Case Report

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Enabling the control of reperfusion parameters in out-of-hospital cardiac arrest: First applications of the CARL system

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Abstract

Introduction: There is increasing evidence for extracorporeal cardiopulmonary resuscitation (ECPR) as a rescue therapy for selected patients in refractory cardiac arrest (CA). Besides patient selection, the control of reperfusion parameters is of eminent importance. Especially in out-of-hospital CA, monitoring and individualized, targeted reperfusion remains a great challenge for emergency personnel. The CARL® system is designed to enable an early control of a variety of reperfusion parameters and to pursue a targeted reperfusion strategy in ECPR.

Case presentation: We report the first 10 ECPR applications of the CARL® system in Regensburg, Germany. Early blood gas analysis, oxygen titration and pressure monitoring were feasible and enabled an individualized and targeted reperfusion strategy in all patients. After suffering from refractory CA and prolonged resuscitation attempts, five out of the first 10 patients survived and were successfully discharged from the hospital (CPC one on hospital discharge).

Conclusion: Application of the CARL® system contributed to early monitoring and control of reperfusion parameters. Whether targeted ECPR may have the potential to improve outcomes in refractory OHCA remains the subject of future investigations.

Keywords

extracorporeal cardiopulmonary resuscitation, out-of-hospital cardiac arrest, targeted reperfusion, ischemia-reperfusion injury

Introduction

Across Europe, depending on the region, only 1-18% of all patients with an out-of-hospital cardiac arrest (CA), who receive cardiopulmonary resuscitation (CPR), survive and can be discharged from the hospital alive.[1] A great number of those patients suffer from neurological sequelae.[2] An increasing body of evidence suggests that the use of extracorporeal membrane oxygenation (ECMO) in cardiopulmonary resuscitation - a method called extracorporeal cardiopulmonary resuscitation (ECPR) - may improve survival after CA.[3] Therefore, ECPR is already acknowledged by the current guidelines of the European Resuscitation Council: "We suggest that ECPR may be considered as a rescue therapy for selected patients with cardiac arrest when conventional CPR is failing in settings in which it can be implemented (weak recommendation, very low certainty of evidence".[4] Besides patient selection, the control of reperfusion parameters is of eminent importance to enable a neurological recovery after CA.[5,6]

Especially in out-of-hospital CA, monitoring and thus individualized, targeted reperfusion remains a great

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challenge for emergency personnel. The CARL® system (Resuscitec GmbH, Freiburg, Germany) is the first ECMO system specifically designed for application in resuscitation outside of an intensive care unit or an operation room. The core system consists of the CARL® Controller, which includes a two-pump reperfusion set, and CARL® MOX, a mobile gas blender. The system can be amended by a mobile cooling unit (CARL® Cooler), which can be operated without an external energy source. The combination of CARL® Controller with CARL® MOX enables an immediate control of a variety of reperfusion parameters (i.e. flow, arterial pressure, temperature, venous hemoglobin, oxygen saturation and built-in blood gas analysis) and thereby empowers the ECMO team to pursue a targeted reperfusion strategy in ECPR from the very start[7–9] (Figure 1). By mixing ambient air with oxygen (using the blower technology), CARL® MOX can work independently of an external air supply and needs only an oxygen source for oxygen titration in sweep gas. Besides an oxygenator (hilite 7000 LT, Xenios AG, Heilbronn, Germany), the CARL® reperfusion set contains two diagonal pumps (DP3, MEDOS Medizintechnik AG, Stolberg, Germany), which can be used to generate pulsatile flows and therefore higher reperfusion pressures. To improve the transportability of the CARL® system, weight reduction is achieved by using a carbon frame and other low-weight components (weight CARL® Controller: 17.6 kg, CARL® MOX: 8.9 kg). In Regensburg, out-of-hospital ECPR is always performed by at least a team of two: A physician, who performs the cannulation and a cardio technician, who oversees the ECMO system. Inclusion and exclusion criteria are based on the German interdisciplinary consensus statement, which is supported by the German Resuscitation Council.[10] The ECPR team and its strategy have been described previously.[11–13]

Case presentation

We present data of the first 10 consecutive patients who were treated with the CARL® system after out-of-center CA in Regensburg, Germany (Figure 1). Nine patients suffered out-of-hospital CA and one patient suffered CA in an external hospital. The data was collected from the Regensburg ECLS Registry, which was approved by the

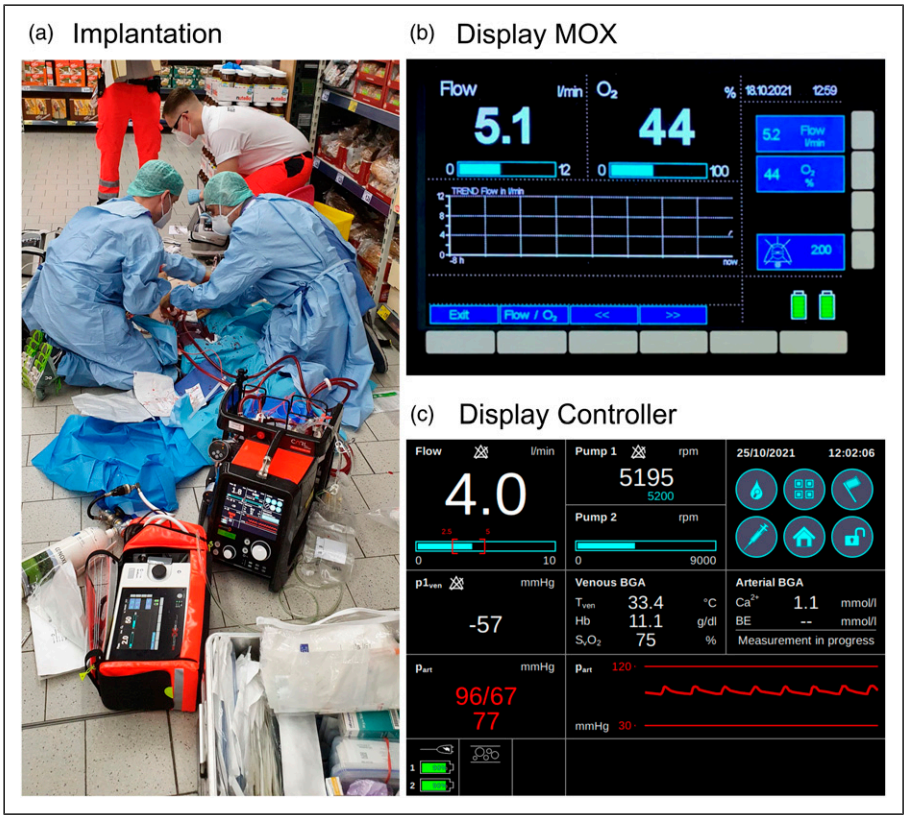

Figure 1. (a) Application of the CARL® system (CARL® controller and CARL® MOX) in a supermarket. (b) Display of CARL® MOX. (c) Display of CARL® controller with online monitoring of reperfusion parameters (i.e. flow, pulsatility, arterial pressure, temperature, venous and arterial blood gas analysis).

University of Regensburg Ethics Committee (number 21-2401-104). The need to obtain an informed consent was waived due to the retrospective design.

Table 1 shows general patient and case characteristics. Seven of the 10 patients were male. The median age of the patients at the time of cardiac arrest was 54.5 years [interquartile range (IQR): 48.5–60.2 years]. Nine patients suffered from cardiac arrest outside of a hospital (four patients at home, four patients in the workplace, one patient on the street while driving), while one patient underwent surgery due to a kidney tumor in an external hospital. Nine out of the 10 patients were witnessed by either bystanders or medical personnel during their collapse. Bystander CPR was performed in all cases. Eight patients displayed ventricular fibrillation as the initial rhythm in the first electrocardiogram. A mechanical resuscitation device was only used in one case. Median duration from collapse (or in case of the unwitnessed arrest from start of CPR) until start of the CARL® Controller was 39.0 min [IQR: 30.5–59.7 min]. All patients underwent femoro-femoral cannulation. In three cases a distal leg perfusion was added after return to the hospital. Acute myocardial infarction was identified as primary cause for the CA in four cases. Four cases showed no pathological findings in the coronary angiography and were suspected to have a rhythmogenic or otherwise unknown pathogenesis (classified as "unknown" in Table 1).

Table 2 shows patient parameters at hospital admission and neurological outcome. Three patients were

Table 1. Patient/case characteristics.

#	Sex	Age [years]	Distance to center [km]	Arrest location	Pathogenesis	Witnessed arrest	Bystander CPR	First rhythm	mCPR	Time from arrest/initial call to CARL [min]	First recorded NIRS on scene
1	Male	20	32	Workplace	Unknown	Yes	Yes	VF	Yes	85	27
2	Female	62	5	External hospital	PulmEmb	Yes	Yes	Asys	No	65	15
3	Male	53	12	Home	Drowning	Yes	Yes	Asys	No	50	n.a.
4	Male	77	17	Home	AMI	Yes	Yes	VF	No	25	38
5	Male	47	4	Workplace	AMI	Yes	Yes	VF	No	35	52
6	Male	55	26	Home	Unknown	Yes	Yes	VF	No	63	33
7	Female	41	24	Street	Unknown	Yes	Yes	VF	No	30	60
8	Male	64	10	Home	AMI	No	Yes	VF	No	30	52
9	Female	55	4	Workplace	AMI	Yes	Yes	VF	No	32	62
10	Male	54	8	Workplace	Unknown	Yes	Yes	VF	No	43	49

AMI: acute myocardial infarction, Asys: asystolie, CPR: cardiopulmonary resuscitation, mCPR: mechanical CPR, n.a.: not available, NIRS: near-infrared spectroscopy, PulmEmb: pulmonary embolism, VF: ventricular fibrillation.

Table 2. Parameters at hospital admission/outcome.

#	At hospital admission					Duration [days]			At hospital discharge
	Temp [°C]	pH (arterial)	Lactate [mg dl^{-1}]	MAP [mmHg]	S_vO_2 [%]	On CARL	On ICU	In hospital	CPC
1	33.4	7.19	144	83	75	0	n.a.	0	5
2	32.5	6.97	249	67	62	0	n.a.	0	5
3	28.9	7.13	180	61	87	0	n.a.	0	5
4	33.0	7.47	39	66	86	2	5	12	1
5	31.9	7.06	137	60	86	1	1	1	5
6	34.2	7.36	86	80	73	4	33	39	1
7	33.9	7.42	26	89	88	2	9	23	1
8	33.1	7.39	59	55	86	2	2	2	5
9	32.8	7.36	40	95	93	3	7	12	1
10	33.0	7.49	59	65	89	3	11	15	1

CPC: cerebral performance category, ICU: intensive care unit, MAP: mean arterial pressure, n.a.: not applicable, S_vO_2: venous oxygen saturation, Temp: temperature.

declared dead in the emergency department after hospital admission due to therapy-limiting diagnoses (i.e. retroperitoneal bleeding and miscannulation). As mentioned above three of the remaining seven patients suffered from leg ischemia. All of these cases could be successfully treated by implementation of a six French distal perfusion catheter. No device related complication or technical malfunction appeared. The median venous blood temperature at hospital admission was 33.0°C [IQR: 32.6–33.3°C]. Early oxygen titration and invasive pressure monitoring enabled an individualized reperfusion strategy in each patient already out of hospital and resulted in a median arterial pressure of 66.5 mmHg [IQR: 62–82.2 mmHg], a mean venous oxygen saturation of 86.0% [IQR: 77.7–87.7%], an arterial pH of 7.36 [IQR: 7.14–7.41] and a median lactate of 72.5 mg dl^{-1} [IQR: 44.7–142.2 mg dl^{-1}] at hospital admission. All survivors showed an arterial pH above 7.3 at hospital admission. Five out of the 10 patients survived and were classified as cerebral performance category 1. The surviving patients stayed on intensive care unit for a median time of 9 days [IQR: 7–11 days] and were discharged from the hospital after a median of 15 days [IQR: 12–23 days].

Conclusion

The application of the CARL® system in ECPR is feasible and enables an extended control of reperfusion parameters (i.e. arterial pressure, oxygen saturation and built-in blood gas analysis) in in- and out-of-hospital settings. Early monitoring of reperfusion parameters allows the ECPR team to pursue an individualized and targeted reperfusion strategy. We believe, that immediate targeted ECPR has the potential to improve outcomes in refractory CA, but this belief has still to be verified by randomized trials.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: CB is CTO and shareholder of Resuscitec GmbH, a start-up company of the University Medical Center Freiburg. JP is part-time employee of Resuscitec GmbH. The other authors declare that they have no competing interests.

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