Out-of-Hospital Pediatric Cardiac Arrest: An Epidemiologic Review and Assessment of Current Knowledge

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Study objective: We systematically summarize pediatric out-of-hospital cardiac arrest epidemiology and assess knowledge of effects of specific out-of-hospital interventions.

Methods: We conducted a comprehensive review of published articles from 1966 to 2004, available through MEDLINE, Cumulative Index to Nursing and Allied Health Literature, EmBase, and the Cochrane Registry, describing outcomes of children younger than 18 years with an out-of-hospital cardiac arrest. Patient characteristics, process of care, and outcomes were compared using pediatric Utstein outcome report guidelines. Effects of out-of-hospital care processes on survival outcomes were summarized.

Results: Forty-one studies met inclusion criteria; 8 complied with Utstein reporting guidelines. Included in the review were 5,363 patients: 12.1% survived to hospital discharge, and 4% survived neurologically intact. Trauma patients (n=2,299) had greater overall survival (21.9%, 6.8% intact); a separate examination of studies with more rigorous cardiac arrest definition showed poorer survival (1.1% overall, 0.3% neurologically intact). Submersion injury–associated arrests (n=442) had greater overall survival (22.7%, 6% intact). Pooled data analysis of bystander cardiopulmonary resuscitation and witnessed arrest status showed increased likelihood of survival (relative risk 1.99, 95% confidence interval 1.54 to 2.57) for witnessed arrests. The effect of bystander cardiopulmonary resuscitation is difficult to determine because of study heterogeneity.

Conclusion: Outcomes from out-of-hospital pediatric cardiac arrest are generally poor. Variability may exist in survival by patient subgroups, but differences are hard to accurately characterize. Conformity with Utstein guidelines for reporting and research design is incomplete. Witnessed arrest status remains associated with improved survival. The need for prospective controlled trials remains a high priority. [Ann Emerg Med. 2005;46:512-522.]

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INTRODUCTION

Cardiopulmonary arrest is uncommon in children. The epidemiology and physiology of cardiopulmonary arrest in children is different than in adults, and the American Heart Association recommends resuscitation guidelines targeted to children. Despite extensive provider training in resuscitation practice, outcomes from cardiopulmonary arrest in children remain poor in virtually all out-of-hospital reports. In addition to poor survival, neurologic morbidity is highly prevalent in survivors. A recent review by Young and Seidel[1] found an overall survival to hospital discharge of 13% in all children with cardiopulmonary arrest in out-of-hospital and inhospital settings combined. Among the conclusions drawn from this review were that the state of knowledge and widespread preparedness for pediatric cardiopulmonary resuscitation (CPR) remains poor and that "multicenter, prospective studies are needed to test interventions and improve outcomes."[1]

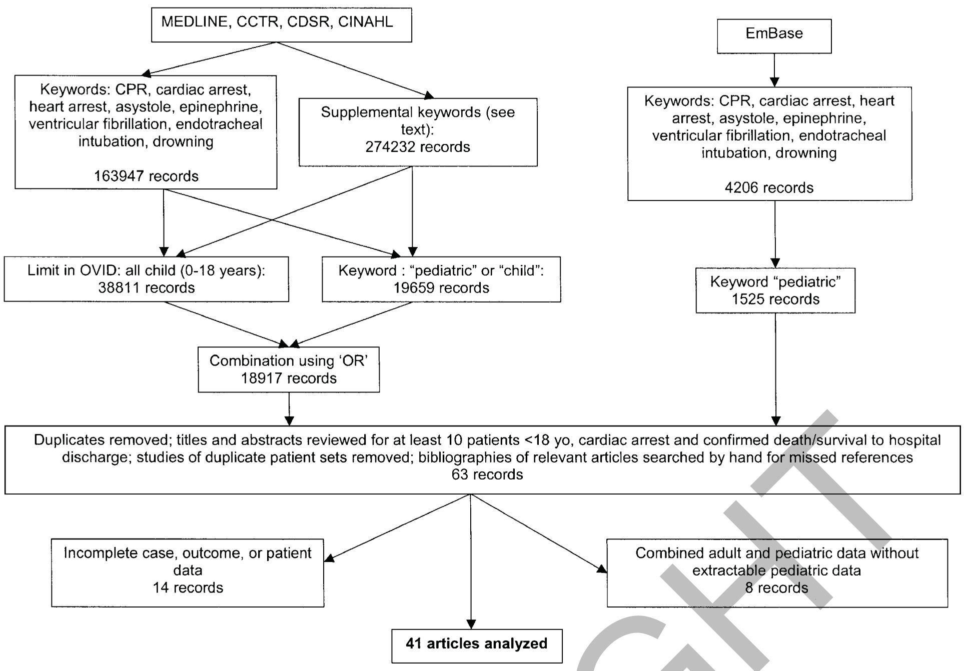

Figure 1. Literature search strategy.

The CanAm Pediatric Cardiac Arrest Group is a collection of researchers from Canada and the United States who met for the first time in 2003. The objective of this group is to design and implement a prospective, multicenter intervention trial to optimize life support measures in the out-of-hospital setting to affect survival outcomes after out-of-hospital pediatric cardiopulmonary arrest. The targets for interventional studies by this group will, in part, be influenced by the results of this review. We performed a systematic literature review to clearly identify the gaps in our knowledge of pediatric cardiopulmonary arrest and CPR, with particular attention to the out-of-hospital setting. We also aimed to analyze the published literature to determine whether the effect of commonly used interventions in the out-of-hospital arena on clinically important outcomes was analyzable systematically.

MATERIALS AND METHODS

Literature Search

Under the supervision of a research librarian from the University of Ottawa, we conducted a literature search using the key words "cardiac arrest," "heart arrest," and "cardiopulmonary resuscitation" using the following databases: MEDLINE, EmBase, the Cochrane Register of Systematic Reviews, the Cochrane Register for Controlled Trials, and CINAHL. Additional keywords of "asystole," "ventricular fibrillation," "epinephrine," "drowning," "endotracheal intubation," "pulse check," "compression to ventilation ratio," "exhaled carbon dioxide," "active compression-decompression" or "ACD," "interposed abdominal compression" or "IAC," "open chest CPR," "extracorporeal membrane oxygenation," "laryngeal mask airway," "impedance threshold valve," "S-100B," "neuron specific enolase," "plasminogen activators," "thrombolysis," "vasopressin," "insulin," and "hypothermia" were searched in the same databases. All articles in all languages published from 1966 to 2004 were considered for inclusion. A hand search of the bibliographies of selected articles was performed to identify articles that were not identified by the above strategy (Figure 1).

Table 1. Utstein outcome definitions.

Outcome	Definition
ROSC	Restoration of perfusing heart rhythm in absence of external chest compressions
Sustained ROSC	ROSC for >20 min
Survival to admission	Patient alive with sustained ROSC at hospital admission
Survival to discharge	Patient alive at hospital discharge

ROSC, Return of spontaneous circulation.

Selection of Articles

Articles were selected that reported clinical outcomes from out-of-hospital cardiopulmonary arrest for patients younger than 18 years. Articles were included when patients were defined as pulseless, defined as in "cardiac arrest" or "cardiopulmonary arrest," or defined as having "received CPR." Outcomes were selected where possible to reflect published consensus Utstein criteria for outcomes from cardiac arrest (ie, any return of spontaneous circulation, sustained return of spontaneous circulation, survival to hospital admission, and survival to hospital discharge (Table 1).[2] At a minimum, selected articles must report survival to hospital discharge as an outcome.

Table 2. Summary of studies included in review.

Author	Year	n	Setting	Study Design	Diagnoses	Survival to Discharge (n)
Eisenberg et al[11]	1983	119	King County, WA	Retrospective	All	8
Rosenberg[34]	1984	24	Detroit, MI	Prospective observational	All	3
Ludwig et al[24]	1984	34	Philadelphia, PA	Retrospective	All	10
Torphy et al[43]	1984	117	Milwaukee, WI	Retrospective	All	7
Nichols et al[27,*]	1986	13	Philadelphia, PA	Prospective observational	All	3
Applebaum and Slater[5]	1986	71	Jerusalem	Prospective observational	All	0
O'Rourke[28]	1986	34	Boston, MA	Retrospective	All	7
Losek et al[22]	1987	114	Milwaukee, WI	Retrospective	All	9
Glaeser et al[15]	1988	29	Milwaukee, WI	Retrospective	All	3
Brunette and Fischer[7]	1988	33	Minneapolis, MN	Retrospective	All	0
Miner et al.[25]	1989	12	Salt Lake City, UT	Prospective observational	All	0
Aijian et al[4]	1989	42	Fresno City, CA	Retrospective	All	2
Losek et al[23]	1989	117	Milwaukee, WI	Retrospective	All	2
Thompson et al[42]	1990	70	WI, MN, IA	Retrospective	All	3
Quan et al[31]	1990	38	Seattle/King County, WA	Retrospective	Drowning	12
Quan and Kinder[32]	1992	29	Seattle/King County, WA	Retrospective	Drowning	6
Safranek et al[35]	1992	353	King County, WA	Retrospective	All	30
Schoenfeld and Baker[37]	1993	58	Philadelphia, PA	Retrospective	All	6
Sheikh and Brogan[39]	1994	27	Sacramento, CA	Retrospective	Trauma	0
Hazinski et al[17]	1994	30	Nashville, TN	Retrospective	Trauma	0
Mogayzel et al[26]	1995	157	Seattle/King County, WA	Retrospective	Excludes SIDS	15
Ronco et al[33]	1995	63	Birmingham, AL	Retrospective	All	6
Dieckmann and Vardis[10,*]	1995	65	San Francisco, CA	Retrospective	All	2
Hickey et al[18]	1995	56	Columbus, OH	Retrospective	All	15
Kuisma et al[19,*]	1995	34	Helsinki	Retrospective	All	5
Schindler et al[36]	1996	80	Toronto	Retrospective	All	6
Siegler[38]	1997	88	Greenville, SC	Prospective observational	All	4
Hassan[16,*]	1997	47	Leicester, UK	Retrospective	All	3
Suominen et al[41,*]	1997	50	Helsinki	Retrospective	All	8
Kumar et al[20]	1997	47	New Haven, CT	Retrospective	All	1
Conroy and Jolin[9,*]	1999	27	Riyadh	Retrospective	All	2
Sirbaugh et al[40]	1999	300	Houston, TX	Prospective observational	All	6
Li et al[21]	1999	957	NPTR database	Multicenter database analysis	Trauma	225
Fisher and Worthen[13]	1999	65	San Diego, CA	Retrospective	Trauma	1
Broides et al[6,*]	2000	20	Beer Sheva, Israel	Retrospective	Excludes trauma	0
Perron et al[29]	2001	586	NPTR database	Multicenter database analysis	Trauma	165
Calkins et al[8]	2002	25	Denver, CO	Retrospective	Trauma	2
Pitetti et al[30]	2002	189	Pittsburgh, PA	Retrospective	All	5
Engdahl et al[12]	2003	94	Goteborg, Sweden	Prospective observational	All	5
Gerein et al[14]	2003	459	Ontario, Canada	Prospective observational	All	9
Young et al[44,*]	2004	594	Los Angeles, CA	Prospective observational	All	51

NPTR, National Pediatric Trauma Registry.
*Studies using the Utstein definition of cardiac arrest (pulseless, apneic, unconscious).

Retrospective, prospective, or databased case series and cohorts were considered for inclusion with sample sizes of 10 or greater. Studies examining children with cardiac arrest, children with other illness or injury that frequently results in arrest in the pediatric population, or undergoing clinical interventions frequently performed on critically ill children were prioritized as sources of data. Articles that reported data on children and adults together in which outcomes on children could not be examined separately from those of adult patients were excluded. Similarly, articles that reported on out-of-hospital and inhospital arrests together in which the data specific to the out-of-hospital arrests could not be extracted were excluded. If multiple articles were found that reported outcomes on the same group of patients, the article that reported the data most completely or on the largest set of patients was included and other articles reporting on the same patients were excluded. Two reviewers (AJD, VN) screened the 63 preliminarily identified articles for inclusion.

Data Extraction

Data extraction on included articles was performed by a single author (AJD). The data extracted from all articles included the case definition, number of patients, study design, and overall survival to hospital discharge. When possible, data on incidence of cardiopulmonary arrest in the relevant population, age, clinical outcomes from the Utstein guidelines other than survival to

Table 3. Clinical outcomes of pediatric cardiac arrest patients.

Table 3A. Outcomes by Utstein category: overall patient set, including National Pediatric Trauma Registry data.

Outcome	Proportion (%)
ROSC	751/2,438 (30.8)
Sustained ROSC*	165/594 (27.8)*
Survival to admit	340/1,423 (23.9)
Survival to discharge	647/5,363 (12.1)
Neurologically intact survival	131/3,272 (4.0)

Table 3B. Outcomes by Utstein category: overall patient set excluding National Pediatric Trauma Registry data.

Outcome	Proportion (%)
ROSC	422/1,850 (22.8)
Sustained ROSC*	165/594 (27.8)*
Survival to admit	340/1,423 (23.9)
Survival to discharge	253/3,752 (6.7)
Neurologically intact survival	50/2,315 (2.2)

*Data on sustained ROSC of >20 min was determinable from only 1 study.[44]

Table 3C. Outcomes by Utstein category: patients with submersion injury.

Outcome	Proportion (%)
ROSC	16/37 (43.2)*
Survival to admit	39/67 (58.2)*
Survival to discharge	63/277 (22.7)
Neurologically intact survival	7/117 (6.0)

*Each proportion is derived from a separate group of studies with incomplete definitions of Utstein outcomes.

Table 3D. Outcomes by Utstein category: patients with traumatic injury (NPTR data included).

Outcome	Proportion (%)
Survival to discharge	401/1,830 (21.9)
Neurologically intact survival	84/1,244 (6.8)

Table 3E. Outcomes by Utstein category: patients with traumatic injury (NPTR data excluded).

Outcome	Proportion (%)
ROSC	12/57 (21.1)
Survival to discharge	11/1,019 (1.1)
Neurologically intact survival	3/1,019 (0.3)

discharge (eg, return of spontaneous circulation, survival to admission), neurologic sequelae, and presenting rhythm were extracted. Subsets of patients with the specific diagnoses of sudden infant death syndrome (SIDS), trauma, and submersion were quantified where possible. Clinical outcomes were separately determined for these diagnostic subgroups.

Data Analysis

Incidence of Utstein outcomes was calculated by weighted averaging for the overall data set, as well as diagnostic subgroups. For the specific interventions of bystander CPR and witnessed arrest, data were pooled and analyzed for heterogeneity. Forest plots were constructed evaluating the effect of these interventions on survival to hospital discharge, with the intention of using random-effect modeling if heterogeneity was present to a significant degree and fixed-effect modeling if no significant heterogeneity was present.

The pediatric Utstein guidelines, published in October 1995, define cardiac arrest as "the cessation of cardiac mechanical activity, determined by the inability to palpate a central pulse, unresponsiveness, and apnea."[3] For the purposes of the review, an article is defined as "using Utstein guidelines" if it does so explicitly or gives a case definition in keeping with these 3 components of the 1995 Utstein definition of cardiac arrest.

For the purposes of this review, the designation of "intact" neurologic survival consists of an outcome in which the patient was described as not having any lasting neurologic deficit, having any impairment subjectively graded as no worse than "mild," or having a score on a validated instrument consistent with mild to no lasting impairment (Pediatric Cerebral Performance Category of 2 or better, Bloom category of 1 or 2).

For the purposes of this review, "trauma" includes patients who were victims of blunt or penetrating trauma, child abuse, burns, and smoke inhalation. "Drowning" and "submersion injury" are used interchangeably and include all patients whose diagnoses include drowning, near-drowning, or submersion.

RESULTS

Sixty-three articles were identified that examined clinical outcomes, including survival to hospital discharge of 10 or more patients, at least some of whom were pediatric, with out-of-hospital cardiac arrest. Fourteen articles were excluded because of incomplete case definition or outcome data; 8 were excluded for data combining pediatric and adult patients, which, although complete, did not allow extraction of outcome data specific to children. All of these articles were independently identified for exclusion by both authors involved in article selection (AJD, VN). Forty-one articles met all prospective criteria for inclusion in our review.[4-44] Nine articles described prospective observational studies,[5,12,14,25,27,34,38,40,44] whereas the remaining 32 were retrospective cohort reports. Thirty studies were identified that involved children with all diagnoses examined collectively; 2 studies involved children who had cardiopulmonary arrest as a result of submersion,[31,32] and 6 studies involved children who had cardiopulmonary arrest as a result of trauma.[8,13,17,21,29,39] Three studies examined all diagnoses, with the exception of a specific exclusion (1 excluded SIDS; 2 excluded trauma patients).[6,11,26] A total of 5,363 patients were represented in the series. Table 2 summarizes the key features of the 41 articles.

Thirty-four of 41 reports were conducted in the United States and Canada. Four studies were conducted in Europe,[12,16,19,41] 2 in Israel,[5,6] and 1 in Saudi Arabia.[9] The incidence of out-of-hospital cardiopulmonary arrest was either reported or calculable in 8 studies, ranging from 2.6 to 19.7 annual cases per 100,000

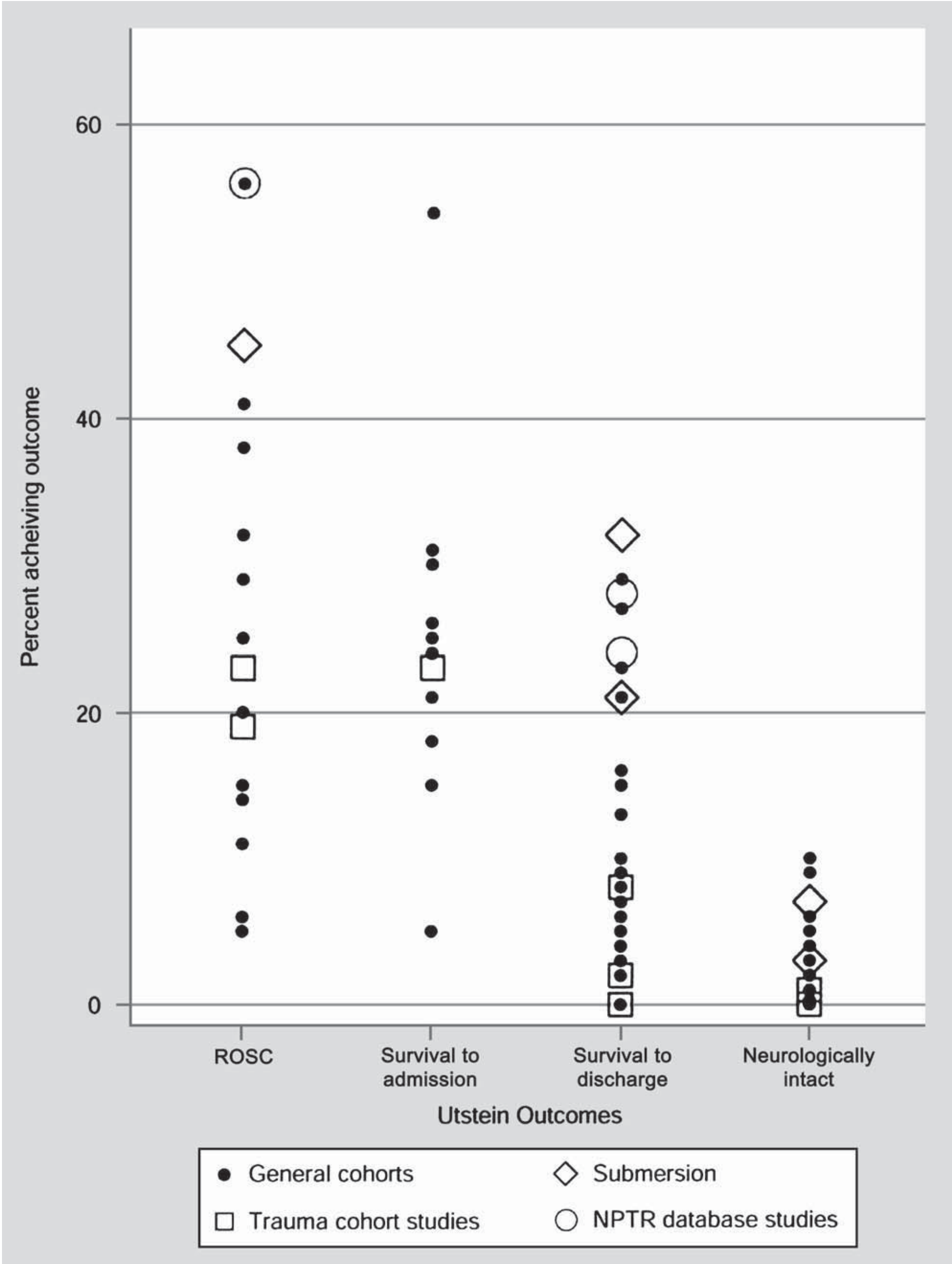

Figure 2. Range of Utstein outcomes by individual study.

pediatric population.[5,11,12,14,16,19,40,42] The majority of the studies were performed in urban areas, with 1 series based on a collection of rural communities in the midwestern United States[42] and 2 based on data collected from the National Pediatric Trauma Registry.[21,29]

Clinical outcomes according to Utstein guidelines for the overall patient set are given in Table 3, along with outcomes for diagnostic subgroups. Figure 2 shows the range of outcomes by individual study. Authors adhered to the Utstein reporting guidelines in a total of 8 of 41 articles.[6,9,10,16,19,27,41,44] Of the articles that were published after October 1995, 5 of 16 articles either cited the Utstein criteria or described an identical set of clinical characteristics[6,9,16,41,44]; by comparison, 3 of the 25 articles before October 1995 (including 1 article published simultaneously with the guidelines) used the triad of unresponsiveness, apnea, and pulselessness as their case definition.[10,19,27] Five of 25 articles before 1995 used none of the 3 criteria in their case definition,[7,11,24,25,39] and 5 of 15 after 1995 used none of the criteria.[8,12,20,21,29] The most common case definition was apnea and pulselessness, used in 19 of 40 articles. Pulselessness alone was used in 4 of 41 articles.[5,13,17,35]

Survival to hospital discharge was observed in 647 of 5,363 (12.1%) patients. Return of spontaneous circulation was achieved in 751 of 2,438 (30.8%) patients. Sustained return of

Table 4. Initial rhythms of pediatric cardiac arrest patients.

Rhythm	Number of patients (percent of total)
A. Initial rhythms: overall patient set (n=2,734)	
Asystole	2,135 (78.0%)
PEA	350 (12.8%)
VF/pulseless VT	222 (8.1%)
Bradycardia	27 (1.0%)
B. Initial rhythms: submersion injury (n=67)	
Asystole	40 (61.4%)
PEA	0
VF/pulseless VT	14 (20.0%)
Bradycardia	11 (15.7%)
Unknown/not recorded	2
C. Initial rhythms: trauma (n=57)	
Asystole	42 (75.0%)
PEA	4 (6.7%)
VF/pulseless VT	3 (5.0%)
Bradycardia	0
Unknown/not recorded	8

PEA, Pulseless electrical activity; *VT*, ventricular trachycardia; *VF*, ventricular fibrillation.

spontaneous circulation was defined in only 1 study, where it was noted in 165 of 170 patients who achieved return of spontaneous circulation.[44] Survival to hospital admission was observed in 340 of 1,423 (23.9%). Of the 37 studies in which there were long-term survivors, neurologic outcomes were described in 27 of the studies. Only 4 articles reported neurologic outcomes using a validated scoring system, with 3 using Pediatric Cerebral Performance Category scoring and 1 using the Bloom classification.[12,19,30,44] All 3 articles using Pediatric Cerebral Performance Category scores were published after the 1995 publication of the pediatric Utstein guidelines. Overall intact neurologic survival occurred in 131 of 3,272 (4.0%) patients (Table 3a).

Age was measured by descriptive statistics in 15 of 41 studies. The range of values for median age, where reported, was 1 to 7 years. The range of values for the mean age was 7.9 months to 5.9 years. The most common characteristic of age reported was the number of patients younger than 1 year, reported in 22 of 41 studies. Overall, 1,036 of 2,180 (47.5%) patients from studies in which age data are interpretable were younger than 1 year at their arrest.

Initial ECG rhythm for the overall patient set, as well as by patient subgroups, is shown in Table 4. Initial cardiac rhythm was described in 25 of 41 studies.

Whether cardiopulmonary arrest events were witnessed was assessed in 12 of 41 studies.[9,11,14,16,18,19,22,23,26,33,41,44] There were 9 studies in which all patients were recorded as either witnessed or unwitnessed[9,11,14,16,18,19,22,41,44]; in the remaining 3 studies, documentation of whether the arrest event was witnessed was incomplete, and results were given as a fraction of patients for whom these data were recorded.[23,26,33] Overall, 532 of 1,725 (30.8%) arrests were witnessed. For patients whose arrest was witnessed, 62 of 475 (13.1%) patients survived to hospital discharge. For patients with unwitnessed arrests, 44 of 956 (4.6%) patients survived to hospital discharge. Pooled data analysis through fixed-effect modeling showed a significant association between witnessed arrest and survival (relative risk 1.99; 95% confidence interval 1.54 to 2.57), with a lack of significant heterogeneity among studies (Cochran's Q 12.1; P=.146; I2 34%) (Figure 3a).

Bystander CPR was quantified in 9 of 41 studies.[14,16,18,19,23,26,40,41,44] The percentage of patients in individual studies receiving bystander CPR varied from 7.8% to 85.1%. Overall, for patients for whom the data were recorded, 540 of 1,755 patients (30.7%) received bystander CPR. Seven of the 9 studies reported survival to hospital discharge between patients who did and did not receive bystander CPR.[14,16,18,19,40,41,44] Forty-one of 433 (9.4%) patients receiving bystander CPR survived to hospital discharge, whereas 49 of 1,042 (4.7%) who did not receive bystander CPR survived. Five studies[18,19,23,40,41] performed univariate analysis associating bystander CPR with survival, and 2 of the 5 found a significantly greater likelihood of survival in patients who received bystander CPR; both of these studies, however, demonstrated no benefit of bystander CPR when applied in a multivariate analysis.[19,41] Pooled data analysis by random-effects modeling demonstrated significant heterogeneity between studies (Cochran's Q 20.8; P=.001; I2 75.9%); one study had zero survivors and as such was excluded from pooled analysis[16] (Figure 3b). Examining the individual influence of each study on the level of heterogeneity by exclusion followed by repeat analysis did not identify one study as a sole source of heterogeneity. Risk ratios for survival to hospital discharge ranged from 0.53 to 4.7. Not all studies clearly stated whether groups of patients who "did not receive bystander CPR" included patients for whom the presence or absence of bystander CPR was not recorded; this was explicitly described in only 3 studies.[16,18,44] In summary, pooled analysis of available studies failed to demonstrate a consistent association between bystander CPR and survival.

SIDS accounted for the greatest subset of cases: 1,075 of 3,339 (32.2%) cases taken from studies that did not exclude SIDS. The diagnosis of SIDS in most studies implied the death of the patient and was either a clinical diagnosis or assigned after autopsy. Consequently, survival statistics are impossible to determine retrospectively for this subgroup. A total of 2 patients who achieved survival to hospital discharge were given the diagnosis of "near-SIDS" or "near-miss SIDS" based on clinical characteristics; 1 of these children survived without neurologic deficit. One study deliberately excluded SIDS cases; outcomes in that study were similar to those of the overall data set (survival 9.5%; intact survival 4.5%).[26]

Trauma patients were included in 34 of 41 studies and accounted for 641 of 2,996 (21.4%) patients in studies in which multiple diagnostic categories including but not limited to trauma were evaluated. Trauma patients were examined exclusively in 6 studies.[8,13,17,21,29,39] Overall, 2,299 children

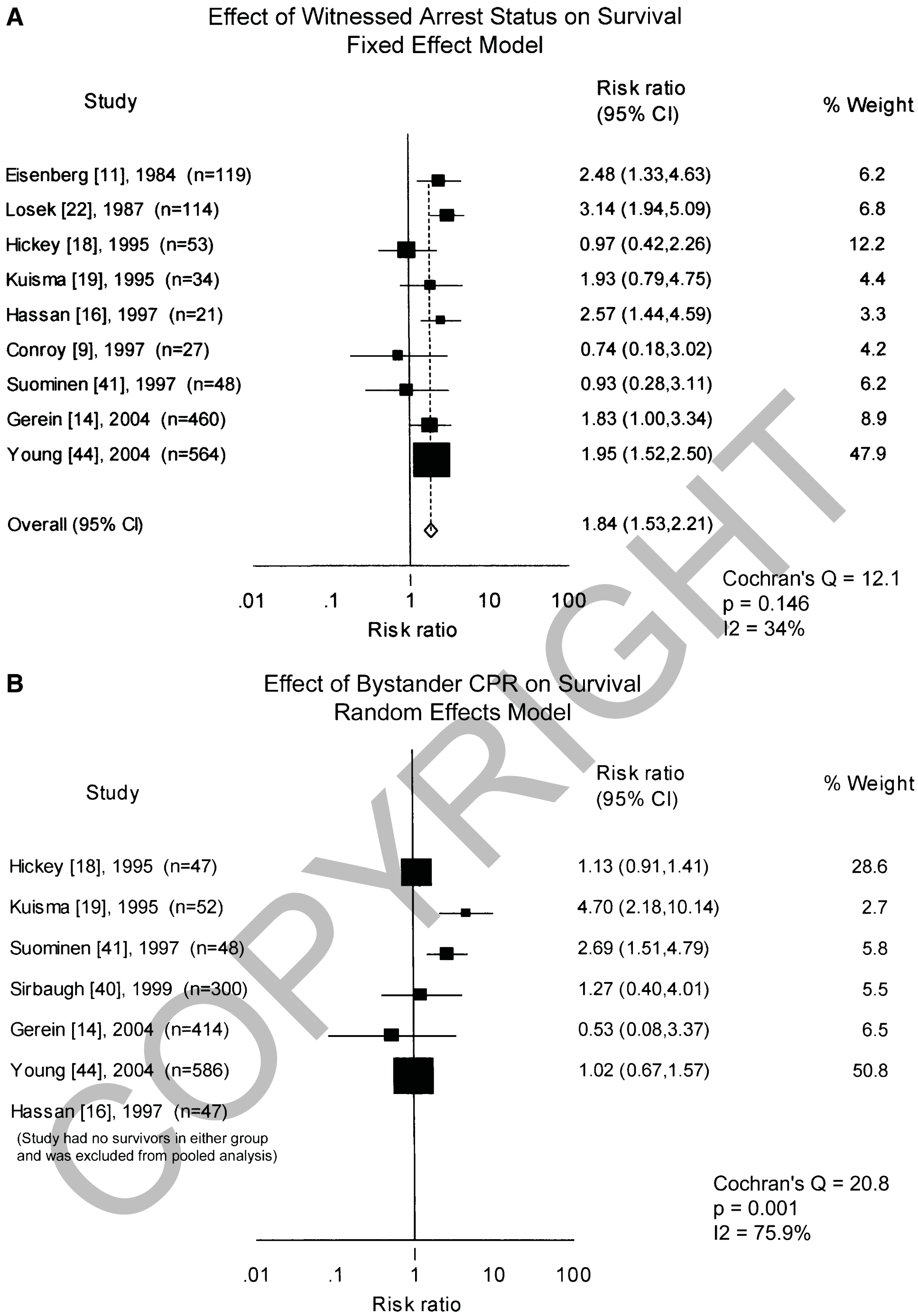

Figure 3. Association between bystander CPR and witnessed status and survival to hospital discharge (pooled data analysis). Size of boxes denote weighing of individual study in pooled analysis. Horizontal lines denote 95% CI. Risk ratio < 1 = association with nonsurvival; risk ratio > 1 = association with survival.

who had cardiopulmonary arrest as a result of trauma are accounted for in the present review. Of the trauma patients whose outcomes were specifically described, 401 of 1,830 (21.9%) survived to hospital discharge. Of the trauma patients for whom neurologic status at discharge was able to be determined, 84 of 1244 (6.8%) did not have significant neurologic sequelae (Table 3d).

There was a significant difference in the definition of cardiac arrest as described by the National Pediatric Trauma Registry, from which 2 studies in our review derived their data.[21,29] A patient in the National Pediatric Trauma Registry is described as "receiving CPR" if he or she received "airway management, chest compressions, intravenous fluid therapy, [or] inotropic drug support," and the authors acknowledge that "It is not possible to make clear distinctions… as any or all of these interventions are categorized as CPR."[21] We therefore recalculated the outcomes of interest for trauma patients in the data set after excluding the National Pediatric Trauma Registry data. In this set, 11 of 1,019 (1.1%) children survived, and 3 of 1,019 (0.3%) survived neurologically intact (Table 3e).

Submersion injury patients were included in 30 of 41 studies and were examined exclusively in 2 studies.[31,32] Submersion accounted for 375 of 3,205 (11.7%) patients in studies in which multiple diagnostic categories including but not limited to submersion were evaluated and data were recorded completely. Overall, 442 children who had cardiopulmonary arrest as a result of submersion are accounted for in the present review. Of the submersion patients whose outcomes were specifically described, 63 of 277 (22.7%) survived to hospital discharge, and 7 of 117 (6.0%) had survival without neurologic sequelae at discharge (Table 3c). One article performed univariate analysis comparing submersion victims to all other patients and found a significantly increased likelihood of survival.[41]

LIMITATIONS

Meta-analyses or pooled analysis of studies of observational data has increased in frequency despite many authors' skepticism about their interpretability. A recent article by Blettner and colleagues[45] saliently summarized the inherent limitations to such reviews. Observational studies tend to have a greater degree of inconsistency in study design, which makes it important to define prospectively the characteristics of studies that will make them suitable for inclusion. There may be increased likelihood of exploratory analyses or smaller patient cohorts failing to reach the medical literature, leading to publication bias. If this occurs in such a way as to favor the publication of unexpected significant results instead of inconclusive studies, an overestimate of the effect in question may result. Additionally, combining different study designs into a single analysis implies that the same crude estimate of effect of an intervention can be inferred from each study, despite methodologic differences.

The limitations of our study are largely delineated by the limitations of the data we were reviewing and the inherent difficulty of reviewing observational data. The quality of the studies included in our review varied greatly and was difficult to account for systematically. It is difficult to restrict a review of pediatric CPR by study design; even with our set of criteria for study inclusion, the variability in case and outcome definitions constitutes a significant obstacle to accurately quantifying outcomes and effects of interventions. We did not attempt to systematically appraise study quality in the course of our search, and we acknowledge that this is a significant limitation in our review.

Even among studies whose case definitions were more appropriate and analyzable, numerous clinical circumstances exist that have potential to affect their results. Inclusion of SIDS patients, a group of children whose likelihood of survival is exceptionally poor, has been recommended against by some authors. Only 1 author deliberately excluded SIDS patients in a study that was otherwise inclusive of all diagnoses.[26] SIDS was the most prevalent diagnosis in our review, and it is likely that survival statistics are influenced negatively by this prevalence. Additionally, it is likely that significant inaccuracy exists in the assessment of a state of apnea, pulselessness, and unconsciousness by out-of-hospital care providers. Accurate assessment of peripheral pulses and recognition of pulselessness has been shown to be poor for adults and children.[46,47] Some children who undergo CPR in the out-of-hospital arena are likely to never have been pulseless. Conversely, children who achieve return of spontaneous circulation through bystander CPR alone (eg, drowning) may or may not be included in a given study. DeMaio et al[48] described a series of CPR-only survivors from the Ontario Prehospital Advanced Life Support data; no data exist examining this phenomenon in children. The presence of patients included in these studies who were never pulseless would influence survival statistics positively; conversely, the exclusion of children who survive an arrest with return of spontaneous circulation before first-responder arrival would have the opposite effect. Accurately determining the extent of these sources of bias is difficult.

Finally, our analyses of the effect of bystander CPR and witnessed arrest status highlight the importance of heterogeneity as a source of bias and inaccuracy in pooled data analysis. We found no statistical association between bystander CPR and survival to discharge and that considerable heterogeneity makes the interpretation of the results of that analysis difficult. By contrast, there was a significant association between witnessed arrest status, and the studies pooled in the analysis appeared sufficiently homogeneous to interpret the results accordingly. We believe this observation to be illustrative of one of the major points of this review, namely, data collected on children with cardiac arrest remain troublingly inconsistent, but when data are collected accurately and according to uniform guidelines, an interpretable estimate of the effects of specific interventions is possible.

DISCUSSION

Our systematic review confirms poor overall survival outcomes reported in previous nonsystematic reviews of pediatric cardiopulmonary arrest. However, important new assessments of survival outcomes accounting for known traumatic etiology, SIDS, and submersion injury provide additional important outcome data to serve as the basis of future intervention study design. Witnessed arrest status was significantly associated with survival in pooled analysis. Patients receiving bystander CPR had improved survival in some individual studies, but the effect was inconsistent when all studies reporting outcome data were considered. Patient survival appears to be affected by cause of arrest; most notably, an increased percentage of patients who had submersion injury survived. Our review suggests that research efforts in pediatric cardiopulmonary arrest and CPR have improved in their cohesion and clinical uniformity, converging on consensus Utstein definitions. However, studies still have considerable methodologic inconsistency. Our review highlights to an even greater extent the continued need for investigative studies. We were unable to find definitive retrospective data to prove, in an evidence-based fashion, that the advanced life support interventions recommended by Pediatric Advanced Life Support improved clinical outcome.

In 1999, Young and Seidel[1] published a collective review summarizing the state of knowledge of the efficacy of CPR in the arrested pediatric patient. Their findings showed that survival was uncommon and that neurologic morbidity was common. More importantly, they documented the many shortcomings of the current state of research on pediatric cardiac arrest and the effectiveness of basic and advanced lifesaving techniques for the arrested child. Among the recommendations those authors made were greater uniformity in case definition, universal application of Utstein recording guidelines, and a more consistent approach to evaluating neurologic outcome. Pediatric resuscitation is counted among the high-priority areas for pediatric research by a recent consensus statement from the Emergency Medical Services for Children Research Agenda Consensus Committee.[49]

This review of cardiopulmonary arrest in children in the out-of-hospital setting demonstrates a similarly dismal set of outcomes. After exclusion of data from the National Pediatric Trauma Registry studies because of methodologic concerns (see below), 6.7% of children survived to hospital discharge, and only 2.2% achieved "intact" neurologic survival (Table 3b). The subset of patients with out-of-hospital cardiopulmonary arrest in the Young and Seidel[1] review achieved 8.4% survival to hospital discharge, but 41% of those were determined to have "good neurologic outcome." The reason for these differences is unclear. Intact neurologic survival is significantly worse in our review, though the ability to accurately quantify this outcome is impaired by the incompleteness with which it is reported.

The lack of uniformity of case definition continues to be a problem in studies of pediatric cardiopulmonary arrest, although some improvement can be noted. We chose to exclude articles that did not report survival to hospital discharge as an outcome based on the fact that it was the most widely reported outcome in studies eligible for this review and arguably a more meaningful one in terms of long-term functional outcome than other Utstein categories of return of spontaneous circulation and survival. The ideal outcome measure, that of the overall change in neurocognitive function from the prearrest to postarrest periods, is not evaluable from the majority of these studies. Young and Seidel[1] recommended that neurologic outcomes be reported uniformly, when possible in the framework of a validated scoring system such as the Pediatric Cerebral Performance Category. This recommendation represents the most important clinical outcome for the arrested child and at the same time is one of the most difficult to study in a well-designed fashion in that it requires long-term follow-up data that are challenging to collect, as well as subjective, which renders them difficult to accurately quantify in some cases. The most recent study in this review designated a separate category of "Pediatric Cerebral Performance Category unchanged from baseline."[44] Although the overall change in neurologic status is possibly the outcome that best reflects the effectiveness of a patient's resuscitation, the interpretation of an unchanged Pediatric Cerebral Performance Category is difficult if the initial Pediatric Cerebral Performance Category is abnormal. The designation of "intact neurologic survival" used in this article should be inferred as being based on the best interpretation possible from the present literature, acknowledging the inconsistencies described above.

Bystander CPR has been well documented in several adult studies to have a favorable impact on outcome in the arrested adult. In the first phase of the Ontario Prehospital Advanced Life Support study, Stiell and colleagues found that 14.5% of adults received bystander CPR and that bystander CPR was an independent predictor of survival in arrested adults.[50] Rates of bystander CPR were higher in children in this review, with an overall rate of 32%. Existing studies of pediatric CPR suggest that rates of bystander CPR in children are worse than in adults. As mentioned above, cases in which bystander CPR is successful (ie, return of spontaneous circulation is achieved before EMS arrival) are frequently not included in studies of pediatric arrests. Our review suggests that bystander CPR remains an understudied intervention with significant potential to improve outcomes for arrested children.

Children who have submersion injury (Tables 3c and 4b) demonstrated some important differences with respect to clinical features and outcomes. Overall survival to hospital discharge and intact neurologic survival was better than the overall sample (22.7% versus 12.1% survival and 6.0% versus 4.0% intact neurologic survival) for patients with submersion injury. Debate has existed historically about the utility of aggressive resuscitation of submersion victims with cardiac arrest or coma in the out-of-hospital phase. Some authors suggest that certain patients need not undergo drastic efforts in light of the extreme unlikelihood of meaningful survival.[51-53] Orlowski[54] found that the early institution of resuscitative efforts had the greatest impact on survival for submersion victims. Studies by Lavelle and Shaw[55] in 1993 and Allman et al[56] in 1986 found that outcomes of submersion victims were positively affected by emergency resuscitative efforts but failed to demonstrate any positive influence of aggressive cerebral resuscitation in the intensive care setting. The results of the present review suggest that the survivability of cardiac arrest may be improved for patients who arrest as a result of submersion.

Trauma patients represented a significant subset of cardiopulmonary arrest patients in all studies from which they were not excluded. Discrepancies in the results yielded by the inclusion of data from the National Pediatric Trauma Registry exemplify that case definition in studies of pediatric cardiopulmonary arrest lacks uniformity. The overall survival and intact neurologic survival of trauma patients in this review, including the National Pediatric Trauma Registry data, were

21.9% and 6.8%, respectively, higher than the survival of the larger data set. These findings are inconsistent with the Young and Seidel[1] review, in which 9 of 207 patients survived (4%); of the 7 survivors with available data, 3 achieved good neurologic outcome. In our review, excluding the National Pediatric Trauma Registry data, survival from trauma was similarly poor, with 1.1% survival to discharge. Rates of survival varied considerably in individual studies, from 0% to 28.2%. Of the 6 articles dealing exclusively with trauma patients, only 2 used the clinical criterion of pulselessness to characterize their patients; those 2 studies account for 95 trauma victims, of whom 1 child survived in a persistent vegetative state.[13,17] The authors of this review believe that the overall outcomes of the data set are more accurately reflected by the exclusion of the National Pediatric Trauma Registry studies. A clearer definition of cardiac arrest in the National Pediatric Trauma Registry, particularly one requiring pulselessness and the performance of chest compressions, would yield much more illustrative data on this common cause of pediatric arrests.

Conclusions and Recommendations

The rarity and lethality of out-of-hospital cardiac arrest in children make it a difficult entity to study in a controlled fashion. Our systematic review of out-of-hospital pediatric cardiac arrest literature corroborates the dismal clinical outcomes that have been described in previous studies of pediatric cardiac arrest. More important, our review highlights the fact that the pediatric Utstein guidelines have set forth a template by which to design and interpret cardiac arrest research, and adherence to these guidelines has improved since their publication. However, considerable inconsistency still exists in pediatric cardiac arrest research.

This review highlights areas of knowledge where data are still lacking. It also demonstrates that data collected in an optimal fashion, with adherence to Utstein style reporting, have a much greater level of usefulness for determining impact of specific interventions. Data in this review can be used to guide the design of well-constructed clinical trials to more clearly elucidate the effectiveness of evidence-based out-of-hospital interventions after cardiac arrest in infants, children, and adolescents.

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