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Consciousness induced during cardiopulmonary resuscitation: An observational study☆

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ABSTRACT

Background: Cardiopulmonary resuscitation-induced consciousness (CPRIC) is a phenomenon that has been described in only a handful of case reports. In this study, we aimed to describe CPRIC in out-of-hospital cardiac arrest (OHCA) patients and determine its association with survival outcomes.
Methods: Retrospective study of registry-based data from Victoria, Australia between January 2008 and December 2014. Adult OHCA patients treated by emergency medical services (EMS) were included. Multivariable logistic regression was used to determine the association between CPRIC and survival to hospital discharge.
Results: There were 112 (0.7%) cases of CPRIC among 16,558 EMS attempted resuscitations, increasing in frequency from 0.3% in 2008 to 0.9% in 2014 ($p = 0.004$). Levels of consciousness consisted of spontaneous eye opening (20.5%), jaw tone (20.5%), speech (29.5%) and/or body movement (87.5%). CPRIC was independently associated with an increased odds of survival to hospital discharge in unwitnessed/bystander witnessed events (OR 2.09, 95% CI: 1.14, 3.81; $p = 0.02$) but not in EMS witnessed events (OR 0.98, 95% CI: 0.49, 1.96; $p = 0.96$). Forty-two (37.5%) patients with CPRIC received treatment with one or more of midazolam (35.7%), opiates (5.4%) or muscle relaxants (3.6%). When stratified by use of these medications, CPRIC in unwitnessed/bystander witnessed patients was associated with improved odds of survival to hospital discharge if medications were not given (OR 3.92, 95% CI: 1.66, 9.28; $p = 0.002$), but did not influence survival if these medications were given (OR 0.97, 95% CI: 0.37, 2.57; $p = 0.97$).
Conclusion: Although CPRIC is uncommon, its occurrence is increasing and may be associated with improved outcomes. The appropriate management of CPRIC requires further evaluation.

Introduction

Cardiopulmonary resuscitation (CPR) typically generates only a fraction of the circulation required to maintain normal physiological function.[1] However, when performed optimally, CPR could theoretically generate sufficient cerebral blood flow to induce levels of consciousness in cardiac arrest patients.[2] Almost 30 years ago, a report by Lewinter et al. described this phenomenon in a 60 year old woman who suffered an in-hospital cardiac arrest and maintained responsiveness throughout a near three-hour resuscitation attempt.[3] Since then, a handful of case reports involving both in-hospital and out-of-hospital cardiac arrest (OHCA) patients have reported variants of CPR-induced consciousness (CPRIC), including spontaneous eye opening, increased jaw tone, speech and body movement.[4] The phenomenon may also be an extension of other undetectable levels of consciousness, such as awareness, which has been reported in survivors of cardiac arrest.[5]

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Despite the paucity of data, CPRIC may not be as uncommon as initially thought. A recent cross-sectional study of experienced resuscitationists suggests that most have observed CPRIC at least once.[6] The use of chemical sedation and paralysis are typically supported by clinicians to reduce pain and emotional distress, and to maximise the effectiveness of the resuscitation attempt.[7] However, empirical evidence supporting pharmacological interventions for CPRIC are unavailable,[8] and both the safety and efficacy of these treatments are unclear. In addition, the clinical factors associated with the development of CPRIC are also not well known.

The primary aim of this study was to identify consecutive cases of CPRIC among a large register of OHCA patients, and to describe its incidence, characteristics and association with survival to hospital discharge. In addition, we sought to describe the frequency of prehospital pharmacological interventions used to manage CPRIC, and to assess their influence on survival.

Methods

Study design

A retrospective study of registry-based data from the Victorian Ambulance Cardiac Arrest Registry (VACAR) between 1st January 2008 and 31st December 2014 was conducted. We included adult OHCA patients (aged $\geq$ 16 years or missing age) who underwent an attempted resuscitation by EMS personnel. Cases involving CPRIC were identified through electronic and manual review of prehospital patient care records. The study was approved by the Alfred Human Research Ethics Committee (Project No.: 293/15).

Setting

The state of Victoria, Australia operates a single EMS servicing almost 5.8 million people across more than 227,000 square kilometres. Paramedics are dispatched to suspected cardiac arrest events in a two-tiered system, including advanced life support and intensive care paramedics. In the city of Melbourne and select rural areas of Victoria, a third tier response by defibrillation-capable first responders is provided by fire-fighters and community volunteers.[9] Resuscitation guidelines in Victoria are aligned with the recommendations of the Australian and New Zealand Committee on Resuscitation.[10] Clinical practice guidelines authorize the use of laryngeal mask airway insertion and intravenous adrenaline (epinephrine) for advanced life support paramedics, and other skills such as capnography-guided endotracheal intubation (including rapid sequence intubation) and the administration of cardiotropic medications can be undertaken by intensive care paramedics. While there are no formal guidelines in Victoria on the management of CPRIC, sedation with midazolam was authorised during the study period for the management of agitated or combative patients, and to facilitate intubation in the presence of a gag reflex. Paramedics are authorised to cease resuscitation in the field if there has been no response to advanced life support interventions after 30 min.

Data sources

The VACAR has been described in detail elsewhere.[11] Since 1999, the registry has captured over 80,000 OHCA episodes attended by paramedics. The registry collects over 150 patient and treatment variables including the Utstein-style elements.[12] Data sources include electronic patient care records, first responder treatment records, call logs, hospital medical records, and telephone follow-up surveys at 12-months post-arrest for known survivors. Potential cardiac arrest cases are identified by the registry using an extremely sensitive search filter of electronic patient care records. Case ascertainment is supplemented by review of emergency call logs and first responder case records. Shortlisted cases are checked and validated manually by registry personnel. In approximately 99% of transported cases, hospital discharge status and direction is obtained from over 100 participating hospitals. Deaths are also cross-referenced against official statewide death records from the Victorian Registry of Births, Deaths and Marriages.

Case ascertainment and definitions

We defined CPRIC on the basis of limited case reports describing the event.[4] A working definition incorporating 'one or more of spontaneous eye opening, jaw tone, speech or body movement in pulseless patients undergoing active CPR' was adopted and used as the inclusion criteria. Potential cases of CPRIC were identified using a broad keyword search of select areas of the electronic patient care record, including case histories, text fields, and treatment fields. The keyword search was developed a-priori using a small number of known cases involving CPRIC, and included the following terms: 'Moving', 'held down', 'combative', 'eyes open', 'opening eyes', 'awake', 'pushing', 'pulling', 'increased motor', 'aware', 'groaning', 'reaching', and 'localising'. Keywords were used with truncation operators to improve the sensitivity of the search.

The search was initially applied to all electronic patient care records and potential matches were then cross-referenced against records of confirmed OHCA cases in the VACAR. As all cases in VACAR retain the original ambulance case identifier, the linkage does not rely on probabilistic methods of data linkage. Two investigators (A.O. and M.S.) then manually reviewed patient care records searching for inclusion criteria. Cases were excluded if the keyword matches were unrelated to the content area; or if consciousness occurred before cardiac arrest (e.g. EMS witnessed events) or post return of spontaneous circulation (ROSC). Disputes regarding case inclusion were referred to a third investigator (Z.N.). Cases meeting the eligibility criteria underwent standardised data extraction for: (i) the description of consciousness; (ii) the cardiac rhythm in which consciousness was observed; and (iii) the pharmacological agents administered to manage CPRIC. The pharmacological agents used to manage CPRIC were collected independently of any agents used to facilitate intubation.

Statistical analysis

Statistical analyses were performed using Stata Statistical Software 14 (StataCorp, 2015, College Station, TX). Given the exploratory nature of the study, a two-sided p-value of less than 0.05 was considered statistically significant for statistical analyses. The primary outcome measure was survival to hospital discharge. Continuous variables were summarized using median with interquartile range (IQR) and discrete variables were summarized using counts with proportions. A Wilcoxon-type test for trend was used to assess the yearly number of CPRIC cases across the study period. Differences in arrest characteristics and unadjusted outcomes of cases with and without CPRIC were compared using the chi-square test or the Wilcoxon rank-sum test as required. Using the same approach, we tested differences in the baseline characteristics of CPRIC patients who did and did not receive consciousness-altering medication by paramedics.

To identify arrest characteristics associated with CPRIC, we performed stepwise logistic regression analyses. To reduce the risk of confounding arrest characteristics with witness status, we performed analyses separately for unwitnessed/bystander witnessed and EMS witnessed populations. In the unwitnessed/bystander witnessed population, we included the following candidate variables in the model: age (continuous), male gender (binary), estimated time between collapse and EMS arrival exceeds 15 min (binary), time from call to EMS arrival (continuous), public location (binary),

Table 1
Characteristics of patients with and without CPRIC.

	Overall N = 16,558	Without CPRIC N = 16 446	With CPRIC N = 112	P-value
Age in years, median (IQR)	67 (53, 80)	68 (53, 80)	63 (55, 71)	0.01
Missing, n (%)	59 (0.4)	59 (0.4)	0	–
Male sex, n (%)	11 279 (68.1)	11 186 (68.0)	93 (83.0)	0.001
Estimated time between collapse and EMS arrival exceeds 15 min[a], n (%)	5043 (36.7)	5038 (36.9)	5 (8.2)	<0.001
Time from call to EMS arrival[a], median (IQR)	8.2 (6.4, 11.3)	8.2 (6.5, 11.3)	7.5 (6.0, 10.3)	0.10
Missing, n (%)	12 (<0.1)	12 (<0.1)	0	–
Public location, n (%)	3297 (19.9)	3259 (19.8)	38 (33.9)	<0.001
Presumed cardiac aetiology, n (%)	12 439 (75.1)	12 334 (75.0)	105 (93.8)	<0.001
Witness status, n (%)				
Unwitnessed	5939 (36.1)	5928 (36.3)	11 (9.8)	<0.001
Bystander witnessed	7794 (47.4)	7744 (47.4)	50 (44.6)	0.56
EMS witnessed	2725 (16.6)	2674 (16.4)	51 (45.5)	<0.001
Missing	100 (0.6)	100 (0.6)	0	–
Bystander CPR[a], n (%)	8613 (62.7)	8572 (62.7)	41 (67.2)	0.47
First monitored arrest rhythm, n (%)				
VF/VT	5096 (31.2)	5019 (30.9)	77 (70.0)	<0.001
PEA	4070 (24.9)	4047 (24.9)	23 (20.9)	0.33
Asystole	7119 (43.5)	7109 (43.8)	10 (9.1)	<0.001
Other non-shockable	74 (0.5)	74 (0.5)	0	0.48
Metropolitan region, n (%)	11 957 (72.5)	11 869 (72.5)	88 (78.6)	0.15
Prehospital intubation, n (%)	10,126 (61.2)	10,053 (61.1)	73 (65.2)	0.38
Description of CPRIC[b], n (%)				
Eye opening	23 (0.1)	–	23 (20.5)	–
Jaw tone	23 (0.1)	–	23 (20.5)	–
Any speech	33 (0.2)	–	33 (29.5)	–
Incomprehensible speech	29 (0.2)	–	29 (25.9)	–
Comprehensible speech	4 (<0.1)	–	4 (3.6)	–
Any movement	98 (0.6)	–	98 (87.5)	–
Purposeful movement/localising	77 (0.5)	–	77 (68.8)	–
Combative	22 (0.1)	–	22 (19.6)	–

CPR denotes cardiopulmonary resuscitation, IQR interquartile range, EMS emergency medical services, VF/VT ventricular fibrillation/pulseless ventricular tachycardia, PEA pulseless electrical activity.

[a] Excludes EMS witnessed arrests.

[b] Categories are not mutually exclusive.

presumed cardiac aetiology (binary), bystander witnessed (binary), bystander CPR (binary), first monitored arrest rhythm is ventricular fibrillation or pulseless ventricular tachycardia (VF/VT) (binary), metropolitan region (binary). In the EMS witnessed population, we omitted the following covariates from the model as they were not relevant: estimated time between collapse and EMS arrival exceeds 15 min, time from call to EMS arrival, bystander witnessed, and bystander CPR. The models were optimised by backward eliminating covariates with the largest p-values until a parsimonious model was achieved, retaining all variables with p-values < 0.10.

To assess the association between CPRIC and survival to hospital discharge we performed multivariable logistic regression adjusting for the arrest characteristics specified above. In an alternative model, we assessed the impact of consciousness-altering medication use by paramedics by including an indicator variable with three categories: (1) cases without CPRIC (reference); (2) cases with CPRIC, medication not given, and; (3) cases with CPRIC, medication given. In our study, consciousness-altering medication included midazolam, opiates (morphine and/or fentanyl) or muscle relaxants (pancuronium and/or suxamethonium). Results from all regression analyses were presented as odds ratios (OR) and 95% confidence intervals (CI). Cases with one or more missing data points were excluded from the analyses.

Results

Sample population

Between January 2008 and December 2014, there were 125,379 paramedic patient care records meeting the initial keyword search criteria (Fig. S1 in the Supplementary Appendix). A total of 2514 cases were confirmed OHCA events in the VACAR, of which 1629 adult cases with an attempted resuscitation underwent manual review. Of these, 1517 were excluded because the keyword match was unrelated to the content area (n = 1354) or consciousness occurred before arrest or post-ROSC (n = 163). From a possible sample of 16,558 adult OHCA patients with an EMS attempted resuscitation, 112 (0.7%) cases were identified with CPRIC.

Incidence and characteristics

The proportion of cases with CPRIC increased over the study period from 0.3% in 2008 to 0.9% in 2014 (p for trend = 0.004). Characteristics of patients with and without CPRIC are presented in Table 1. Patients with CPRIC were younger, were more often male, experienced fewer delays from collapse to arrival of EMS, were more often EMS witnessed, and more frequently presented with an initial rhythm of VF/VT. Patients with CPRIC exhibited one or more of spontaneous eye opening (20.5%), jaw tone (20.5%), speech (29.5%) and/or body movement (87.5%). Almost one in five (19.6%) patients was described as being combative.

Multivariable stepwise logistic regression of the association between arrest characteristics and CPRIC is shown in Table 2. In unwitnessed and bystander witnessed cases, the odds of CPRIC increased with younger age, presumed cardiac aetiology, an initial arrest rhythm of VF/VT, and a time between collapse and EMS arrival of ≤15 min. In the EMS witnessed population, presumed cardiac aetiology, an initial arrest rhythm of VF/VT, and public arrest location significantly increased the odds of CPRIC.

Association between CPRIC and survival

Unadjusted outcomes of patients with and without CPRIC are presented in Table 3. Hospital discharge data was unavailable in

Table 2
Association between arrest characteristics and CPRIC using multivariable stepwise logistic regression.

Variable	Unwitnessed & bystander witnessed population N = 13 527[c]		EMS witnessed population N = 2598[d]	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age, per year increase	0.98 (0.96, 1.00)	0.01	Eliminated[a]	
Male sex	Eliminated[a]		Eliminated[a]	
Estimated time between collapse and EMS arrival exceeds 15 min	0.21 (0.07, 0.59)	0.003	Omitted from model[b]	
Time from call to EMS arrival (per min increase)	Eliminated[a]		Omitted from model[b]	
Public location	1.65 (0.96, 2.83)	0.07	2.63 (1.31, 5.29)	0.007
Presumed cardiac aetiology	3.63 (1.05, 12.56)	0.04	4.87 (1.66, 14.27)	0.004
Bystander witnessed	Eliminated[a]		Omitted from model[b]	
Bystander CPR	Eliminated[a]		Omitted from model[b]	
First monitored arrest rhythm = VF/VT	3.16 (1.65, 6.03)	<0.001	2.79 (1.52, 5.12)	0.001
Metropolitan region	Eliminated[a]		Eliminated[a]	

CPR denotes cardiopulmonary resuscitation, CI confidence interval, EMS emergency medical services, VF/VT ventricular fibrillation/pulseless ventricular tachycardia.
[a] P-value ≥ 0.10.
[b] Variable not tested in model.
[c] Patients with one or more missing variables were excluded (n = 206, 1.5%).
[d] Patients with one or more missing variables were excluded (n = 127, 4.7%).

Table 3
Unadjusted outcomes of patients with and without CPRIC.

	Overall N = 16,558	Without CPRIC N = 16 446	With CPRIC N = 112	P-value
Efforts ceased at scene, n (%)	9907 (59.9)	9875 (60.1)	32 (28.6)	<0.001
ROSC at any time, n (%)	6783 (41.0)	6702 (40.8)	81 (72.3)	<0.001
Survived to hospital, n (%)	5625 (34.1)	5562 (34.0)	63 (56.8)	<0.001
Missing	82 (0.5)	81 (0.5)	1 (0.9)	–
Survived to hospital, but died during admission[a], n (%)	3403 (61.9)	3388 (62.3)	15 (25.0)	<0.001
Missing	129 (2.3)	126 (2.3)	3 (4.8)	–
Survived to hospital discharge, n (%)	2163 (13.2)	2115 (13.0)	48 (44.0)	<0.001
Missing	154 (0.9)	151 (0.9)	3 (2.7)	–
Discharged home from hospital[b], n (%)	1826 (85.7)	1782 (85.5)	44 (91.7)	0.23
Missing	31 (1.5)	31 (1.5)	0	–

ROSC denotes return of spontaneous circulation.
[a] As a proportion of patients surviving to hospital.
[b] As a proportion of patients surviving to hospital discharge.

Table 4
Association between CPRIC and survival to hospital discharge using multivariable logistic regression.

Variable	Unwitnessed & bystander witnessed population N = 13 430[b]		EMS witnessed population N = 2552[c]	
	Odds ratio (95% CI)	P-value	Odds ratio (95% CI)	P-value
Age, per year increase	0.97 (0.97, 0.97)	<0.001	0.98 (0.97, 0.99)	<0.001
Male sex	0.91 (0.78, 1.06)	0.23	1.14 (0.91, 1.43)	0.27
Estimated time between collapse and EMS arrival exceeds 15 min	0.33 (0.27, 0.42)	<0.001	Omitted from model[a]	
Time from call to EMS arrival (per min increase)	0.95 (0.93, 0.97)	<0.001	Omitted from model[a]	
Public location	1.79 (1.57, 2.05)	<0.001	1.00 (0.72, 1.39)	0.99
Presumed cardiac aetiology	1.17 (0.93, 1.46)	0.18	2.40 (1.83, 3.13)	<0.001
Bystander witnessed	1.62 (1.36, 1.92)	<0.001	Omitted from model[a]	
Bystander CPR	1.29 (1.11, 1.50)	0.001	Omitted from model[a]	
First monitored arrest rhythm = VF/VT	9.20 (7.73, 10.96)	<0.001	10.71 (8.61, 13.33)	<0.001
Metropolitan region	1.51 (1.29, 1.78)	<0.001	1.47 (1.17, 1.86)	0.001
CPRIC	2.09 (1.14, 3.81)	0.02	0.98 (0.49, 1.96)	0.96

CPR denotes cardiopulmonary resuscitation, CI confidence interval, EMS emergency medical services, VF/VT ventricular fibrillation/pulseless ventricular tachycardia.
[a] Variable not tested in model.
[b] Patients with one or more missing variables were excluded (n = 303, 2.2%).
[c] Patients with one or more missing variables were excluded (n = 173, 6.3%).

a small proportion of the included population (n = 31, 1.5%). Compared to patients without CPRIC, scene and hospital outcomes were consistently in favour of patients with CPRIC, including higher unadjusted rates of ROSC (40.8% vs. 72.3%, p < 0.001), survival to hospital (34.0% vs. 56.8%, p < 0.001), and survival to hospital discharge (13.0% vs. 44.0%, p < 0.001). Table 4 shows that after adjustment for arrest factors, CPRIC increased the odds of survival to hospital discharge (OR 2.09, 95% CI: 1.14, 3.81; p = 0.02) in unwitnessed/bystander witnessed cases, but not in EMS witnessed cases (OR 0.98, 95% CI: 0.49, 1.96; p = 0.96).

Influence of consciousness-altering medication administration on survival

Table 5 shows the characteristics of CPRIC cases stratified by whether consciousness-altering medication was administered by paramedics. Of the 112 patients with CPRIC, 42 (37.5%) received paramedic treatment with one or more of midazolam (35.7%), opiates (morphine and/or fentanyl [5.4%]) or muscle relaxants (pancuronium and/or suxamethonium [3.6%]). The remaining

Table 5
Characteristics and outcomes of 112 cases with CPRIC, stratified by whether consciousness-altering medication (including midazolam, opiates and muscle relaxants) was administered by paramedics.

Characteristic	Overall N = 112	Managed without medication N = 70	Managed with medication N = 42	P-value
Arrest characteristics, n (%)				
Age in years, median (IQR)	63 (55, 71)	61 (53, 71)	65 (55, 71)	0.22
Male sex	93 (83.0)	59 (84.3)	34 (81.0)	0.65
Public location	38 (33.9)	26 (37.1)	12 (28.6)	0.35
Presumed cardiac aetiology	105 (93.8)	65 (92.9)	40 (95.2)	0.61
EMS witnessed	51 (45.5)	36 (51.4)	15 (35.7)	0.11
VF/VT initial arrest rhythm	77 (70.0)	51 (73.9)	23 (63.4)	0.25
Description of consciousness[a], n (%)				
Eye opening	23 (20.5)	13 (18.6)	10 (23.8)	0.51
Jaw tone	23 (20.5)	11 (15.7)	12 (28.6)	0.10
Any speech	33 (29.5)	27 (38.6)	6 (14.3)	0.006
Any movement	98 (87.5)	60 (85.7)	38 (90.5)	0.46
Arrest rhythm during CPRIC, n (%)				
VF/VT	77 (68.8)	50 (71.4)	27 (64.3)	0.43
PEA	29 (25.9)	17 (24.3)	12 (28.6)	0.62
Asystole	6 (5.4)	3 (4.3)	3 (7.1)	0.52
Medication used to manage consciousness[a], n (%)				
Opiate	6 (5.4)	0	6 (14.3)	–
Midazolam	40 (35.7)	0	40 (95.2)	–
Muscle relaxant	4 (3.6)	0	4 (9.5)	–
Mechanical CPR device used, n (%)	5 (4.5)	1 (1.4)	4 (9.5)	0.05
Outcome, n (%)				
Efforts ceased at scene	32 (28.6)	13 (18.6)	19 (45.2)	0.002
ROSC at any time	81 (72.3)	52 (74.3)	29 (69.1)	0.55
Survived to hospital	63 (56.8)	45 (64.3)	18 (43.9)	0.04
Survived to hospital discharge	48 (44.0)	39 (58.2)	9 (21.4)	<0.001
Time between EMS starting CPR and first ROSC in minutes[b], median (IQR)	10 (5, 20)	8 (4, 16)	16 (9, 26)	0.007

CPR denotes cardiopulmonary resuscitation, IQR interquartile range, VF/VT ventricular fibrillation/pulseless ventricular tachycardia, PEA pulseless electrical activity, ROSC return of spontaneous circulation.
[a] Categories are not mutually exclusive.
[b] In the sub-group of patients achieving ROSC (n = 81).

70 (62.5%) patients were managed with reassurance, physical restraint, or no specific intervention. For patients receiving midazolam, the median dose was 2 mg intravenously (interquartile range [IQR], 1–3 mg). Nine patients (22.5%) received doses ≥5 mg.

Compared to patients with CPRIC who did not receive consciousness-altering medication, patients receiving consciousness-altering medication (including midazolam, opiates and muscle relaxants) had similar arrest characteristics. Patients receiving these medications also had a higher rate of mechanical CPR device use (9.5% vs. 1.4%, p = 0.045), and experienced significantly poorer unadjusted survival to hospital discharge outcomes (21.4% vs. 58.2%, p < 0.001) compared to those not receiving medication. Although rates of ROSC were similar across groups, the median time between EMS starting CPR and achieving first ROSC was significantly lower in CPRIC patients not treated with consciousness-altering medication compared to those who received either midazolam, opiates or muscle relaxants (8 vs. 16 min, p = 0.007).

After stratification for consciousness-altering medication use and adjustment for arrest factors, the impact of CPRIC on survival to hospital discharge is presented in Fig. 1. In the unwitnessed/bystander witnessed population, compared to patients not experiencing CPRIC, CPRIC patients not given consciousness-altering medication observed higher odds of survival (OR 3.92, 95% CI: 1.66, 9.28; p = 0.002) than patients who did receive medication (OR 0.97, 95% CI: 0.37, 2.57; p = 0.97). In the EMS witnessed population, CPRIC patients receiving consciousness-altering medication observed poorer odds of survival compared to patients not experiencing CPRIC (OR 0.25, 95% CI: 0.10, 0.99; p = 0.05).

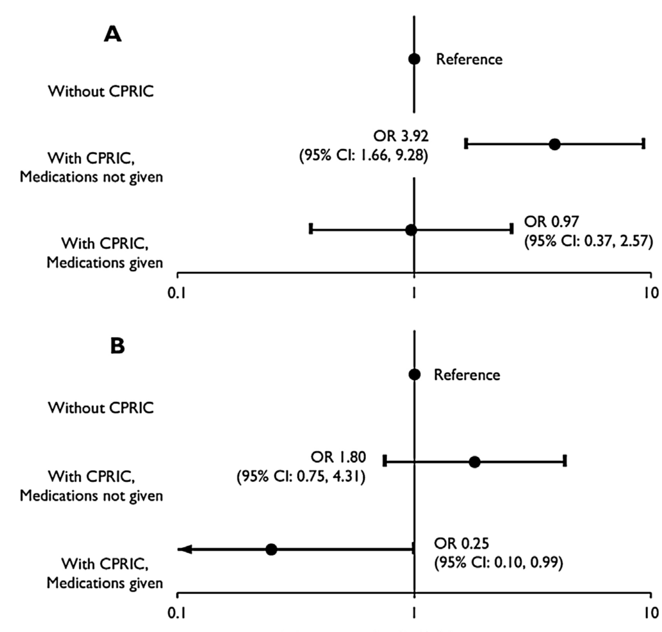

Fig. 1. Adjusted logistic regression analyses of the association between CPRIC and consciousness-altering medication use (including midazolam, opiates and muscle relaxants) on survival to hospital discharge in (A) Unwitnessed and bystander witnessed events, and; (B) EMS witnessed events. Models adjusted for variables listed in Table 4.

Discussion

This study identified OHCA patients developing detectable levels of consciousness during CPR. To our knowledge, this is the largest collection of data describing this phenomenon, which we estimate affects less than one percent of OHCA cases with an EMS attempted resuscitation. Among the 112 patients with CPRIC included in our study, the description of consciousness varied broadly from eye opening to combativeness, with the vast majority experiencing some degree of limb or body movement (87.5%). CPRIC was associated with favourable arrest characteristics and better outcomes among unwitnessed and bystander witnessed events, but was not associated with survival to hospital discharge among EMS witnessed cases.

Cases involving CPRIC were more often witnessed to arrest by EMS, had a first monitored arrest rhythm of VF/VT, and had fewer delays between collapse and EMS arrival. These findings may suggest that CPRIC is dependent on the duration of no-flow time before the commencement of CPR. Animal studies indicate that when compared to delayed CPR, the application of immediate CPR following arrest requires lower coronary perfusion pressures to yield similar levels of cerebral blood flow.[13] CPRIC could therefore be a surrogate of the duration and extent of cerebral ischaemia during arrest. Precipitating factors such as overdoses, hangings, and respiratory conditions could worsen pre-arrest hypoxia, and this could explain why fewer episodes of CPRIC occurred among non-cardiac causes of arrest.

There are several plausible explanations supporting the association between CPRIC and improved OHCA outcomes. It is possible that cases with CPRIC represent residual confounding from other favourable arrest factors not measured in our models, such as the duration of CPR efforts and the presence of agonal respirations post-arrest.[14,15] Both of these factors could help augment cerebral blood flow and reduce cerebral ischemia in the early stages of arrest. CPRIC may also be a surrogate for the quality of CPR delivered by emergency crews. Targeted resuscitation practices have been associated with improved ROSC and survival outcomes following OHCA,[16,17] which could theoretically lead to an increase in cerebral perfusion and rates of CPRIC.[2,3] It is also possible that CPRIC delays prognostication by medical personnel, and leads to longer and more aggressive resuscitation attempts. A recent systematic review suggests that the length of resuscitation in patients with CPRIC could exceed two hours.[4]

CPRIC could also be a surrogate of sustained high levels of regional cerebral oxygen saturation, which has been associated with increased ROSC and neurologically favourable survival following cardiac arrest.[18,19] Previous case reports of patients experiencing CPRIC have reported that medical personnel will often prolong resuscitation efforts, believing that survivors could be less likely to sustain neurological sequelae.[20] Although our study identified significantly higher rates of ROSC among patients with CPRIC compared to those without, there was no difference in the proportion of survivors being discharged home following OHCA. Despite this, the rate of early in-hospital mortality among admitted patients was significantly lower for patients with CPRIC compared to those without, and this could reflect fewer deaths from hypoxic brain injury which is a common cause of premature death post-arrest.[21]

The administration of consciousness-altering medications such as midazolam, opiates and muscle relaxants was not associated with survival benefits in our population. These findings contribute to concerns that sedatives, such as benzodiazepines, could impair vasomotor tone leading to a reduction in coronary perfusion pressures.[22] As a result, several regions have implemented clinical practice guidelines which recommend the use of ketamine for sedation during CPRIC.[7] Unlike benzodiazepines, ketamine stimulates the sympathetic nervous system, increasing both heart rate and vasomotor tone.[23] Due to the small sample size of our population, it is difficult to determine whether the association between medication use and survival is medication-specific or dose-dependent.

While differences in arrest characteristics were not significant across cases treated with and without medication, cases treated with medication were less likely to arrest in public locations, be witnessed by EMS personnel and experience an initial VF/VT arrest rhythm. Because medication is less likely to be administered if cardioversion occurs soon after cardiac arrest (e.g. EMS witnessed arrest), its association with survival could reflect residual confounding from arrest duration.[15,24] This may explain why CPRIC patients treated with medication had a significantly higher median time to first ROSC compared with patients not receiving medication. In addition, despite the presence of CPRIC, patients receiving medication were more likely to have their resuscitation efforts ceased on scene compared with patients not receiving medication. It is possible that sedation prejudices the positive prognostication bias which is typically observed in cases with CPRIC,[4] and this may lead rescuers to perform shorter resuscitation attempts. As such, guidance is needed around both the ongoing use of medication in the treatment of CPRIC and prognostication decisions after their administration.

Limitations

Identification of CPRIC was performed using a broad keyword search of electronic patient care records and therefore reliance on recording of the events by paramedics may have under-estimated the number of cases. However, given its relatively rare occurrence and challenges associated with management, it is unlikely that CPRIC cases would have gone undocumented. Although this is the largest collection of cases of CPRIC described in medical literature, the sample remains relatively small. As such, it is possible that our analysis was unpowered to detect meaningful differences between groups. In particular, the association between medication use and survival outcome requires validation in larger prospective studies. Future evaluations would also benefit from the inclusion of other arrest factors which could confound the association between CPRIC and survival, such as the quality and duration of CPR. In addition, the assessment of blood pressures post-ROSC may also be a valuable approach to measuring vasomotor impairment associated with sedative administration.

Conclusion

Consciousness induced during the delivery of CPR occurs infrequently in OHCA patients, although the proportion of cases appears to be increasing over time. Favourable arrest characteristics, including reduced downtime before the arrival of EMS, are likely to influence the development of CPRIC. Patients with CPRIC had improved survival outcomes, but this association may be dependent on management. Treatment guidelines regarding the use of sedation to manage episodes of CPRIC and in-field prognostication decisions would help standardise care and minimise treatment bias.

Conflicts of interest statement

None to declare.

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None reported.

Disclosures

None reported.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.resuscitation.2017.01.018.

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