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CLINICAL PAPER

Effectiveness and long-term outcome of cardiopulmonary resuscitation in paediatric intensive care units in Spain[☆]

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Received 8 June 2005; received in revised form 11 November 2005; accepted 14 November 2005

KEYWORDS

Child;
Intensive care;
Cardiac arrest;
Resuscitation;

Summary

Objective: To analyse the immediate effectiveness of resuscitation and long-term outcome of children who suffered a cardiorespiratory arrest when admitted to paediatric intensive care units (PICU).

Design and setting: Secondary analysis of data from an 18-month prospective, multi-centre study analysing cardiorespiratory arrest in children in 16 paediatric intensive care units in Spain.

[☆] A Spanish translated version of the summary of this article appears as Appendix in the online version at [doi:10.1016/j.resuscitation.2005.11.020](https://doi.org/10.1016/j.resuscitation.2005.11.020).

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Cardiopulmonary
resuscitation;
Outcome

Patients and methods: We studied 116 children between 7 days and 17 years of age. Data were recorded according to the Utstein style. Analysed outcome variables were sustained return of spontaneous circulation (ROSC), survival to hospital discharge and survival at 1 year. Neurological and general performance outcome was assessed by means of the Paediatric Cerebral Performance Category (PCPC) and the Paediatric Overall Performance Category (POPC) scales.

Interventions: None.

Measurements and results: In 80 patients (69%) ROSC was achieved and it was sustained >20 min in 69 (59.5%). At one-year follow-up, 40 children (34.5%) were alive. Survival was not associated with sex, age or weight of patients. Mortality from cardiac arrest was higher than respiratory arrest (69.8% versus 40%, $p=0.01$). Patients with sepsis had a higher mortality than other diagnostic groups. Mechanically ventilated children and those treated with vasoactive drugs had a higher mortality. Initial mortality was slightly higher in patients with slow ECG rhythms (35.7%) compared to those with ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) (27.2%). Duration of resuscitation effort was correlated with mortality ($p<0.0001$). Patients who required one or more doses of adrenaline had also a higher mortality (77.8% versus 20.7%, $p<0.0001$) and survivors needed less doses of adrenaline (0.85 ± 1.14 versus 4.4 ± 2.9 , $p<0.0001$). At hospital discharge 86.8 and 84.6% of patients had scores 1 or 2 (normal or near-normal) in the PCPC and POPC scales. At 1-year follow-up these figures were 90.8 and 86.3%, respectively.

Conclusion: One-third of children who suffer a cardiac or respiratory arrest when admitted to PICU survive, and most of them had a good long-term neurological and functional outcome. The duration of cardiopulmonary resuscitation attempts is the best indicator of mortality.

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Introduction

Critically ill children have a high risk of complications that can lead to cardiorespiratory arrest (CRA). Resuscitation includes procedures and treatments that are immediately available in the critical care setting and the best possible results in terms of survival and neurological outcome should be obtained.^{1–3} However, little has been published about the actual effectiveness and long-term outcome of resuscitation in this subset of patients, and most of the data are difficult to interpret because the studies have been retrospective or included patients having suffered CRA at different in-hospital sites.^{4–8}

The Utstein style provides uniform guidelines for reporting characteristics and outcome for in-hospital and out-of-hospital CRA in children.^{8,10} To date, only one prospective study that analyses, in a single centre, the outcome of in-hospital CRA in children following the Utstein style guidelines has been reported.⁵

The purpose of the present study was to provide an Utstein style prospective and multicentre report of children who suffered a CRA when admitted to PICU and to evaluate factors associated with survival as well as short and long-term neurological outcome.

Patients and methods

An invitation to participate in the study was sent to 26 paediatric intensive care units (PICU) in Spain.^{11,12} A protocol was drawn up in accordance with the Utstein style guidelines.^{9,10} This is a secondary analysis of data from a study of cardiopulmonary arrest in Spain; the methodology and primary results of which have been described elsewhere.^{11,12} Patients admitted to PICU and aged from 7 days to 18 years were eligible to be included in the present study if they presented emergency non-induced respiratory arrest (RA), defined as the absence of respiration requiring assisted ventilation, or cardiac arrest (CA), defined as the inability to palpate a central pulse, unresponsiveness and apnea or severe bradycardia lower than 60 bpm with poor perfusion in infants requiring external cardiac compressions and assisted ventilation. Patients who presented with RA but developed CA during resuscitation were retained in the RA group.

Treatment protocol consisted of the recommendations for cardiopulmonary resuscitation released by the Spanish Paediatric Resuscitation Working group following the international guidelines available at the time of the study.^{13,14} The record included: patient-related variables (age, sex, weight, cause of the arrest and personal back-

ground), arrest and life support related variables (type of arrest, monitored variables, assisted ventilation an/or vasoactive drugs administered before the arrest, the staff who performed the resuscitation manoeuvres and procedures, first ECG rhythm, and total duration of CPR). The outcome-related variables were: (a) initial survival, defined as the return of spontaneous circulation (ROSC) sustained more than 20 min, (b) return of spontaneous breathing, (c) neurological status at the end of the CPR, (d) later complications in the PICU: respiratory, shock, renal failure, nosocomial infection, intracranial hypertension, and (e) cause and time of death. Paediatric cerebral performance category (PCPC) and paediatric overall performance category (POPC) scales¹⁵ were applied at PICU discharge, at hospital discharge and at 1-year follow-up. The study period was from 1 April 1998 to 30 September 1999 (18 months).

The statistical study was performed using version 12 of the SPSS software statistical programme. Pearson's chi-squared test was used for qualitative variables analysis, and Fisher's exact test when n was less than 20 or when any value was less than 5. Student's t -test was used to compare quantitative variables between independent groups and the Mann-Whitney U -test for variables not normally distributed. Multivariate logistic regression was performed to assess the influence of each one of the factors on the initial and final mortality. All the individual factors with statistically significance in the univariate analysis were included in the multivariate analysis. Results are expressed as mean \pm standard deviation (S.D.). A less than 0.05 p -value was considered significant. The data relating to mortality at hospital discharge and final mortality were very similar and therefore only the hospital discharge mortality is presented in tables.

Results

We studied 116 children who presented with a cardiorespiratory arrest while they were hospitalised in 16 PICUs (in-PICU CRA), 71 males (61.2%) and 45 females (38.8%), with a mean age of 37.7 ± 48.7 months (range: 0.1–204 months) and mean weight of 14.3 ± 15.6 kg (range: 2.3–80 kg). This population represents 41% of the 283 children with CRA previously reported.^{11,12}

In 80 patients (69.0%) resuscitation (CPR) achieved ROSC, that was sustained in 69 (59.5%). In 20 patients (17.2%) restoration of spontaneous ventilation was also achieved at the end of the resuscitation procedure.

A total of 76 children died (65.5%); 47 did not respond to resuscitation attempts, 5 children died in the first 24 h after the arrest, 9 survived more than 24 h but died in the first week, and 14 died in hospital after 1 week. Only one patient died in hospital after been discharged from PICU and another died 15 days after hospital discharge due to a new cardiorespiratory arrest (Figure 1).

No significant differences were observed when survivors and children who subsequently died were compared in terms of sex, age and weight (Table 1). The causes of death were: no response to CPR in 47 patients (61.8%), multiorgan failure in 20 (26.3%), brain death in 6 (7.9%), do-not-resuscitate order in 2 (2.6%) and new arrest after hospital discharge in one (1.3%) (Figure 1).

When the event was detected, the arrest was respiratory in 20 patients (17.2%) and cardiac in 96 (82.8%). Ten (50%) of the RA patients developed cardiac arrest and required chest compressions during resuscitation. Mortality at hospital discharge after cardiac arrest (68.9%) was significantly higher than in cases of respiratory arrest (40.0%) ($p = 0.01$) (Table 1).

The underlying diseases of patients were cardiac in 39 (33.6%), sepsis in 26 (22.4%), respiratory in 25 cases (21.6%), neurological in 15 (12.9%), metabolic in 5 (4.3%) and "other" in 6 cases (5.2%). The relative risk of mortality was significantly higher for septic patients (1.35, 95% CI: 1.02–1.78) (Table 1).

Seventy-nine patients (68.1%) were ventilated mechanically and 69 (59.5%) were treated with vasoactive drugs at the moment of arrest. Mortality at hospital discharge in the children mechanically ventilated (72.2%) was significantly higher than in the other patients (48.6%) ($p = 0.012$), as was the mortality of those treated with vasoactive drugs (81.2% versus 40.4%, $p < 0.0001$) (Table 1).

The ECG tracing was recorded at the moment of arrest in 110 patients (94.8%) (Table 1). There were slow rhythms (asystole, severe bradycardia and atrioventricular blockade) in 74.5% of cases, pulseless electrical activity (PEA) in 10.9%, ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) in 10.0%, and sinus rhythm in 3.6%. Initial mortality was slightly higher in patients who showed slow rhythms (35.7%), than in those with ventricular fibrillation or pulseless ventricular tachycardia (27.2%); however, the difference did not achieve statistical significance. The same occurred when hospital discharge and final mortality were assessed in relation to the initial rhythm. There were no differences in initial and final mortality between asystole, PEA and VF/pulseless VT (Table 1). A mean of 4.1 doses of adrenaline (epinephrine) (range: 1–14) was administered to 81 patients (69.8%). Mortal-

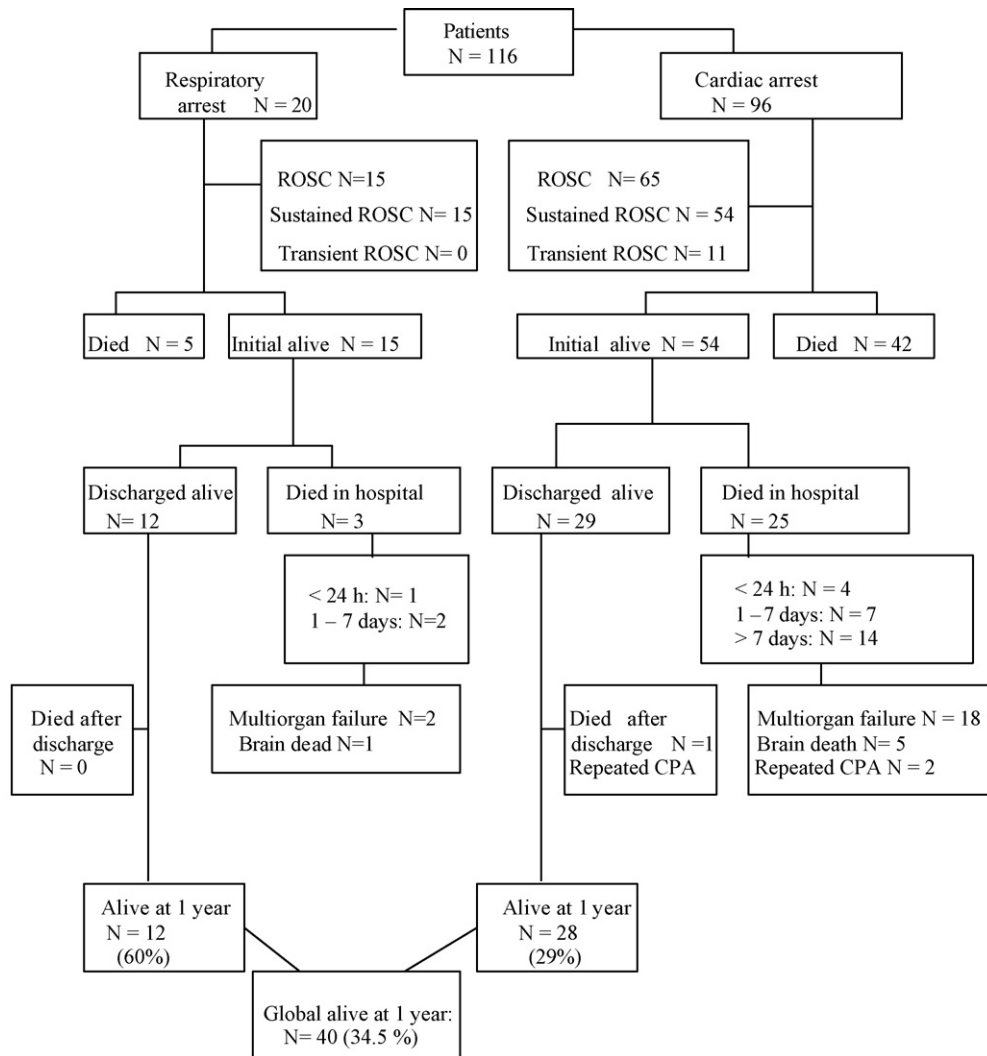


Figure 1 Paediatric Utstein style template for recording outcome from respiratory and cardiopulmonary arrest.

ity at hospital discharge in patients who required adrenaline (77.8%) was significantly higher than in those who did not receive the drug (20.7%) ($p < 0.0001$). Children who subsequently died received more doses of adrenaline than survivors (4.4 ± 2.9 versus 0.85 ± 1.14 , $p < 0.0001$). The final mortality in those who required less than three doses of adrenaline was 50.0%; however, it was 90.3% for those who required three or more doses ($p < 0.0001$) (Table 2). Bicarbonate (mean number of doses = 2.3, range: 1–4) was given to 67 patients (57.7%). Mortality in these patients was significantly higher than the rest (83.6% versus 30.2%, $p < 0.0001$) (Table 2). The number of bicarbonate doses was also higher in non-survivors (2.0 ± 1.5 versus 0.3 ± 0.7 , $p < 0.001$). Twenty-seven patients (23.2%) were treated with volume load; the mortality in this group was also higher than the rest of patients (77.8% versus 57.8%, $p = 0.049$) (Table 2).

Initial, mortality at hospital discharge and final mortality were higher in patients with longer resuscitation times. The relative risk of mortality became statistically significant with a period of resuscitation that was longer than 20 min (Table 2).

At the end of the resuscitation attempt, the neurological status of survivors was alert in 10 (14.0%), 10 responded to voice or physical stimulus (14.0%), 6 did not respond to physical stimulus (8.4%) and 45 were sedated with drugs (63.3%). Mortality was 83.3% in patients who did not respond to stimuli, 46.7% for those sedated, 30.0% for those who responded to stimulus and 10.0% in those who were alert ($p = 0.03$).

Patients who presented clinical complications (with the exception of respiratory infection) after the arrest episode had a significantly higher mortality (Table 2). Logistic regression analysis found that duration of resuscitation longer than 20 min

Table 1 Clinical characteristics of patients and mortality

	Number of patients	Initial mortality (%)	Mortality at hospital discharge (%)	Relative risk of mortality	95% CI	p-value
Sex						0.405
Female	45	42.2	62.2	0.88	0.64–1.21	NS
Male	71	32.4	66.2	1.13	0.82–1.55	NS
Age						0.697
<1 month	9	33.3	55.6	0.89	0.46–1.72	NS
1–12 months	48	39.6	60.4	0.91	0.66–1.24	NS
1–8 years	44	31.8	68.2	1.03	0.76–1.39	NS
>8 years	15	40	31.8	1.18	0.84–1.67	NS
Type of arrest						0.013
Respiratory	20	25	40	0.53 ^a	0.29–0.96	<0.05
Cardiac	96	38.5	68.9	1.90	1.04–3.48	<0.05
Underlying disease						
Cardiac	39	30.8	61.5	0.93	0.67–1.28	NS
Sepsis	26	53.8	80.8	1.35	1.02–1.78	< 0.05
Respiratory	25	24	52	0.79	0.5–1.25	NS
Neurological	15	33.3	73.3	1.05	0.69–1.62	NS
Metabolic	5	40	60	0.94	0.45–1.95	NS
Other	6	50	50	0.78	0.34–1.74	NS
Previous treatments						
Mechanical ventilation	79	41.8	72.2	1.69	1.52–1.89	0.012
Vasoactive drugs	69	46.4	81.2	2.08	1.39–3.1	<10 ⁻³
Initial ECG						
Asystole	29	31	69	1.13	0.84–1.52	NS
PEA	12	33.3	83.3	1.38	1.02–1.85	NS
VF-VT	11	27.2	81.8	1.34	0.97–1.84	NS
Other	58					

PEA: pulseless electrical activity; VF-VT: ventricular fibrillation, ventricular tachycardia.
^a RR of mortality less than 1.

was the variable that displayed the strongest association with initial and final mortality. The odds ratio (confidence interval 95%) for initial mortality and mortality at hospital discharge were 168.7 (28.9–983.1) and 60.3 (7.2–504.9), respectively.

Neurological outcome scales were available for 39 patients at PICU and hospital discharge (95.1% of survivors) and for 22 children at 1-year follow-up (55% of survivors). At hospital discharge 86.8 and 84.6% of patients had scores 1 or 2 (normal or near-normal) in the PCPC and POPC scales. At 1-year follow-up these figures were 90.8 and 86.3%, respectively (Tables 3 and 4).

Discussion

Cardiorespiratory arrest is a rare but relatively expected event in critically ill children.^{1,7,8} However, there is a surprisingly lack of data about the immediate and long-term results of CPR in this spe-

cific population.^{1–7} The aim of our study was to focus on the data of paediatric CRA occurring in all types of patients admitted to PICU, and to assess the long-term neurological outcome. This is the first prospective and multicentre study of paediatric CPR in PICUs using the Utstein guidelines for uniform data reporting.^{9,10} Previous studies of in-hospital paediatric cardiac arrest are difficult to compare and interpret because of inconsistent definitions of cardiac arrest, CPR, event times and intervals, specific interventions, and outcomes.⁴ Reis et al.⁵ reported data from 129 in-hospital CPR (94 children arrested in PICU), in a single centre, following the Utstein style; however this study did not include cardiac surgery nor trauma patients. Suominen et al.⁶ used Utstein-style epidemiological definitions but the data were abstracted from retrospective chart reviews. In this series 64% of CPR occurred in the ICU and the sample included mainly patients after cardiac surgery, without neurosurgical or trauma patients. Horisberger et al.¹

Table 2 Treatment of patients, duration of CPR, PICU complications and mortality

	Number of patients	Initial mortality (%)	Mortality at hospital discharge (%)	Relative risk of mortality	95% CI	p-value
Adrenaline	81	44.4	77.8	3.76	1.83–7.73	<10 ⁻³
0 doses	29	0	20.7	0.34	0.18–0.65	<10 ⁻³
1 dose	11	0	20	0.30	0.09–1.04	NS
2 doses	17	12.5	68.8	1.21	0.81–1.8	NS
3 or more doses	53	61.5	90.3	2.52	1.7–3.73	<0.05
Bicarbonate	67	46.3	83.6	2.77	1.67–4.67	<10 ⁻³
0 doses	43	11.6	30.2	0.41	0.26–0.64	<0.05
1 dose	23	27.3	68.2	1.18	0.84–1.65	NS
2 or more doses	44	57.1	90.4	1.94	1.43–2.61	<0.05
Volume load	27	51.9	77.8	3.50	2.1–5.83	0.049
Duration of CPR	108					
<4 min	34	0	20.6	0.26	0.13–0.53	<0.05
5–9 min	11	9.1	36.4	0.52	0.2–1.33	NS
10–19 min	22	4.5	72.7	1.12	0.77–1.63	NS
20–29 min	7	57.1	100	1.71	1.43–2.03	<0.05
30–60 min	26	88.5	96.2	1.97	1.52–2.55	<0.05
>60 min	8	62.5	100	1.73	1.45–2.08	<0.05
PICU complications						
Respiratory infection	41	29.4	68.3	1.52	1.03–2.23	0.060
Shock	36	30	86.1	2.26	1.53–3.33	<10 ⁻³
Cardiac failure	33	28.6	75.8	1.60	1.11–2.3	0.009
Renal failure	29	31.8	89.7	2.28	1.65–3.15	<10 ⁻³
Sepsis	28	39.1	75	1.78	1.27–2.51	0.025
Intracranial hypertension	7	42.9	100	1.89	1.52–2.36	0.019

reported the long-term outcome of resuscitation in a retrospective study of 89 in in-patients and out-patients (only 36% were resuscitated during PICU admission). Two other studies have reported the results of resuscitation in children admitted to specialised paediatric cardiac intensive care units.^{16,17} In contrast, our sample was collected prospectively from 16 different PICUs and included all types of critically ill patients, from infectious or metabolic diseases to postoperative neurosurgical or cardiac

cases. Slonim et al.⁸ reported patient survival to hospital discharge, and the predictors of survival after resuscitation within the PICU in a diverse population admitted to one of 32 PICUs. They collected the data from the 1.8% admitted children who experienced an event requiring resuscitation for at least 2 min, but long-term neurological outcome was not assessed.⁸

Our results compare favourably with other studies in terms of survival and long-term outcome

Table 3 Paediatric cerebral performance category (PCPC) and paediatric overall performance category (POPC) scale scores at PICU discharge, hospital discharge and at 1 year in patients with cardiac arrest

Score	Number of patients (%)					
	At PICU discharge (27) ^a		At hospital discharge (27) ^a		At 1 year (14) ^a	
	PCPC	POPC	PCPC	POPC	PCPC	POPC
1	21 (77.7)	20 (74)	19 (70.3)	19 (70.3)	12 (85.7)	11 (78.5)
2	3 (11.1)	3 (11.1)	4 (14.9)	4 (14.9)	1 (7.1)	1 (7.1)
3	1 (3.7)	2 (7.4)	2 (7.4)	2 (7.4)	1 (7.1)	2 (14.2)
4	2 (7.4)	2 (7.4)	2 (7.4)	2 (7.4)	0	0
5	0	0	0	0	0	0

^a Number of patients.

Table 4 Paediatric cerebral performance category (PCPC) and Paediatric overall performance category (POPC) scale scores at PICU discharge, hospital discharge and at 1 year in patients with respiratory arrest

Score	Number of patients					
	At PICU discharge (12) ^a		At hospital discharge (12) ^a		At 1 year (8) ^a	
	PCPC	POPC	PCPC	POPC	PCPC	POPC
1	10	10	10	10	7	7
2	0	0	0	0	0	0
3	1	1	1	1	1	1
4	0	0	0	0	0	0
5	1	1	1	1	0	0

^a Number of patients.

(Table 5).^{1,5,6,16,18} Resuscitation was deemed effective in PICU: sustained ROSC was attained in 59.5% of initial CPR attempts and 34% of patients were alive 1 year later. In concordance with other reports,^{1,5,6} independent factors associated with mortality were septic disease, previous treatment with vasoactive drugs, mechanical ventilation, need for treatment with adrenaline, bicarbonate or volume load and duration of CPR attempts. The logistic regression analysis showed that a period of resuscitation longer than 20 min was the variable that displayed the strongest association with mortality. Although some patients who required resuscitation lasting from 20 to 60 min and were alive at 1 year have been reported,¹ our results and most of studies of in- and out-of-hospital resuscitation suggest that, while decision to discontinue unsuccessful CPR is difficult and should not depend on duration of resuscitation alone, to maintain resuscitation without positive effects longer than 20 min seems to be futile.⁴ Recently, encouraging results with extracorporeal support in refractory in-

hospital cardiac arrest have been reported. If these results are confirmed, in the centres where extracorporeal support is available it should be considered and initiated early in patients with refractory cardiac arrest.¹⁹

As was expected, patients monitored and rapidly assisted by intensive care staff, respiratory arrest had a better prognosis than cardiac arrest. However, the mortality at hospital discharge of patients with respiratory arrest was 40%, a figure that could be related with the underlying disease in these children.

The precipitating cause of the arrest can be an important determinant of outcome.⁵ In our study, sepsis was the only underlying disease that was significantly associated with an increased risk of mortality. Other studies, difficult to compare due to the different definitions used, have already noted the bad outcome from resuscitation in patients with sepsis. Reis et al.⁵ reported a 5% rate of survival at hospital discharge. Similarly, Torres et al.¹⁸ noted that none of 44 cardiac arrest victims with the sep-

Table 5 Recently reported long-term outcomes of resuscitation after in-PICU cardiorespiratory arrest

Author (country) (year published)	Number of patients	One-year survival (%)	Good neurological outcome (%)	Notes/Limitations
Torres (USA) (1997)	92	10	78	
Parra (USA) (2000)	32	34 (6 months survival)	72	Most patients were infants ^a post cardiac surgery
Suominen (Finland) (2000)	76	18	—	No trauma, no neurosurgery patients
Reis (Brazil) (2002)	129 in-hospital (94 in-PICU)	15	83	No heart diseases, no trauma patients
Horisberger (Switzerland) (2002)	89 in- and out-of-hospital (32 in-PICU)	54 ^b	77 ^b	Retrospective study. Data of PICU patients no specified.
Rodríguez-Núñez (Spain) (2005)	116	34.5	90	Multicentre, prospective study

^a Median of age: 1 month.

^b Results referred to the whole sample.

sis syndrome survived and Slonim et al.⁸ reported a 7% survival to hospital discharge among children with an infectious disease. In contrast, our hospital discharge rate for septic patients was 19%.

When patients needed treatment with vasoactive drugs and/or mechanical ventilation before the arrest, the relative risk of mortality after one event of CRA was significant. This is not surprising and we consider that these factors are indirect markers of the severity of the underlying disease and of organ failure.

Adrenaline treatment and the number of doses administered have been noted as factors associated with mortality after resuscitation.⁵ In our study the relative risk of mortality at hospital discharge of the group who needed adrenaline was 3.76 (95% CI: 1.83–7.73). More interestingly, the number of doses of adrenaline given should be considered as a factor related to a bad prognosis and even as a factor for termination of resuscitation efforts.^{5,8} In our study the relative risk of mortality became significant when two or more doses were needed; when three or more doses were needed, the hospital discharge mortality was 90%. We think this fact should promote investigations to search for additional treatments in this setting.

As it was expected, complications arising after initial resuscitation, including sepsis, renal failure, shock, intracranial hypertension and cardiac failure, increased the risk of mortality at hospital discharge. Respiratory infections were the most frequent complication in these patients, but they did not achieve statistical significance as a mortality factor. However, the possible association of complications with mortality must be regarded with caution because several confounders could be occurring in our patients.

Although the immediate survival rate is an important end-point, there is a general consensus that the main goal of resuscitation should be survival with a long-term good neurological status.^{1,4,12} The PCPC and POPC scores are simple but useful tools to assess general performance and neurological disability.^{9,10} Recent reports indicate that the neurological outcome in children who survive after CPR is quite good with rates of "good outcome" (normal or mild disability) ranging from 72 to 83%.^{1,5,6,12,16,18} In our sample 86.8 and 84.6% of children had scores 1 or 2 by the PCPC and POPC scales at hospital discharge, and 90.8 and 86.3% of those evaluated had scores 1 or 2 at 1-year follow-up (Table 5). In our opinion, this encouraging fact must be noted as a positive point for the emergency and critical care staff who sometimes become frustrated by the perceived dismal results of resuscitation in terms of survival.

Ethical aspects are also fundamental during and after resuscitation. One of these aspects is the futility of a treatment that sometimes cannot achieve any increase in length or quality of life.²⁰ In the light of this principle, do not attempt resuscitation (DNAR) orders should be considered and might be indicated in some PICU patients; in this sense, Horisberger et al.¹ from Switzerland, reported that they applied a DNR order to 35% of those who survived initially. In contrast, only 2.6% of our patients had such an order. This is a striking difference, suggesting a great heterogeneity of ethical attitudes on resuscitation depending on the geographical and socio-cultural area.²¹

Our study has several limitations that must be considered. Some of the PICUs in Spain did not participate in the study and this could produce some bias on results. Resuscitation may be an uncontrolled activity even inside the PICU and we cannot certify that procedures were done uniformly in all patients. The small number of survivors make it difficult to ascertain if one or several confounders had influence on results. Finally, some patients were lost in follow-up and these could lead to overestimation of good outcomes.

In conclusion, about one-third of children who suffered a cardiac or respiratory arrest when hospitalised in PICUs survived, and most of them had a good long-term neurological and functional outcome. Several factors have influence on survival: type of arrest, underlying disease, need of mechanical ventilation or vasoactive drugs, duration of CPR, treatment with adrenaline and bicarbonate, as well as complications after resuscitation. Among them, duration of cardiopulmonary resuscitation attempts is the best indicator of mortality in these children.

Conflict of interest

None.

Acknowledgment

This study has been supported by a Grant from the Fondo de Investigaciones Sanitarias, 00/0288.

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