

# Obstetrical and Pediatric Anesthesia

## An evaluation of pediatric in-hospital advanced life support interventions using the pediatric Utstein guidelines: a review of 203 cardiorespiratory arrests

*[Une évaluation des interventions de réanimation cardiorespiratoire avancée en pédiatrie hospitalière à l'aide des directives Utstein pour enfants : une revue de 203 cas]*

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**Purpose:** Evaluate the efficacy of advanced life support interventions using the pediatric Utstein guidelines.

**Methods:** Charts from all patients for whom a cardiorespiratory arrest code was called during a six-year period in a university affiliated centre were reviewed. Data were recorded according to the pediatric Utstein guidelines and a  $P < 0.05$  was considered significant.

**Results:** Of the 234 calls, 203 were retained for analysis. The overall survival rate at one year was 26.0% of which 10% had deterioration of their neurologic status compared to the pre-cardiorespiratory arrest evaluation. Time to achieve sustained return of spontaneous circulation (ROSC;  $P < 0.0001$ ) and sustained measurable blood pressure ( $P = 0.002$ ), to perform endotracheal intubation ( $P = 0.04$ ) and the dose of sodium bicarbonate ( $P < 0.0001$ ) were indicators of long-term survival. Two patients were alive at one year with unchanged neurologic status despite a time to achieve sustained ROSC longer than 30 min (38 and 44 min). The mean first epinephrine dose of patients for whom ROSC was achieved but unsustainable was higher than those for whom ROSC was achieved and sustained ( $0.038 \pm 0.069 \text{ mg}\cdot\text{kg}^{-1}$  vs  $0.011 \pm 0.006 \text{ mg}\cdot\text{kg}^{-1}$ ;  $P = 0.004$ ). Survival rate and mean first epinephrine dose of patients who received their first epinephrine dose endotracheally ( $13.3\%$ ;  $0.011 \pm 0.004 \text{ mg}\cdot\text{kg}^{-1}$ ) were comparable to those of patients who received their first epinephrine dose intravenously ( $7\%$ ;  $0.015 \pm 0.027 \text{ mg}\cdot\text{kg}^{-1}$ ).

**Conclusions:** For intravenously administered epinephrine, a dose of  $0.01 \text{ mg}\cdot\text{kg}^{-1}$  seems appropriate as the first dose. The endotracheal route is a valuable alternative for epinephrine administration and, for infants, the dose does not need to be increased. A minimal resuscitation duration time of 30 min can be misleading if ROSC is used as the indicator.

**Objectif :** Évaluer l'efficacité des interventions de réanimation cardiorespiratoire avancée à l'aide de la technique Utstein pédiatrique.

**Méthode:** Les dossiers de tous les enfants pour lesquels un appel de réanimation cardiorespiratoire a été demandé sur une période de six années consécutives dans un centre hospitalier universitaire ont été revus. Les données ont été recueillies selon la technique Utstein pédiatrique. Un  $P < 0,05$  a été retenu.

**Résultats :** Des 234 appels, 203 ont été retenus pour analyse. Le taux de survie globale à un an est de 26,0 % avec 10 % de détérioration neurologique chez les survivants. Le délai pour l'obtention de la récupération d'une activité circulatoire spontanée (ROSC;  $P < 0,0001$ ) et d'une pression artérielle mesurable soutenue ( $P = 0,002$ ), pour réaliser l'intubation trachéale ( $P = 0,04$ ) et la dose de bicarbonate de sodium ( $P < 0,0001$ ) sont des indicateurs de survie à long terme. Deux patients sont vivants un an après l'arrêt sans modification de statut neurologique malgré un délai pour le ROSC supérieur à 30 min (38 et 44 min). La dose moyenne d'adrénaline administrée comme première dose est plus élevée pour les patients avec ROSC obtenu mais non soutenu que ceux pour qui le ROSC est soutenu ( $0,038 \pm 0,069 \text{ mg}\cdot\text{kg}^{-1}$  vs  $0,011 \pm 0,006 \text{ mg}\cdot\text{kg}^{-1}$ ;  $P = 0,004$ ). Le taux de survie et la première dose d'adrénaline des patients qui ont reçu l'adrénaline par voie intratrachéale (13,3 %;  $0,011 \pm 0,004 \text{ mg}\cdot\text{kg}^{-1}$ ) sont similaires à ceux qui l'ont reçue par voie iv (7 %;  $0,015 \pm 0,027 \text{ mg}\cdot\text{kg}^{-1}$ ).

**Conclusions :** Une dose de  $0,01 \text{ m}\cdot\text{kg}^{-1}$  d'adrénaline est appropriée comme première dose par voie iv. La voie intratrachéale est une solution de rechange adéquate et, pour les moins d'un an, la dose peut être identique à la dose recommandée pour la voie iv. Un temps minimal de réanimation de 30 min peut être insuffisant si le ROSC est choisi comme paramètre.

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**P**EDIATRIC cardiorespiratory arrests carry a poor prognosis that has unfortunately not changed over the last two decades. Report of small series using different terminologies may in part have contributed to the difficulty of developing new interventions that could have improved the prognosis of cardiorespiratory arrests in this age group. In their last guidelines publication the American Heart Association (AHA) clearly underlined this lack: "There is a need for more and better data regarding the epidemiology, treatment, and outcome of pediatric cardiorespiratory arrest".<sup>1</sup> In order to make possible data pooling from different centres, the American Academy of Pediatrics, the AHA and the European Resuscitation Council have proposed a uniform style to report pediatric cardiorespiratory arrest data based on the Utstein symposium.<sup>2,3</sup> Availability of more pediatric cardiorespiratory arrest data in this uniform style may help in the development of guidelines and/or recommendations that may ultimately improve the prognosis of these children.

Epinephrine remains the most useful and widely used drug in pediatric cardiorespiratory arrest. It improves cerebral and coronary blood flow, a critical determinant for return of spontaneous pulse, and is the first line drug for treatment of bradycardia with poor perfusion and asystole, the two most common initial rhythms observed in in-hospital pediatric cardiorespiratory arrests.<sup>4,5</sup> However, despite its widespread use, there are actually few available human data on the optimal dose of epinephrine that should be administered during pediatric cardiorespiratory resuscitation (CPR). Three studies, two retrospective and one prospective, have compared what are actually considered standard doses for *iv* epinephrine (0.01 or 0.02 mg·kg<sup>-1</sup>) to "high" epinephrine doses (0.1 or 0.2 mg·kg<sup>-1</sup>) with contradictory results.<sup>6-8</sup> The possible efficacy of lower or intermediate doses has not been evaluated so far.

The aims of this study were to report data from a six-year experience of in-hospital pediatric CPR in a tertiary care centre according to the pediatric Utstein style and to evaluate the influence of advanced life support (ALS) interventions including various dosages of epinephrine on survival and functional outcome after pediatric CPR.

### Methods

The hospital is a 673-bed university-affiliated tertiary maternal and pediatric care centre with 19,000 hospital admissions annually. Of these, 940 to 1,100 are pediatric critical care admissions. The CPR team includes a nurse with ALS training, two pediatric resi-

dent (one senior and one junior), and the on-call anesthesiologist. During the daytime, the pediatric intensivist also answers the call. The resuscitation team is mobilized for every cardiorespiratory arrest except those happening in the operating room or the neonatal intensive care unit.

With institutional Review Board approval, all charts of patients for whom a cardiorespiratory arrest code had been called between January 1 1983 to December 31 1987 were reviewed by one of the two investigators. We abstracted data on patient demographics and details on the cardiorespiratory arrest (Table A, available as Additional Material at [www.cja-jca.org](http://www.cja-jca.org)). We classified the etiology of the arrest by the system involved (cardiac and / or respiratory) and by the disease. Since there is a difference in severity between respiratory and cardiac arrests, we first classified each arrest as respiratory, cardiac, or cardiorespiratory. To provide a more detailed picture of the etiology for future allocation of educational resources and monies, we then classified each arrest by the etiological factor that preceded the respiratory and/or cardiac compromise.

From the abstracted data, a pediatric cerebral performance category (PCPC) score, from 1 to 6, was attributed before cardiac arrest and at 24 hr, seven, 30, and 365 days post-arrest, and at discharge from hospital. When data were not available from the chart, the requisite information was sought via a telephone interview with the child's parents or the child's primary physician. The PCPC score is a six-point score describing neurological and cognitive disability and function (Table B, available as Additional Material at [www.cja-jca.org](http://www.cja-jca.org)).<sup>2</sup> The difference between the pre-arrest score and the hospital discharge or one-year score was calculated for each patient (i.e., pre-arrest PCPC - discharge or one-year PCPC). When a negative difference was observed, the reason for the increased disability or lower function was classified as secondary to the illness or injury that led to the arrest, secondary to the arrest or resuscitation, or unrelated to the index arrest. When a patient suffered from more than one cardiorespiratory arrest within a year, only the first event was studied and the patient was considered dead (PCPC = 6) from the date of the second event.

Data were analyzed using the JMP 5.01 software (SAS Institute Inc. 2002, Cary, NC, USA). Nominal and ordinal data were analyzed with survival analysis, likelihood ratio tests, and nominal logistic regression. Continuous variables were described using mean  $\pm$  standard deviation and were analyzed with linear and stepwise regressions. Epinephrine dosages among the different ROSC groups (ROSC never achieved, ROSC achieved but unsustainable, and ROSC achieved

and sustained for 20 min or longer) were compared using ANOVA. A *P*-value of less than 0.05 was considered to be statistically significant.

## Results

The Figure outlines results for long-term survival. Two hundred and thirty-four patients had one or more cardiorespiratory arrests. Of these, 31 episodes were excluded: 17 occurred out of hospital, eight occurred within a year of a previous arrest, three occurred in patients aged over 21 yr, two occurred in patients for whom resuscitation was not attempted, and one was an erroneous call (Figure). Of the 203 patients retained for analysis, 11 could not be followed up to one year. Data from these patients, up to the time at which they were lost to follow-up, were included.

Details of the study population are described in Table I. At one year, 50 patients were alive, 142 patients were dead, and 11 had an unknown status (Figure). Of those who were alive, five had negative differences of -1 (two patients), -2 (one patient), or -3 (two patients) between their pre-arrest and one-year PCPC scores. These were attributed to the illness or injury that led to the arrest for one patient, to the event or the resuscitation for two patients, and to causes unrelated to the arrest for two patients. Thus, of the patients whose fates were known at one-year post-arrest, 45/192 (23.4%) were neurologically unchanged while 5/192 (2.6%) survived with some degree of deterioration from their initial neurological status.

The effects of ALS interventions on survival are given in Table II. For continuous variables, those that were significantly correlated with the number of days before death or loss to follow-up were time to achieve a sustained ROSC ( $P < 0.0001$ ), time to achieve a sustained measurable blood pressure ( $P = 0.002$ ), time to perform endotracheal intubation ( $n = 84$ ,  $P = 0.04$ , no long-term survival after 20 min), and the dose of sodium bicarbonate in  $\text{mEq}\cdot\text{kg}^{-1}$  ( $P < 0.0001$ ). Long-term survival did not occur in individuals who required defibrillation at  $18.5 \text{ j}\cdot\text{kg}^{-1}$  or higher (as the total dose) or had a pre-cardiorespiratory arrest hemoglobin concentration lower than  $57 \text{ g}\cdot\text{L}^{-1}$ , but was observed in individuals with arterial pHs as low as 6.85 and as high as 7.63 during the arrest period.

There was no relationship between blood glucose and survival duration or change in neurological status. There was no correlation between the pre-arrest blood glucose (range  $0.5$  to  $38.6 \text{ mmol}\cdot\text{L}^{-1}$ ) and the number of days before death or loss to follow-up ( $n = 88$ ,  $P = 0.45$ ) or the pre-arrest - one-year PCPC difference ( $n = 85$ ,  $P = 0.38$ ) nor between the post-arrest blood glucose (range  $3.3$  to  $32.4 \text{ mmol}\cdot\text{L}^{-1}$ ) and the number

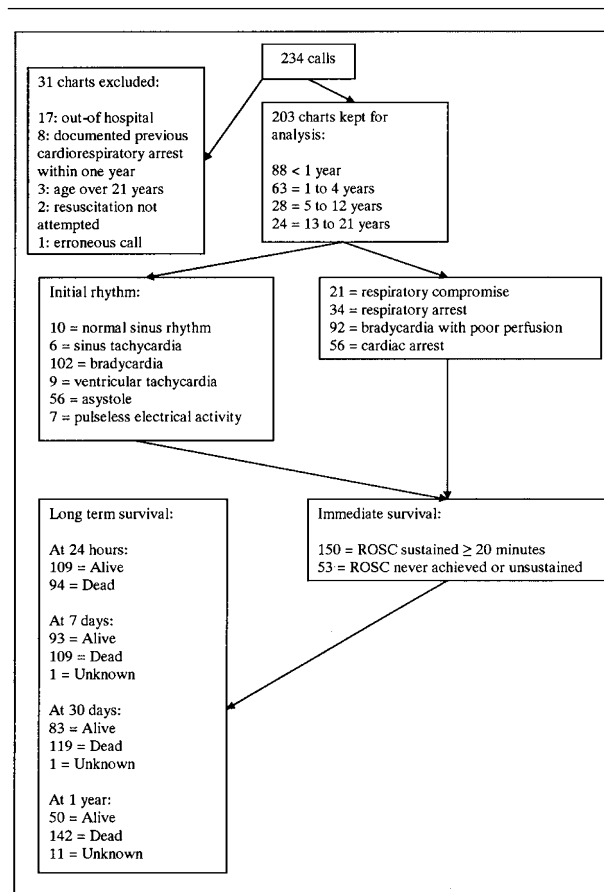


FIGURE Flowchart of short and long-term survival of patients according to the pediatric Utstein guidelines.

of days before death or loss to follow-up ( $n = 73$ ,  $P = 0.26$ ) or the pre-arrest - one-year PCPC difference ( $n = 68$ ,  $P = 0.44$ ).

Factors that were associated with one-year survival ( $P < 0.25$ ) were the need for at least one dose of epinephrine ( $P = 0.002$ ), type of cardiorespiratory arrest ( $P = 0.09$ ), initial rhythm ( $P = 0.12$ ), pre-existing chronic disease ( $P = 0.21$ ), and the time required to perform endotracheal intubation ( $P = 0.21$ ).

Two patients had a one-year survival without neurological deterioration despite requiring 38 and 44 min respectively to achieve a sustained ROSC. One of these patients also required 34 min to achieve a sustained measurable blood pressure.

The first epinephrine dose varied from  $0.0004$  to  $0.24 \text{ mg}\cdot\text{kg}^{-1}$  ( $n = 97$ ). The mean first dose was  $0.013 \pm 0.009 \text{ mg}\cdot\text{kg}^{-1}$  for patients for whom a ROSC was never achieved,  $0.038 \pm 0.069 \text{ mg}\cdot\text{kg}^{-1}$  for those for

TABLE I Description of the study population

Factor ( <i>P</i> -value)	Number	One-year survival rate (%)
Age ( <i>P</i> = 0.05)		
Under 1 yr	88	34.1
1 to 4 yr	63	31.8
5 to 12 yr	28	25
13 to 21 yr	24	8.3
Gender ( <i>P</i> = 0.90)		
Female	88	29.6
Male	115	28.7
Witnessed arrest ( <i>P</i> = 0.80)		
Yes	171	28.7
No	29	31.0
Site of arrest ( <i>P</i> = 0.03)		
Emergency room	6	50
Ward	70	30
Pediatric intensive care unit	109	22
Radiology suite	13	61.5
Cardiac catheterization room	2	50
Other sites	3	66.7
Type of arrest ( <i>P</i> = 0.009)		
Respiratory compromise	21	33.3
Respiratory arrest	34	38.2
Bradycardia with poor perfusion	92	34.8
Cardiac arrest	56	12.5
Initial rhythm ( <i>P</i> = 0.006)		
Normal sinus rhythm	10	60
Sinus tachycardia	6	50
Bradycardia	102	30.4
Ventricular tachycardia	9	22.2
Asystole	56	14.3
Pulseless electrical activity	7	0
Etiology of arrest by affected system ( <i>P</i> < 0.0001)		
Respiratory compromise	119	40.3
Circulatory compromise	78	12.8
Cardiorespiratory compromise	6	16.7
Etiology of arrest by disease ( <i>P</i> = 0.0007)		
Congenital cardiac disease	45	13.3
Non-congenital cardiac disease	6	16.7
Trauma	5	0
Airway related	92	37.0
Neurological disorder	21	38.1
Intoxication	7	85.7
Severe infection other than respiratory	10	10
Other	16	18.8
Pre-existing chronic disease ( <i>P</i> < 0.0001)		
None	16	12.5
Hepatic	13	30.8
Cardiac	62	12.9
Oncological / hematological	14	7.1
Prematurity	8	37.5
Neurological	28	35.7
Pulmonary	16	68.8
Genetic	9	22.2
Metabolic	6	16.7
Malformations	18	61.1
Renal	8	50
Acquired immune deficiency syndrome	5	40

*P* values indicate the effect of the category as a marker for survival.

whom a ROSC was achieved but unsustainable, and  $0.011 \pm 0.006$  mg·kg<sup>-1</sup> for those for whom a sustained ROSC was achieved (*P* = 0.004). For patients with bradycardia as initial rhythm the first dose of epinephrine was  $0.014 \pm 0.013$  mg·kg<sup>-1</sup> for patients for whom a ROSC was never achieved,  $0.055 \pm 0.085$  mg·kg<sup>-1</sup> for those for whom a ROSC was achieved but unsustainable, and  $0.011 \pm 0.005$  mg·kg<sup>-1</sup> for those for whom a sustained ROSC was achieved (*P* = 0.01). For patients who received epinephrine, there was no immediate survivor (ROSC sustained for 20 min or higher) if the first dose of epinephrine was lower than 0.0018 mg·kg<sup>-1</sup> or higher than 0.0357 mg·kg<sup>-1</sup> and there was no 24 hr survival if the first dose of epinephrine was lower than 0.0018 mg·kg<sup>-1</sup> or higher than 0.019 mg·kg<sup>-1</sup>. The total dose of epinephrine was  $0.096 \pm 0.21$  mg·kg<sup>-1</sup> for patients for whom a ROSC was never achieved,  $0.15 \pm 0.157$  mg·kg<sup>-1</sup> for patients for whom a ROSC was achieved but unsustainable, and  $0.032 \pm 0.047$  for those in whom a sustained ROSC was achieved (*P* = 0.007). The mean epinephrine dose of patients who received their first epinephrine dose intravenously was  $0.015 \pm 0.027$  mg·kg<sup>-1</sup> (*n* = 86) and their survival rate was 7%. The mean epinephrine dose of patients who received their first epinephrine dose through their endotracheal tube was  $0.011 \pm 0.004$  mg·kg<sup>-1</sup> and their survival rate was 13.3% (*n* = 15). The mean age of patients who received their first epinephrine dose endotracheally was  $2.30 \pm 4.56$  yr (median 0.58 yr; 25 and 75% quartiles 0.33 and one year).

## Discussion

A pediatric cardiorespiratory arrest is a devastating event. Even with the inclusion of respiratory compromises in this cohort (as suggested by the Pediatric Utstein Symposium), the overall one-year survival rate was only 26.0% with 10% of these survivors showing a deterioration of their neurologic status from their pre-arrest state as measured by the PCPC score. Though chronic pre-existing disease was certainly an important determinant of the long-term prognosis and the poor overall survival rate, cardiorespiratory arrest and subsequent CPR themselves resulted in extremely poor prognosis as demonstrated by a 24-hr survival rate of 53.7% and a seven-day survival rate of 45.8%. For the subgroup of patients with cardiac arrests, the one-year survival rate was only 12.5%. Standardization of definitions as proposed by the Pediatric Utstein Symposium should help in evaluating efficacy and real benefits of ALS interventions.

In the present study, the time from initiation of CPR to intubation of the trachea was an important factor for long-term survival (*P* = 0.04). For patients requiring

TABLE II Effects of advanced life support interventions on survival

Intervention ( <i>P</i> -value)	Number	Survival rate (%)
Endotracheal intubation ( <i>P</i> < 0.0001)		
Not intubated	55	54.6
Intubated prior to arrest	58	15.5
Intubated during resuscitation	90	22.2
Vascular access ( <i>P</i> = 0.007)		
No vascular access	25	56
Vascular access inserted prior to arrest	154	26.6
Vascular access inserted during resuscitation	23	17.4
Type of vascular access ( <i>P</i> = 0.001)		
None	24	58.3
Peripheral vein	120	29.2
Femoral vein	17	11.8
Central vein other than femoral	35	14.3
Route of administration, first epinephrine dose ( <i>P</i> = 0.0001)		
No epinephrine given	100	51
<i>iv</i>	86	7.0
Endotracheal	15	13.3
Route of administration, all epinephrine doses ( <i>P</i> = 0.0001)		
No epinephrine given	99	51.5
<i>iv</i> only	79	7.6
Endotracheal only	6	33.3
Combination of <i>iv</i> and endotracheal	15	0

*P* values indicate the effect of the need for a specific intervention before a sustained ROSC could be achieved on survival rate.

endotracheal intubation, none survived long-term when the trachea was intubated 20 min or later during CPR. These results suggest that early endotracheal intubation by a well trained resuscitator should probably be recommended for all these patients.

Vascular access is often difficult to achieve in small children. To obviate this problem, intraosseous cannulation has been recommended. In the present study, time to obtain vascular access did not correlate significantly with long-term survival ( $n = 25$ ). When the first dose of epinephrine was administered endotracheally, the survival rate was equivalent to that of patients receiving their first dose of epinephrine intravenously (13.3% *vs* 7%). These results suggest that the endotracheal route is a valuable alternative for the first dose of epinephrine during pediatric resuscitation and that it should be used while *iv* or intraosseous access is sought. In adults, it has been suggested that, during resuscitation, drugs administered through central venous access would be more effective than peripherally administered drugs. In the present study, the long-term survival rate was not better in patients for

whom central venous access was present (13.5% for all sites) than for those in whom only a peripheral access was available (29.2%), suggesting that a patent peripheral vein can be as effective as a central vein in pediatric CPR (Table II). However, these results should be interpreted cautiously since many of our patients with *in situ* femoral or internal jugular venous access before their arrests were patients hospitalized in the pediatric intensive care unit after an operation for a cardiac congenital defect and the long-term survival rate of these patients was poor (13.3%; Table I).

In its most recent publication, the AHA recommends that the first dose of intravenously administered epinephrine should be 0.01 mg·kg<sup>-1</sup> followed by the same dose or a dose of 0.1 mg·kg<sup>-1</sup> in the absence of an adequate response to the first dose after three to five minutes.<sup>9</sup> Our results suggest that the recommendation for the first dose of intravenously administered epinephrine is appropriate since the mean dose of patients in whom a sustained ROSC was achieved was 0.011 ± 0.006 mg·kg<sup>-1</sup> compared to 0.038 ± 0.069 mg·kg<sup>-1</sup> for those in whom a ROSC was achieved but unsustainable (*P* = 0.004). Our results indirectly suggest that a higher initial dose might be dangerous since the mean dose of patients in whom a ROSC was achieved but unsustainable was significantly higher (all patients and subgroup of patients with bradycardia as initial rhythm).

For endotracheally administered epinephrine, current recommendations suggest an initial dose of 0.1 mg·kg<sup>-1</sup>. In the present study, the mean dose of patients who received their first epinephrine dose intratracheally was 0.011 ± 0.004 mg·kg<sup>-1</sup> and their survival rate (13.3%,  $n = 15$ ) was comparable to those who received their first epinephrine dose intravenously (7%,  $n = 86$ ). These results suggest that in infants, increasing the first dose of epinephrine when it has to be administered endotracheally might not be necessary.

In a retrospective study on 20 near-drowning pediatric patients, Ashwal *et al.* reported that an elevated initial blood glucose was highly predictive of those patients who died (mean 28.4 ± 6.1 mmol·L<sup>-1</sup>) or remained in a vegetative state (25.8 ± 5.8 mmol·L<sup>-1</sup>) compared with those who recovered completely (13.2 ± 9.4 mmol·L<sup>-1</sup>).<sup>10</sup> Despite a higher number of observations and a wide range of blood glucose levels, we did not find a correlation between either pre- or post-arrest blood glucose levels and survival or neurological prognosis. However, this does not imply that hyperglycemia should not be appropriately treated but that high blood glucose levels measured before or after a cardiorespiratory arrest should not be taken as a predictor of poor prognosis and used as an argument to withhold subsequent ALS interventions in children.

In the past, the definition of resuscitation was not always the same from one study to another; thus, it was difficult to determine what should be an appropriate duration of resuscitative efforts before declaring a patient dead. In adults, the interval time between collapse and achievement of a ROSC is a powerful indicator of ultimate survival and the Pediatric Utstein Symposium proposed its use in children. In a way, our results are in agreement with this recommendation since there was a good correlation between time to establish a sustained ROSC and survival ( $P < 0.0001$ ). However, if this definition had been used and resuscitative effort had been terminated after 30 min, two of our intact survivors would have died. Time to achieve return of a sustained spontaneous ventilation is not very useful in this population, since sedatives and/or neuromuscular blocking agents are often used after resuscitation and, indeed, did not correlate with long-term survival in our patients. In the present study, return of a measurable blood pressure was also an indicator of long-term survival ( $P = 0.002$ ).

The longest time to achieve a sustained measurable blood pressure that was associated with intact survival at one year was 34 min. Thus, absence of return of a sustained measurable blood pressure within 40 min might be an alternative to help determine the optimal minimum duration of CPR in children. Further studies will be needed to solve this issue.

In conclusion, the pediatric Utstein guidelines proved to be a valuable and easy to use tool to evaluate the efficacy of ALS interventions in pediatric in-hospital cardiorespiratory arrests. When an endotracheal tube is needed, its insertion should be done within 20 min by a trained resuscitator. For intravenously administered epinephrine, a dose of  $0.01 \text{ mg}\cdot\text{kg}^{-1}$  seems appropriate as the first dose. The endotracheal route is a valuable alternative while waiting for *iv* or intraosseous access. For infants (less than one year of age), a dose of  $0.01 \text{ mg}\cdot\text{kg}^{-1}$  administered via the endotracheal route seems as effective as the same dose administered via the *iv* route. Finally although the time to achieve a ROSC is an indicator of long-term survival in pediatric CPR, it could be misleading if a limit of 30 min is chosen to determine the minimum acceptable duration of resuscitation before termination of resuscitative efforts.

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