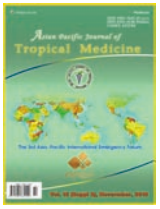

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Practice of extracorporeal cardiopulmonary resuscitation in China after publication of the 2015 AHA guidelines for resuscitation: A multi-institution survey

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ABSTRACT

Objective: To investigate the current practice of extracorporeal cardiopulmonary resuscitation (ECPR) for Chinese cardiac arrest patients after the publication of 2015 American Heart Association guidelines for cardiopulmonary resuscitation.

Methods: A questionnaire was distributed to healthcare providers of emergency departments (EDs) and/or Intensive Care Units (ICUs) across 52 hospitals in China from August to November 2016. Data collection ended in February 2017. The questionnaire included three parts: (1) characteristics of the departments and the respondents; (2) knowledge about ECPR; (3) practice of ECPR in cardiac arrest patients (case volume, inclusion/exclusion criteria, ECPR procedure). The characteristics of the departments/hospitals were only answered by the head of the department.

Results: A total of 1 952 (86.8%) respondents fulfilled the survey. Only 2.5% of the respondents from 3 of 52 hospitals performed ECPR. Among the three hospitals, the case number of ECPR were ≤5 per year and none of them had written ECPR procedures. Only one hospital had formal inclusion/exclusion criteria. The inclusion criteria included age between 18 to 60 years, suspected cardiogenic cardiac arrest, beginning of cardiopulmonary resuscitation <5 min after cardiac arrest and duration of cardiopulmonary resuscitation >10 min. The top three reasons for the nonuse of ECPR were unknown fields (31.2%), potential ECMO-related side effects (26.9%) and cost (18.7%).

Conclusions: ECPR for cardiac arrest patients are not well understood by healthcare providers in the emergency department or ICUs and its application is still in the early stage in China. Educational training and other interventions are needed to promote the clinical practice.

1. Introduction

The survival rate till discharge is not high and the neurological outcome remains poor among patients with cardiac arrest (CA) despite improvements in conventional cardiopulmonary resuscitation (CCPR)[1,2]. Previous studies have revealed that the survival rate till discharge ranged from 7% to 26% in CA patients[3,4]. But if the duration of cardiopulmonary resuscitation (CPR) exceeds 10 min, the survival rate declines greatly[3]. It is difficult for CA patients to have a return of spontaneous circulation (ROSC)[4]. For patients with refractory CA, the extracorporeal membrane oxygenation (ECMO)-assisted CPR (ECPR) is a therapeutic choice and its

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application is increasing all over the world.

It was reported that only 30% to 40% of normal blood flow was provided to the target organ even when CCPR was performed under optimal conditions[5]. ECPR can provide near-full or full cardiopulmonary support by circulating blood outside the body with extracorporeal oxygenation. Observation studies have shown an improved survival rate and better neurological outcomes in CA patients receiving ECPR compared to CCPR[6,7]. On the basis of these findings, ECPR is recommended as a mechanical cardiopulmonary support for patients with reversible etiology of CA according to the 2015 American Heart Association (AHA) guidelines for CPR.

The application of ECPR in CA patients has rarely assessed in China. So we perform this investigation to determine the knowledge about ECPR and the practice of ECPR among healthcare providers in emergency departments (EDs)/ICUs in China.

2. Materials and methods

2.1. Study design and data collection

This was a cross-sectional multicenter study. Hospitals were selected by multistage convenience sampling. First, 10 representative provinces that were well geographically distributed were selected. Among the 10 provinces, 5 provinces were selected from developed east and south of China, 3 provinces were selected from underdeveloped west and north of China, 2 provinces were selected from the middle of China). Then at least one university-affiliated hospital and hospitals in the second- and third-tier cities were chosen based on the number of the province's hospitals in an attempt to cover hospitals with different developing levels. Among those hospitals, we were more likely to choose hospitals that have a good cooperation with us for high response rate and high-quality control. Finally, 52 hospitals were included, of which 5 are level Ⅱ and 47 are level Ⅲ hospitals. All healthcare providers in the EDs and/or ICUs participated in the survey. An anonymous questionnaire was distributed to the participants. Informed consent was obtained from all participants.

The questionnaire was developed by a senior emergency physician and was discussed three times by an expert team consisting of epidemiologists and emergency specialists experienced in CA management and ECPR. The questionnaire included three parts: (1) Characteristics of the departments and the respondents; (2) knowledge about ECPR; (3) practice of ECPR in CA patients (case volume, inclusion/exclusion criteria, ECPR procedure). The characteristics of the departments/hospitals were only answered by the head of the department. The test-retest reliability and split-half reliability of the questionnaire were tested. A total of 100 healthcare providers fulfilled the questionnaire two times in an interval of two weeks. The Pearson correlation coefficient was 0.85. Split-half reliability was analyzed after data collection and the Guttman split-half coefficient of the questionnaire was 0.94. The questionnaires were sent to the participants from August to November 2016. Data collection ended in February 2017. All the procedures were in accordance with the ethical standards of the institutional committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the local ethics committee (Peking university third hospital ethics committee, the committee's reference number: 2017-147-02). And the study has been approved by all participating centers.

2.2. Statistical methods

The data were analyzed by SPSS 20.0. Data were tested for normality using the Shapiro-Wilk Normality Test. Quantitative variables were expressed as mean±standard deviation when following a Gaussian distribution or median (interquartile range) otherwise. Qualitative variables were expressed as frequencies.

3. Results

Finally, 64 departments including 49 EDs and 15 ICUs in 52 hospitals participated in the study. A total of 2 250 questionnaires were sent and the response rate was 86.8%. General characteristics of departments and respondents are described in Table 1. Doctors account for nearly 50% of respondents. Regardless of doctor or nurse, the distribution of different titles was appropriate. A total of 59.4% of the departments had more than 300 CA patients admitted during one year prior to the study.

The awareness of ECPR in CA patients is shown in Table 2. A total of 63.0% of respondents had knowledge about ECMO and only 15.9% for ECPR. More than 80% believed that ECPR could improve the survival rate and neurological outcomes of CA patients comparing with CCPR. The indication of ECPR was considered as reversible underlying etiology by 30.3% of respondents, cardiogenic arrest by 28.1%, middle-aged or young patients by 24.7% and duration of CPR more than 10 min by 16.7%.

The practice of ECPR in CA patients is shown in Table 3. Only 3 of 52 hospitals had performed ECPR in CA patients. Among these three hospitals, the ECPR team was available 24 h×7 d in only 1 hospital and none of them had written ECPR procedure. Only 1 hospital (Peking university third hospital) had formal inclusion/exclusion criteria as shown in Table 4. The number of ECPR cases in the performed hospitals were all less than 5 during the one-year period prior to the study. Only 2.5% of respondents reported that they had applied ECPR to CA patients. The top three reasons for the nonuse of ECPR were unknown fields (31.2%), potential ECMO-related side effects (26.9%) and expensive cost (18.7%) (Figure 1).

Table 1. Characteristics of departments and respondents [*n* (%)].

Type of departments (*n*=64)	
EDs	49 (76.6)
ICUs	15 (23.4)
Type of respondents (*n*=1 883)	
Doctors	905 (48.1)
Nurses	978 (51.9)
Title of doctor (*n*=866)	
Resident doctor	421 (48.6)
Attending doctor	301 (34.8)
Associate chief physician	104 (12.0)
Chief physician	40 (4.6)
Title of nurse (*n*=826)	
Nurse	421 (51.0)
Nurse-in-charge	301 (36.4)
Associate chief nurse	104 (12.6)
Admission of CA patients among different departments (*n*=64)	
<100 CA patients admitted	8 (12.5)
100-300 CA patients admitted	18 (28.1)
>300 CA patients admitted	38 (59.4)

ED: Emergency department; CA: Cardiac arrest.

Table 2. Healthcare providers' understanding of ECPR [*n* (%)].

Knew the knowledge of ECMO (*n*=1 805)	
Yes	1 137 (63.0)
No	668 (37.0)
Knew the knowledge of ECPR (*n*=1 884)	
Yes	299 (15.9)
No	1 585 (84.1)
Which of the following do you think is the indication of ECPR? (*n*=773)	
Middle-aged or young patients	191 (24.7)
Cardiogenic arrest	217 (28.1)
Reversible underlying disease of CA	234 (30.3)
ROSC more than 10 min of CPR	129 (16.7)
Others	2 (0.3)
Compared with CCPR, do you think ECPR can improve the survival rate of CA patients (*n*=299)	
Yes	254 (85.6)
No	26 (2.4)
Unknown	19 (11.1)
Compared with CCPR, do you think ECPR can improve the neurological outcomes of CA patients (*n*=297)	
Yes	257 (86.5)
No	7 (2.4)
Unknown	33 (11.1)

ECMO: Extracorporeal membrane oxygenation; CPR: cardiopulmonary resuscitation; ECPR: Extracorporeal cardiopulmonary resuscitation; CA: Cardiac arrest.

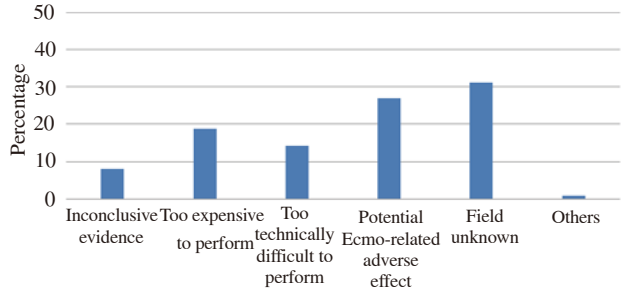

Figure 1. Reasons for nonuse of ECPR for CA patients in respondents (*n*=892 respondents; 2 465 answers expressed as percentage of response). ECPR: Extracorporeal cardiopulmonary resuscitation; CA: Cardiac arrest.

Table 3. Practice of ECPR in CA patients [*n* (%)].

Implementation of ECMO (*n*=52)	
Yes	16 (30.8)
No	36 (69.2)
If yes, is the ECMO team available 24 h×7 d? (*n*=16)	
Yes	12 (75.0)
No	4 (25.0)
Cases of ECMO performed for CA patients during one year period prior to the present study(*n*=16)	
<5	11 (68.8)
5-10	3 (4.7)
10-20	1 (0.6)
20-30	1 (0.6)
>30	0 (0.0)
Implementation of ECPR in CA patients (*n*=52)	
Yes	3 (5.8)
No	49 (94.2)
If yes, is the ECPR team available 24 h×7 d? (*n*=3)	
Yes	1 (33.3)
No	2 (66.7)
Does the hospital have formal inclusion and exclusion criteria for ECPR in CA patients? (*n*=3)	
Yes	1 (33.3)
No	6 (66.7)
Use of a written ECPR procedure (*n* =3)	
Yes	0 (0.0)
No	3 (100.0)
The cases of ECPR performed for CA patients during one year period prior to the present study (*n*=3)	
<5	3 (100.0)
5-10	0 (0.0)
10-15	0 (0.0)
Implementation of ECPR in CA patients (*n*=1 800)	
Yes	48 (2.5)
No	1 752 (97.5)
Cases of ECPR performed for CA patients during one year period prior to the study	
<5	48 (100.0)
5-10	0 (0.0)
10-15	0 (0.0)

ECMO: Extracorporeal membrane oxygenation; ECPR: Extracorporeal cardiopulmonary resuscitation; CA: Cardiac arrest.

Table 4. Inclusion/exclusion criteria of ECPR in Peking university third hospital.

Inclusion criteria	Exclusion criteria
Age 18-65	Disease in the terminal stage
CPR >10 min without ROSC	Previous severe neurologic damage
Beginning of CPR <5 min after CA	Current intracranial hemorrhage
Suspected cardiogenic cardiac arrest	Serious infectious diseases
	Severe bleeding tendency
	Pregnant and lactating women

ECPR: Extracorporeal cardiopulmonary resuscitation; ROSC: Return of spontaneous circulation.

4. Discussion

In the 1960s, ECPR was introduced to improve survival rate and neurological outcomes[8]. For decades, advances in ECMO technologies and devices have made it a more powerful resuscitation tool. The Extracorporeal Life Support Organization international

registry reports that until 2016 there are more than 9 000 ECPR patients from 329 centers[9]. The ECPR patients have increased by greater than ten-fold since 2004 all over the world and increased dramatically since 2008 when Chen *et al.* reported that ECPR provided better outcomes for CA patients as compared to CCPR[10]. In America, emergency ECPR programs were used to reduce the initiation time of ECPR although most of the programs were less than 5 years old and performed ≤3 cases per year[11]. ECPR was started in the late 1990s and developed rapidly in Taiwan. The ECPR cases were as high as 230 in a 5-year period between 2007 to 2012 in only one hospital[12].

In 2010, it was concluded by the International Liaison Committee on Resuscitation guidelines that there was very little evidence as to whether the routine use of ECPR for CA should be recommended. Given the prevalence of ECPR and broad evidence for improved survival, the 2015 AHA guidelines recommended that ECPR should be considered for CA patients with suspected and potentially reversible etiology (Class Ⅱb, C).

But ECPR is still in the early stage in mainland China. Our study showed that ECPR was an unfamiliar field for more than 80% of the healthcare providers in EDs/ICUs who were more likely to care for CA patients. The top reason for the nonuse of ECPR was the unknown field. Only 3 in 52 hospitals had implemented ECPR in practice and the cases performed per year were all less than 5. Only 2.5% of the respondents had applied ECPR for CA patients. It reveals that there is a huge gap between the ECPR practice and recommendation by guidelines in China, and healthcare providers fail to catch up with clinical developments, reflecting the need for education to promote ECPR awareness and practice.

In our study, more than 80% of the respondents believe that ECPR can improve survival and neurological outcomes when compared with CCPR. In fact, more and more evidence supports this view. Several factors, including rapid recognition of CA, CPR on time, the time to ROSC, rapid defibrillation, initial rhythm as well as comprehensive post-CA care, are related to the outcomes of CA patients[13,14]. ECPR has the potential to modify some of these factors theoretically. ECPR provides definitive and immediate circulatory support to the vital organs which are not possible in CCPR, thereby reducing the ischemic damage. Improved perfusion of a failing myocardium may increase the success rate of defibrillation and ROSC.

In fact, it is increasingly clear that ECPR has saved the life of thousands of CA patients. According to the Extracorporeal Life Support Organization registry, the cumulative survival rate of 3 995 adult CA patients receiving ECPR was 28%[9]. Some observational studies had reported survival till discharge in CA patients with ECPR ranged widely from 20%-46%[15,16]. Although a randomized controlled study has not been performed, well propensity-score matching analyses suggested that ECPR could improve survival and neurological outcomes of CA patients when compared with CCPR[6,7,10]. In addition, the benefit of ECPR was confirmed in two recent meta-analyses of studies. Although little difference of survival in OHCA patients, improved survival to discharge and better neurologic outcome at 3-6 months in patients receiving ECPR for IHCA was observed[17,18]. Maybe ECPR led to more favorable outcomes in IHCA patients than in OHCA patients because the latter were more likely to have variable-quality CPR and a longer duration to initiation of ECPR. But when ECPR can be performed immediately, the outcomes of OHCA patients may be similar to that of IHCA patients[7,12], especially when combined with other treatments such as target temperature management[19].

To date, there are no standardized protocols for the use of ECPR, making the use of this therapy a complex clinical challenge. In general, old age is one of the factors that make the physician reluctant to initiate ECPR. In our study, age <65 was an inclusion criterion in the hospital which had formal inclusion and exclusion criteria. Although most studies considering age as an inclusion criterion, the age range was variable ranging from less than 70 to less than 80[20]. With the improvement of the ECMO's technologies and devices, the age criterion of ECPR may extend to an older upper limit.

One of the difficult decisions to make is when to initiate ECPR. The duration of pre-ECPR resuscitation which was negatively associated with outcomes varies in observational studies, ranging from 10-30 min[20]. Similar to our study, more and more studies and ECPR centers had set CPR >10 min without ROSC as an inclusion criterion on the basis of Chen *et al.*[6,10,20]. The rate of ROSC decreases with prolonged CPR. More than half of CA patients recovered within 10-15 min, and the most majority within 20 min[21,22]. Maybe decision making within 10 min after CCPR would allow for ECPR within the allowable time limits and allow identification of patients with a low chance of ROSC[3].

The AHA proposed that ECPR for patients should be considered when the duration of the no-flow is brief. As in the present study and previous investigations, the no-flow duration should be less than 5 min. It was especially challenging for OHCA, so many centers had set witnessed CA or bystander CPR as an indication of ECPR[16]. Etiologies of ECPR were heterogeneous ranging from hypothermia to refractory arrhythmias[3]. But ECPR patients with underlying cardiac pathology demonstrated superior survival to CA patients with non-cardiac reasons[23]. Because ECPR was in the early stage, the hospital in our study only enrolled suspected cardiogenic cardiac arrest. In conclusion, careful selection of reasonable patients guarantees optimal use of medical resources and a better outcome.

We found that the top three reasons for the nonuse of ECPR were unknown fields, potential ECMO-related side effects, and expensive cost. ECPR did have complications. Severe bleeding of an internal organ such as gastrointestinal tract (4.0%) or the central nervous system (2.2%) and life-threatening complications such as disseminated intravascular coagulation (4.1%) and cardiac tamponade (5.4%) was reported[24]. In addition, ECPR is a highly costly intervention. The cost was variable and related to many factors, including advanced ECLS equipment, broad multi-disciplinary team involvement, and increased length of care[25]. Part of the cost of ECPR was not covered by insurance in China, and most patients can't afford the huge expense.

Our study used convenience sampling rather than random sampling

in order to get a high response rate. It did have disadvantages of convenience sampling, although selected hospitals were geographically well distributed. The survey might have been subject to bias as level Ⅲ hospitals were over-represented, which makes the degree of ECPR awareness and practice reflected in our survey an optimistic perspective. The true proportion might be lower than that reported in this study.

ECPR for CA patients has not been well understood by healthcare providers in EDs or ICUs and its application is still in the early stage in China. Educational actions and other interventions are needed to promote knowledge awareness and clinical practice.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Author's contribution

L.F.D., H.X.G., Q.B.M. have made contributions to the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article and final approval of the version. B.L.G., J.Z.Y., Y.H.M., Y.X.Z. have made important contributions to the conception and design of the study and acquisition of data.

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