracorporeal cardiopulmonary resuscitation (ECPR). Both patients were breathing spontaneously upon arrival. One patient was asystolic and the other experienced pulseless electrical activity followed by ventricular fibrillation. Agonal respiration was observed in both and ECPR was implemented, leading to a favorable neurological outcome at discharge.

Conclusion: The presence of agonal respiration has the potential to confer a favorable neurological outcome in patients with refractory cardiac arrest if maintained, even when the initial cardiac rhythm is not shockable. In these cases, resuscitation should not be abandoned, and ECPR should be considered.

Key words: Agonal respiration, cardiac arrest, extracorporeal membrane oxygenation, non-shockable cardiac arrest, out-of-hospital cardiac arrest

BACKGROUND

DURING CARDIAC ARREST resulting from ventricular fibrillation (VF) and ventricular tachycardia (VT), continuous breathing is commonly observed in the first minute following the cardiac arrest episode.[1] However, shortly thereafter, the frequency of regular breathing decreases.[1,2] Cases of agonal respiration after a witnessed cardiac arrest have been reported,[1,3] suggesting that the presence of spontaneous respiration during cardiac arrest might represent the early phase of an arrest episode.

Agonal respiration appears to be a natural biomarker for the presence of brainstem activity, predicting the preservation of neurological function[2,4] and possible favorable neurological outcomes in patients with cardiac arrest.[4] Agonal respiration also facilitates respiratory gas exchange, increasing aortic, coronary, and cerebral perfusions,[5] resulting in favorable neurological outcomes in patients with cardiac arrest. Therefore, in refractory cardiac arrest, resuscitation efforts should continue while agonal respiration persists.

Resuscitation using extracorporeal membrane oxygenation (ECMO) for refractory cardiac arrest was proposed in the 1960s.[6] Several recent studies have reported better neurological outcomes in patients with refractory cardiac arrest receiving extracorporeal cardiopulmonary resuscitation

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(ECPR).[7] Although ECPR is a prospective approach, the definitive inclusion criteria for patients to receive ECPR remain unclear. Some variables including initial shockable cardiac rhythm (VF and pulseless VT), witnessed cardiac arrest, presence of bystander cardiopulmonary resuscitation (CPR) attempt, and shorter interval from cardiac arrest to ECMO are suggested for the successful introduction of ECPR.[8,9] Based on these previous studies, in cases of cardiac arrest with non-shockable cardiac rhythm and unwitnessed cardiac arrest, ECPR should not be initiated. The prognostic significance of persisting agonal respiration during CPR as a potential candidate of ECPR has not been described.

In some cardiac arrest patients, despite the persistence of agonal respiration during CPR a return of spontaneous circulation (ROSC) never occurs, although cerebral function might be present during CPR. Thus, it is not clear whether introducing ECPR in such patients might lead to favorable outcomes. Here, we report two cases of refractory cardiac arrest in patients with non-shockable rhythms who maintained agonal respiration and were subsequently successfully resuscitated through ECPR.

CASE PRESENTATION

Case 1

A 73-YEAR-OLD MAN collapsed in a crowded public place. A member of the public immediately started chest compressions and called emergency medical services (EMS). When EMS arrived, the man was in cardiac arrest with asystole. His respiration, however, remained. On admission, the patient had not achieved ROSC and still had an asystole cardiac rhythm, but maintained spontaneous respiration. The cardiac arrest was judged as refractory because more than 30 min had passed since its onset and adrenaline administration was not useful to achieve ROSC. We decided to carry out ECPR. After ECMO was started, the patient could follow simple orders and ROSC was achieved 62 min after the initiation of ECMO. After an intra-aortic balloon pump (IABP) was inserted, coronary angiography was carried out and showed that the coronary arteries had no significant stenosis. The patient was conscious and had a low heart rate on admission to the intensive care unit. Hence, therapeutic hypothermia was not administered. Based on an electrocardiogram after the ROSC, he was diagnosed with complete atrioventricular block (Table 1).

Although the patient's cardiac output increased over time, he developed pulmonary edema and bilateral pleural effusion. High positive end-expiratory ventilation pressure was needed to resolve the insufficient oxygenation situation for several days, until the patient's hemodynamic and respiratory status was satisfactory. The ECMO and IABP were removed on days 5 and 6, respectively. He was transferred

Table 1. Details of two cases of refractory cardiac arrest with non-shockable rhythms and agonal respiration

	Case 1	Case 2
Age (years)	73	43
Sex	Male	Male
Witness of collapse	Yes	No
Bystander CPR attempt	Yes	No
Presence of agonal respiration upon arrival of EMS	Yes	Yes
Initial cardiac rhythm	Asystole	PEA
Cardiac rhythm at admission	Asystole	VF
Time from first call to the dispatcher to hospital admission (min)	30	35
No-flow time (min)†	0	Unknown
Low-flow time (min)‡	60	35
Adrenaline administration before ECMO initiation	Yes	Yes
Therapeutic hypothermia	No	Yes
Intra-aortic balloon pumping	Yes	Yes
Duration of ECMO (days)	5	8
Etiology of cardiac arrest	Complete atrioventricular block	Dilated cardiomyopathy
Survival at discharge	Yes	Yes
Cerebral performance category	2	2

†Defined as the delay between diagnosis of cardiac arrest and onset of cardiopulmonary resuscitation.
‡Defined as the delay between onset of cardiopulmonary resuscitation and initiation of extracorporeal membrane oxygenation (ECMO).
CPR, cardiopulmonary resuscitation; EMS, emergency medical services; PEA, pulseless electrical activity; VF, ventricular fibrillation.

to another hospital for rehabilitation on day 29 with a cerebral performance category of 2.

Case 2

A 43-year-old man was found unresponsive by a colleague who came to his residence as he had not shown up for work. On arrival of EMS, the patient was in cardiac arrest and showed pulseless electrical activity (PEA). Although intubation was undertaken, and adrenaline was given during transportation, ROSC was not achieved. On admission, the patient was showing VF with agonal respiration. Because of the refractory cardiac arrest, we decided to initiate ECPR; ROSC was achieved 4 min after starting ECMO. After coronary angiography and computed tomography, the patient was admitted to the intensive care unit with an inserted IABP and was treated with therapeutic hypothermia. A diagnosis of dilated cardiomyopathy was made (Table 1).

The patient's hemodynamic status gradually improved; ECMO was discontinued and the IABP was removed on days 8 and 9, respectively. He was moved to a rehabilitation ward on day 63 and transferred to another hospital for further rehabilitation on day 100 with a cerebral performance category of 2.

DISCUSSION AND CONCLUSIONS

IN PATIENTS WITH refractory cardiac arrest, the presence of agonal respiration might be linked to favorable neurological outcomes, even when the patient's cardiac rhythm is not initially shockable (e.g., asystole or PEA). In this situation, resuscitation should not be abandoned and ECPR should be considered.

The initial cardiac rhythm after an arrest is associated with the patients' prognosis. Cardiac arrest due to VF/VT is associated with better outcomes than one due to PEA/asystole, as the former is thought to be predominantly caused by ischemic cardiac disease,[10] whereas the etiology of the latter is commonly hypoxia, non-ischemic cardiac disease, or intracranial hemorrhage,[11] and has a worse prognosis than that due to cardiac disease. Asystole is considered a final rhythm degenerated from VF/VT and PEA and represents a terminal cardiac rhythm state signifying poor prognosis.[10,12] The prognosis of a PEA/asystole arrest is therefore worse than that of a VF/VT arrest. However, whereas cardiac arrest rhythm does not directly reflect cerebral function, agonal respiration partly does. For this reason, persisting agonal respiration is more important than the initial cardiac arrest rhythm in predicting a patient's neurological outcome.

As mentioned above, in the setting of preserving agonal respiration, the chances of achieving a favorable neurological outcome seem to be higher with agonal respiration than without it, even in cases of non-shockable cardiac arrest.[4] Extracorporeal membrane oxygenation produces definite systemic blood flow. However, it is impossible to accurately determine whether systemic blood flow should be restarted or not by continuing standard advanced cardiovascular life support alone, as it depends on the probability. Additionally, administration of adrenaline implemented with standard advanced cardiovascular life support could sacrifice microvascular cerebral blood flow and might result in worse neurological outcome.[13] Hence, we recommend that ECPR should be selected when agonal respiration is preserved during CPR.

In conclusion, agonal respiration has the potential to lead to favorable neurological outcomes in patients with refractory cardiac arrest, even if the initial cardiac rhythm is not shockable (e.g., asystole or PEA). Therefore, resuscitation should not be halted and ECPR should be carried out in patients who maintain agonal respiration after a cardiac arrest.

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DISCLOSURE

Approval of the research protocol: Formal ethical approval from the University Research Ethics Board was not required for the completion of this study.
Informed consent: Written informed consent for publication of this case report was obtained from the patients.
Registry and registration no. of the study: N/A.
Animal studies: N/A.
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