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Clinical paper

Prognostic impact of the conversion to a shockable rhythm from a non-shockable rhythm for patients suffering from out-of-hospital cardiac arrest

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Abstract

Objective: For patients suffering from an out-of-hospital cardiac arrest (OHCA), having an initial shockable rhythm is a marker of good prognosis. It has been suggested as one of the main prognosticating factors for the selection of patients for extracorporeal resuscitation (E-CPR). However, the prognostic implication of converting from a non-shockable to a shockable rhythm, as compared to having an initial shockable rhythm, remains uncertain, especially among patients that can otherwise be considered eligible for E-CPR. The objective of this study was to evaluate the association between the initial rhythm and its subsequent conversion and survival following an OHCA, for the general population and for E-CPR candidates.

Methods: This study used a registry of OHCA in Montreal, Canada. Adult patients suffering from a non-traumatic OHCA for whom the initial rhythm was known were included. The association between the initial rhythm and its subsequent conversion or not and survival to discharge was assessed using a multivariable logistic regression.

Results: Of 6681 included patients, 1788 (27%) had an initial shockable rhythm, 1749 (26%) had pulseless electrical activity (PEA) and no subsequent shockable rhythm, 295 (4%) had PEA and a subsequent shockable rhythm, 2694 (40%) had asystole and no subsequent shockable rhythm, and 155 (2%) asystole and a subsequent shockable rhythm. As compared to patients having an initial shockable rhythm, patients in all other groups had significantly lower odds of survival to hospital discharge ($p < 0.001$ for all comparisons). Univariate analyses were performed for E-CPR candidates. Among these 556 (8%) patients, more patients with an initial shockable rhythm survived than patients in all other groups ($p < 0.001$ for all comparisons).

Conclusions: The initial rhythm remains a much better prognostic marker than subsequent rhythms for all patients suffering from an OHCA, including in the subset of potential E-CPR candidates.

Keywords: Out-of-hospital cardiac arrest, Rhythm conversion, Extracorporeal resuscitation, Prognosis

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https://doi.org/10.1016/j.resuscitation.2019.04.044
Received 16 December 2018; Received in revised form 27 February 2019; Accepted 27 April 2019

Introduction

Over 325,000 North Americans die each year from a non-traumatic out-of-hospital cardiac arrest (OHCA).[1,2] Among all patients who suffer from an OHCA, survival is low, with only 5–10% of all OHCA surviving to hospital discharge.[2–4] The use of extracorporeal cardiopulmonary resuscitation (E-CPR) has been proposed as a way to improve the mortality associated with OHCA since it has been shown to perform favorably when compared to traditional resuscitation.[5–8] This technique incorporates an extracorporeal cardiopulmonary bypass circuit to obtain cardiopulmonary support during resuscitation.[9–11] However, given the material, human and economic resources required to provide this treatment, its use is usually limited to the patients deemed to have a good prognosis, that is without significant comorbidities and with an underlying reversible etiology for their OHCA.[12,13]

One of the main prognostic factors used for the selection of patients for E-CPR is the initial rhythm.[14–18] Indeed, having an initial shockable rhythm, such as ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT), is considered a marker of good prognosis compared to having a non-shockable initial rhythm (pulseless electrical activity [PEA] or asystole).[3,19–21] A systematic review also recently concluded that the conversion from a non-shockable rhythm to a shockable rhythm during the course of the resuscitation is a marker of good prognosis.[22] However, the precise prognostic implications of such a conversion for both PEA and asystole, as compared to having an initial shockable rhythm, were not evaluated in that review, and no specific analyses were performed to better evaluate this matter among patients who otherwise meet E-CPR selection criteria.[5,6,14,23,24] More accurately determining the prognosis of patients who convert to a shockable rhythm during resuscitation may help improve OHCA prognostication and patient selection for E-CPR.

The main objective of this study was therefore to evaluate the association between the initial rhythm, with or without its subsequent conversion if not initially shockable, and the resuscitation outcomes of patients suffering from an OHCA, and more precisely in a targeted population: potential E-CPR candidates.

Methods

Study design and setting

This cohort study was derived from a registry of all OHCA occurring in the region of Montreal, Canada. It was carried out in association with the Hôpital du Sacré-Coeur de Montréal, the regional emergency medical service (EMS) (Urgences-santé) and the Université de Montréal, and was approved by the Research Ethics Board of the Hôpital du Sacré-Coeur de Montréal with a waiver of written informed consent.

In Montreal, a single public tiered-response EMS agency coordinates all prehospital care for a population of over 2,000,000 people. First responders and paramedics treat patients suffering from OHCA following resuscitations protocols based on the American Heart Association guidelines.[25–28] Patients suffering from OHCA are normally transported to the closest of the 20 local hospitals, five of which have the necessary resources and expertise to perform E-CPR (cardiac surgery department and necessary equipment). During the study's period (2010–2015), E-CPR was seldom used to treat patients suffering from an OHCA in all these hospitals.

Study population

All patients aged 18 years and older treated for an OHCA between April 2010 and December 2015 were included in the present study. Patients with traumatic causes for arrest, 'do-not-resuscitate' directives or fitting 'obviously dead' criteria (e.g. decapitation, advanced putrefaction) were excluded from both the registry and this analysis.[26] In addition, patients for whom the initial rhythm was unknown were excluded from the present study.

Methods and measurements

The methods used to collect and extract the data for the initial registry have been described previously.[3,29–31] Patient data are entered by the paramedic on a 'run-sheet' following every call. Patients suffering from an OHCA are identified using these run-sheets. The pertinent information is then entered into a database which comprises demographic and clinical characteristics. Resuscitation outcome data were transferred from the discharge hospitals to the regional EMS agency or were readily available. The extracted data was subsequently validated.

Study groups

All included patients were divided into five groups according to the nature of their initial rhythm and its subsequent evolution for initially non-shockable rhythms: (1) initially shockable rhythm (VF or pVT), (2) PEA without conversion to a shockable rhythm (PEAwoC), (3) PEA with conversion to a shockable rhythm (PEAwC), (4) asystole without conversion to a shockable rhythm (AwoC) and (5) asystole with conversion to a shockable rhythm conversion (AwC).

Patients were considered otherwise potential E-CPR candidates if they met the following clinical criteria: 65 years of age or younger, absence of return of spontaneous circulation (ROSC) after 15 min of prehospital resuscitation and EMS witnessed collapse or witnessed collapse with bystander cardiopulmonary resuscitation (CPR).[5,6,9,24,32]

Outcome measures

The primary outcome measure was survival to hospital discharge. The secondary outcome measure was occurrence of a prehospital ROSC of a duration of more than 30 s.

Statistical analyses

Continuous variables are presented as means with standard deviations or median and Q1–Q3, as appropriate, and categorical variables are presented as frequencies with percentages.

A Pearson's chi-squared test was first used to evaluate the difference in survival to discharge and ROSC between all five groups. The primary analysis consisted of a multivariable logistic regression model, constructed with a standard direct approach (enter method) using demographic (age, gender) and clinical variables (delay before EMS personnel arrival, witnessed arrest, bystander CPR, presence of first responders, presence of advanced care paramedics) previously selected for their proven or theoretical effect on survival following an

OHCA. The predictive power of the model was evaluated using a Nagelkerke R^2. The reference category used in that analysis was the group of patients with an initial shockable rhythm because these patients are generally the ones considered for E-CPR.[14] Then, two supplemental sets of analyses were performed to evaluate the influence of a subsequent rhythm conversion for patients with an initial PEA and an initial asystole. In the first one, the reference category was the group of patients with PEAwoC and, in the second one, the reference category was the group of patients with AwoC.

Statistical analyses were performed using SPSS Statistics 23 (IBM, Chicago, USA). All results are presented with their 95% confidence intervals (CI). The alpha level was fixed at 0.05 for all comparisons.

Results

During the study period, 7134 patients suffered an OHCA, of whom 6681 (93,7%) had a known initial rhythm (Fig. 1). Among the included patients, 1788 (26,8%) had an initial shockable rhythm, 2044 (30,6%) had PEA and 2849 (42,6%) had asystole. A total of 295 (14,4%) patients with an initial PEA and 155 (5,4%) patients with an initial asystole subsequently converted to a shockable rhythm during prehospital resuscitation. The demographic and clinical characteristics of all included patients are presented in Table 1. Among the entire cohort, 1594 (23,8%) patients experienced prehospital ROSC and 729 (10,9%) survived to hospital discharge.

The probabilities of survival to hospital discharge and prehospital ROSC of all five groups are presented in Fig. 1 and Table 2. Patients with an initial shockable rhythm were more likely to survive than patients in all other groups ($p < 0.001$ for all comparisons). Patients with an initial PEA, regardless of subsequent shockable rhythm conversion, were more likely to survive than patients in both asystole groups (all $p = 0.021$ or less). The conversion to a shockable rhythm was not associated with an improvement in survival for patients with an initial PEA (PEAwC vs PEAwoC), ($p = 0.22$) or an initial asystole (AwC vs AwoC) ($p = 0.89$).

Regarding the prehospital ROSC outcome, patients with an initial shockable rhythm experience prehospital ROSC more often than patients in all other groups ($p < 0.001$ for all comparisons). Patients with an AwoC were less likely to experience prehospital ROSC than patients in all other groups ($p < 0.001$ for all comparisons). There was no difference when comparing the three remaining groups between each other (PEAwC, PEAwoC and AwC) (all $p = 0.13$ or more).

In the main multivariable logistic regression model, as compared to patients having an initial shockable rhythm, patients in all other groups had significantly lower odds of survival to hospital discharge and prehospital ROSC ($p < 0.001$ for all comparisons) (Nagelkerke $R^2 = 0.36$ and Nagelkerke $R^2 = 0.40$, respectively) (Tables 3 and 4). In the first supplemental set of regression models, among patients with an initial PEA, there was no association between evolving to a shockable rhythm and survival to hospital discharge or prehospital ROSC (PEAwC vs PEAwoC) (AOR = 0.74 [95% CI 0.40–1.35], $p = 0.32$, and AOR = 0.88 [95% CI 0.64–1.21], $p = 0.44$, respectively). In the second supplemental set of regression models, among patients with an initial asystole, there was no association between evolving to a shockable rhythm and survival to hospital discharge (AwC vs AwoC) (AOR = 1.37 [95% CI 0.17–10.83], $p = 0.77$), but it was however associated with higher odds of prehospital ROSC (AwC vs AwoC) (AOR = 3.41 [95% CI 2.03–5.70], $p < 0.001$).

A total of 556 (8,3%) patients were considered potential E-CPR candidates according to their clinical characteristics (65 years of age or younger, absence of ROSC after 15 min of prehospital resuscitation and EMS witnessed collapse or witnessed collapse with bystander CPR). Among these patients, 248 (44,6%) had an initial shockable rhythm, 227 (40,8%) had an initial PEA and 86 (15,4%) had an initial asystole. Only 26 (11,5%) patients with an initial PEA and five (5,8%) patients with an initial asystole had a subsequent shockable rhythm during their prehospital resuscitation. The probabilities of survival to hospital discharge and prehospital ROSC of all five groups are presented in Table 5. Given the small number of patients and events in some groups, only univariate analyses were performed using a Fisher's exact test. Patients with an initial shockable rhythm had better odds of survival than patients in all other groups ($p < 0.001$ for all comparisons). No other comparisons yielded significant results ($p = 0.09$–$p = 0.80$). Patients with an initial shockable rhythm were also more likely to experience prehospital ROSC than patients in all other groups (all $p < 0.001$), with the exception of the small group

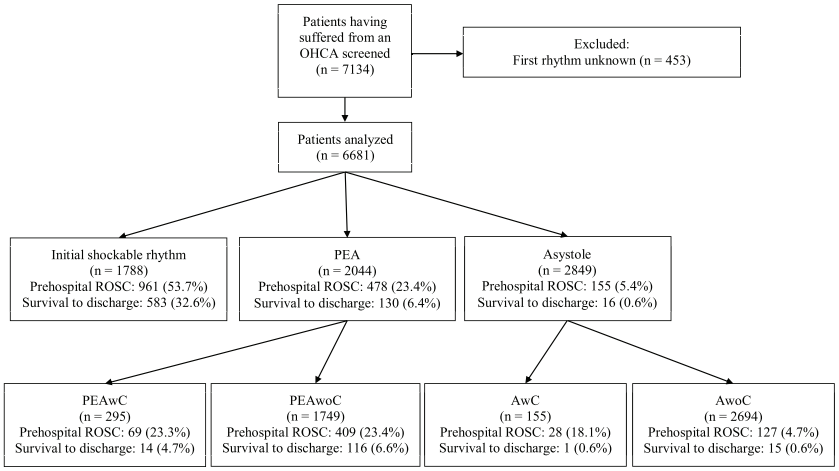

Fig. 1 – Utstein diagram. OHCA: Out-of-hospital cardiac arrest; ROSC: return of spontaneous circulation; PEA: pulseless electrical activity; PEAwC: pulseless electrical activity with a conversion to a shockable rhythm; PEAwoC: pulseless electrical activity without a conversion to a shockable rhythm; AwC: asystole with a conversion to a shockable rhythm; AwoC: asystole without a conversion to a shockable rhythm.

Table 1 – Demographic and clinical characteristics of the included patients.

Variables	Initial shockable rhythm (n = 1788)	PEAwoC (n = 1749)	PEAwC (n = 295)	AwoC (n = 2694)	AwC (n = 155)
Age, years (mean, SD)	64 (16)	70 (16)	71 (16)	69 (17)	70 (16)
Sex, male (N, %)	1396 (78.1)	1011 (57.8)	204 (69.2)	1554 (57.7)	100 (64.5)
Unwitnessed arrest (N, %)	375 (21.0)	593 (33.9)	102 (34.6)	1997 (74.1)	98 (63.2)
Bystander witnessed	1170 (65.4)	792 (45.3)	167 (56.6)	652 (24.2)	56 (36.1)
First responder or paramedic witnessed	243 (13.6)	364 (20.8)	26 (8.8)	45 (1.7)	1 (0.6)
No bystander CPR (N, %)	908 (51.0)	972 (55.8)	179 (61.1)	1966 (73.4)	119 (76.8)
Bystander CPR	629 (35.3)	405 (23.3)	88 (30.0)	667 (24.9)	35 (22.6)
First responder or paramedic witnessed	243 (13.7)	364 (20.9)	26 (8.9)	45 (1.7)	1 (0.6)
Delay from call to arrival of EMS personnel, minutes (mean, SD)	7 (4)	7 (5)	7 (5)	7 (5)	7 (4)
Presence of first responders (N, %)	1040 (58.2)	1086 (62.1)	210 (71.2)	1601 (59.4)	99 (63.9)
Presence of advanced care paramedics (N, %)	536 (30.0)	449 (25.7)	106 (35.9)	765 (28.4)	69 (44.5)
Intubation using an esophageal tracheal airway (N, %)	1177 (65.8)	1423 (81.4)	262 (88.8)	2078 (77.1)	138 (89.0)
At least one dose of epinephrine given (N, %)	295 (16.5)	317 (18.1)	84 (28.5)	441 (16.4)	60 (38.7)

PEAwoC: Pulseless electrical activity without a conversion to a shockable rhythm; PEAwC: pulseless electrical activity with a conversion to a shockable rhythm; AwoC: asystole without a conversion to a shockable rhythm; AwC: asystole with a conversion to a shockable rhythm; SD: standard deviation; CPR: cardiopulmonary resuscitation; EMS: emergency medical service.

Table 2 – Probabilities of survival to hospital discharge and prehospital ROSC among patients with an OHCA according to the initial rhythm and its subsequent evolution.

Variables	Initial shockable rhythm (n = 1788)	PEAwoC (n = 1749)	PEAwC (n = 295)	AwoC (n = 2694)	AwC (n = 155)
Survival to hospital discharge (N, %)	583 (32.6)	116 (6.6)	14 (4.7)	15 (0.6)	1 (0.6)
Prehospital ROSC (N, %)	961 (53.7)	409 (23.4)	69 (23.4)	127 (4.7)	28 (18.0)

ROSC: Return of spontaneous circulation; OHCA: out-of-hospital cardiac arrest; PEAwoC: pulseless electrical activity without a conversion to a shockable rhythm; PEAwC: pulseless electrical activity with a conversion to a shockable rhythm; AwoC: asystole without a conversion to a shockable rhythm; AwC: asystole with a conversion to a shockable rhythm.

comprising patients with an AwC ($p = 0.52$). No other comparisons yielded significant results.

Discussion

In this analysis of a large, unselected OHCA population of almost all cases of a metropolitan region, it was observed that patients with an initial PEA or asystole have significantly lower odds of survival to hospital discharge or ROSC than patients with an initial shockable rhythm, regardless of subsequent conversion to a shockable rhythm. Converting to a shockable rhythm was however associated with an improvement in the odds of prehospital ROSC for patients presenting with an asystole. Rhythm conversion did not show significant impact on survival to hospital discharge. Among potential E-CPR candidates, survival was also higher in patients with an initial shockable rhythm. No E-CPR candidate with an initial asystole survived to hospital discharge. The present study is the first one to address these questions in potential E-CPR candidates.

The initial cardiac rhythm appears to be a much better outcome predictor than subsequent rhythms in patients suffering from an OHCA. Rajan et al. also observed that the conversion to a shockable rhythm was not a strong prognostic marker as compared to the initial rhythm itself.[33] This may be explained by shockable rhythms being a marker of earlier intervention.[34] Indeed, even after a conversion to a shockable rhythm, patients having an initial non-shockable rhythm might have more severe underlying total body ischemia in relation to the duration of their arrest or the quality of their resuscitation.[34] It is also possible that their underlying illness is less easily treatable than for patients having an initial shockable rhythm, regardless of subsequent rhythm conversion.[35]

Patients who had an initial asystole experienced prehospital ROSC more often after conversion to a shockable rhythm, which was not the case for patients with an initial PEA. This is in keeping with the findings of Luo et al. in their recent literature review.[22] Luo et al. also observed that the conversion from an initial asystole to a shockable rhythm was associated with an increase in survival, which we did not observe in our cohort.[22] Asystole consists of a lack of both perceivable electrical and mechanical activity in the heart. Patients with PEA may have persistent organized mechanical activity despite ongoing circulatory collapse. As such, conversion from a lack of activity to any electrical activity (i.e. a shockable rhythm) may be a good prognostic marker, conversion of an organized PEA to a disorganized rhythm such as VF may not have the same positive prognostic significance. On the contrary, among patients suffering from an in-hospital cardiac arrest (IHCA), conversion from a non-shockable to a shockable rhythm has been associated with worse outcomes.[21] This is likely explained by the varying aetiology of cardiac arrest between

Table 3 – Multivariate analysis for the survival to hospital discharge outcome, adjusted for the groups according to the nature of their initial rhythm and its subsequent evolution, demographic and prehospital variables.

Variables	AOR (95% CI)	P value
Initial shockable rhythm	*	
PEAwoC	0.15 (0.12–0.18)	< 0.001
PEAwC	0.12 (0.067–0.21)	< 0.001
AwoC	0.017 (0.010–0.030)	< 0.001
AwC	0.020 (0.003–0.15)	< 0.001
Age (1 year older)	0.97 (0.96–0.97)	< 0.001
Gender, male sex	0.68 (0.56–0.84)	< 0.001
Unwitnessed arrest	*	–
Bystander witnessed	1.96 (1.53–2.51)	<0.001
First responder or paramedic witnessed	4.52 (3.31–6.19)	<0.001
No bystander CPR	*	–
Bystander CPR	1.22 (1.00–1.50)	0.056
First responder or paramedic witnessed	†	†
Presence of first responders	0.93 (0.82–1.20)	0.93
Presence of advanced care paramedics	1.00 (0.82–1.23)	1.00
Delay from call to arrival of EMS personnel (1 more minute before their arrival)	0.97 (0.94–0.99)	0.011

AOR: Adjusted odds ratio; CI: confidence interval; PEAwoC: pulseless electrical activity without a conversion to a shockable rhythm; PEAwC: pulseless electrical activity with a conversion to a shockable rhythm; AwoC: asystole without a conversion to a shockable rhythm; AwC: asystole with a conversion to a shockable rhythm; CPR: cardiopulmonary resuscitation; EMS: emergency medical services.
*Reference category † Not calculated due to collinearity.

Table 4 – Multivariate analysis for the prehospital ROSC outcome, adjusted for the groups according to the nature of their initial rhythm and its subsequent evolution, demographic and prehospital variables.

Variables	AOR (95% CI)	P value
Initial shockable rhythm	*	
PEAwoC	0.25 (0.21–0.29)	< 0.001
PEAwC	0.24 (0.18–0.33)	< 0.001
AwoC	0.051 (0.041–0.064)	< 0.001
AwC	0.18 (0.12–0.29)	< 0.001
Age (1 year older)	0.99 (0.98–0.99)	< 0.001
Gender, male sex	0.73 (0.63–0.84)	< 0.001
Unwitnessed arrest	*	–
Bystander witnessed	2.12 (1.79–2.50)	<0.001
First responder or paramedic witnessed	4.04 (3.20–5.11)	<0.001
No bystander CPR	*	–
Bystander CPR	1.14 (0.97-1.33)	0.11
First responder or paramedic witnessed	†	†
Presence of first responders	0.97 (0.83–1.12)	0.97
Presence of advanced care paramedics	3.97 (3.42–4.62)	<0.001
Delay from call to arrival of EMS personnel (1 more minute before their arrival)	0.97 (0.96–0.99)	0.004

ROSC: Return of spontaneous circulation; AOR: adjusted odds ratio; CI: confidence interval; PEAwoC: pulseless electrical activity without a conversion to a shockable rhythm; PEAwC: pulseless electrical activity with a conversion to a shockable rhythm; AwoC: asystole without a conversion to a shockable rhythm; AwC: asystole with a conversion to a shockable rhythm; CPR: cardiopulmonary resuscitation; EMS: emergency medical services.
* Reference category † Not calculated due to collinearity.

IHCA and OHCA. Patients suffering from an OHCA are acutely sick, and most often have underlying cardiac ischemia.[36] On the contrary, patients with an IHCA most often have an acute respiratory insufficiency or a profound hypotension.[21] In that population, a shockable rhythm mark a necessity to perform prolonged resuscitative efforts or a severe underlying myocardial pathology. The resuscitation of patients suffering from an IHCA is also initiated more rapidly and they usually receive epinephrine more rapidly (especially given the

Table 5 – Probabilities of survival to hospital discharge and prehospital ROSC among patients with an OHCA according to the initial rhythm and its subsequent evolution, including only potential E-CPR candidates.

Variables	Initial shockable rhythm (n = 248)	PEAwoC (n = 201)	PEAwC (n = 26)	AwoC (n = 76)	AwC (n = 5)
Survival to hospital discharge (N, %)	91 (36.7)	9 (4.5)	1 (3.8)	0 (0.0)	0 (0.0)
Prehospital ROSC (N, %)	128 (51.6)	33 (16.4)	4 (15,4)	11 (14.5)	2 (40.0)

ROSC: Return of spontaneous circulation; OHCA: out-of-hospital cardiac arrest; E-CPR: extracorporeal resuscitation; PEAwoC: pulseless electrical activity without a conversion to a shockable rhythm; PEAwC: pulseless electrical activity with a conversion to a shockable rhythm; AwoC: asystole without a conversion to a shockable rhythm; AwC: asystole with a conversion to a shockable rhythm.

relatively low rate of prehospital advanced cardiopulmonary life support provided in the present cohort), which can explain the higher frequency of conversion to a shockable rhythm.[21]

To the best of our knowledge, this is the first study to show that the initial rhythm is a better marker of prognosis than subsequent rhythms among patients in refractory cardiac arrest who would otherwise be potential candidates for E-CPR. This finding adds to the current evidence that the initial rhythm is a marker of good prognosis among patients undergoing E-CPR and supports using the initial rhythm in the selection of patients for E-CPR.[37] In addition to this, we believe that E-CPR selection criteria should be adapted to the local environment. Where resources are more limited, offering E-CPR only to those with an initial shockable rhythm would be reasonable. In settings with more resources available, extending indications to those with initial PEA may be appropriate. Our findings do not support extending E-CPR to those presenting with asystole given the low likelihood of a favorable outcome.[18] The results of our analysis do not support altering the decision to provide E-CPR based on subsequent rhythm conversion for initial non-shockable rhythms and this is in keeping with the current literature.[37] Whether such a dynamic strategy could be beneficial will require appropriately powered prospective studies.

Limitations

The present study is observational in nature and, as such, is subject to ascertainment bias and unmeasured confounding. As all data were derived from prehospital record, the timing of conversion, the final diagnosis and the neurologic outcomes were not available for analysis. While there was a large number of patients in the overall study, the number of E-CPR candidates was relatively small and there were comparatively few events in this group, particularly in certain rhythm categories. As such, the results in this sub-cohort must be interpreted with caution. It was not possible to know exactly how many patients received E-CPR, although it is probable given the period studied that no patient underwent that therapy. Consequently, the impact of that treatment for these patients remains uncertain. It is also possible that the patients who had an asystole as an initial rhythm had less aggressive treatment and that a part of the observed results are due to a self-fulfilling prophecy bias. However, the prehospital treatment patients received were protocol based and a prolonged period of resuscitative efforts must be completed before termination of resuscitation can be considered, which minimizes that potential bias. Finally, although this study included a large and comprehensive multicenter dataset of OHCA, caution should be recommended in extrapolating these results to patients suffering from an in-hospital cardiac arrest, or to regions with EMS systems with improved prehospital advanced care like emergency physicians or intensive care paramedics treating all OHCA patients, varying treatment standards or patient demographics.

Conclusions

The initial rhythm is a much better prognostic marker than subsequent rhythms for patients suffering from an OHCA. This finding also held for the subset of patients considered potential E-CPR candidates. For patients with an initial asystole, the conversion to a shockable rhythm is associated with an improvement in survival, but the overall prognosis for patients with initial asystole remained poor. Future studies are necessary to determine whether or not E-CPR might be appropriate for patients presenting with initial PEA.

Financial support

This project received funding from the 'Fonds des Urgentistes de l'Hôpital du Sacré-Cœur de Montréal' and the 'Département de médecine familiale et de médecine d'urgence de l'Université de Montréal'.

Conflict of interest

Dr André Denault is part of a speakers' bureau for Masimo and CAE Healthcare. All other authors have no conflict of interest to declare.

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