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Energy doses for treatment of out-of-hospital pediatric ventricular fibrillation☆

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Summary
Aim: To investigate the energy dose used to treat out-of-hospital pediatric ventricular fibrillation and the survival rates of these patients.
Methods: We reviewed three emergency medical systems (EMS) for their reports of patients under 1 month to 18 years who received shocks for ventricular fibrillation to determine the energy of each shock as well as other patient and care characteristics. Each patient's weight was estimated at the age-appropriate 50th and 95th percentiles. Patients were then grouped as receiving recommended energy doses (2 to ≤4 J/kg), moderately high energy doses (>4—6 J/kg), and high energy doses (>6 J/kg).
Results: Of 57 patients identified, 54% were male, with a mean age of 11 years, range 2 months to 17 years. Ventricular fibrillation was the initial rhythm in 80% (43/54) of patients. The mean number of shocks delivered was 3, with ≤2 shocks delivered to 28 (49%) and ≥5 shocks delivered to 10 (18%) patients. When evaluating all 185 shocks using the 50th percentile estimated weight, 45 (24%) shocks were at recommended doses, 56 (30%) were at moderately high energy doses, and 84 (45%) were high energy doses. Elevated energy dose was associated with an increasing number of shocks and lack of bystander CPR ($p < .05$). Nineteen (33%) patients survived to hospital discharge having received total doses up to 73 J/kg. Energy dose was not related to survival.

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Conclusion: In this observational, multicenter out of hospital experience, children received a wide range of defibrillation doses, often exceeding recommended doses and equivalent to adult energy levels. Survival occurred at low and very high energy doses.

Introduction

Ventricular fibrillation is not an uncommon rhythm in children with cardiac arrest. It is the initially observed rhythm in up to a quarter of pediatric patients in out-of-hospital arrests not due to sudden infant death syndrome.[1,2] Bradyarrhythmias and ventricular fibrillation (VF) typically degenerate to asystole over the course of a pediatric arrest.[3] Survival and survival with a good neurological outcome are significantly better when the presenting rhythm is VF compared to asystole.[1,4–6] The current international recommendation adopted by the American Heart Association (AHA) for defibrillation of pediatric patients in ventricular fibrillation is 2 J/kg for the initial shock and 4 J/kg for subsequent shocks. This dose range was based on a single inpatient study of 27 patients that demonstrated 2—4 J/kg was the minimal energy dose to provide effective defibrillation.[7] In contrast, recent animal data evaluating monophasic waveforms suggest that 2—4 J/kg may be inadequate to achieve defibrillation.[8] Animal studies using monophasic waveforms suggest much higher doses defibrillate without causing histological evidence of myocardial damage; the mean toxic dose following a single shock in dogs is 30 J/kg.[9] There is evidence from adult studies that repeated shocks at higher energy levels result in more adverse events.[10]

No study has assessed what energy doses are actually used in pediatric out-of-hospital cardiac arrest. The purpose of this study was to describe the energy dose used during out-of-hospital resuscitation of pediatric ventricular fibrillation and the survival rates of these patients.

Materials and methods

Study design, setting and population

We conducted a case series study of patients aged >1 month to <18 years who received shocks for ventricular fibrillation by EMS in the out-of-hospital setting from January 1, 1986 to December 31, 2002. We reviewed three cardiac arrest databases from Emergency Medical Services (EMS) in Seattle and King County, WA and Eastern Iowa. The EMS systems maintain registries of all EMS-treated out-of-hospital cardiac arrests.[11,12] Any cardiac arrest in which the EMS was activated and attempted resuscitation with a shock was included in this study. Two EMS systems serve the population of Seattle and surrounding King County, a total population of 1.75 million persons. A total of 419 EMS systems serve the Eastern Iowa population of approximately 1 million persons.

The EMS in Washington and Iowa are two-tiered systems whose first responders are usually emergency medical technicians trained to perform CPR and automated external defibrillation until the arrival of paramedics. Until 1999, EMS protocols only allowed automated external defibrillator (AED) use in patients ≥12 years or 90 pounds (approx. 40 kg), as recommended by the American Heart Association.[13,14] After 1999, the protocols called for AED use in children >8 years of age or >55 pounds (approx. 25 kg).[15] Emergency medical technicians provided basic life support until paramedics arrived. In all three systems, paramedics are the second tier responders and provided advanced life support: evaluation of cardiac rhythm, use of manual defibrillators or AEDs, intubation, and administration of medications such as epinephrine (adrenaline), lidocaine, or bicarbonate according to the American Heart Association guidelines. During the time period of the study, most of the paramedics were equipped with monophasic defibrillators that permitted the dose to be reduced to 20 J, but did not have AEDs equipped with pediatric cables that attenuate the energy dose. The mean response interval for Seattle EMS was 4 min for first responders and 8 min for second responders.[16] Mean response interval for surrounding King County was 5 min for EMS first responders and 9 min for second-tier responders.[17]

Data collection and definitions

The EMS reports were reviewed by two of the authors (JR for Washington, MK for Iowa) to obtain patients' age, sex, underlying medical condition, location of arrest, presence of bystander cardiopulmonary resuscitation (CPR), initially recorded cardiac arrest heart rhythm, number of defibrillation attempts, energy per shock, duration of CPR, return of spontaneous circulation, admitting diagnosis, and survival to hospital discharge. Since EMS data did not include weight, weight was estimated at the 50th and 95th percentile for age for each patient using standard growth charts.[18] We conducted two sets of analyses: one using the 50th percentile weight estimate and a second using the 95th percentile weight estimate. Patients were classified into one of three categories according to their estimated weight-based energy dose: those who received (1) the recommended energy dose of 2 J/kg for the initial shock and 4 J/kg for subsequent shocks, (2) moderately high energy dose of 2 to ≤4 J/kg for the initial shock and/or >4–6 J/kg for subsequent shocks, and (3) high energy dose, >4 J/kg for their first shock and/or >6 J/kg for subsequent shocks. We also calculated the cumulative weight-based energy (J/kg) delivered during the resuscitation attempt. Resuscitation duration was defined as the total duration of the time resuscitation was provided by EMS and included the duration of bystander CPR when that information was available.

Statistical analysis

We assessed the energy dose for each shock using both the 50th percentile and 95th percentile age-based weight estimates to determine the proportion of shocks (or patients) who received the recommended, moderately high, and high energy dose. Patient and event circumstances were compared for the three energy dose groups. Continuous variables were compared using analysis of variance across the three energy dose groups and *t*-test between two groups. Categorical variables were compared using Chi-square or Fishers exact test.

In a secondary analysis, we also evaluated factors including energy dose group associated with survival to hospital discharge. For this analysis, we incorporated all shocks for each patient. Patients were classified into a dose group based on the highest dose they received during resuscitation. For example, if a patient received the recommended dose for the first shock and then a high dose for a subsequent shock, that patient would be classified in the high dose group. An a priori subgroup for primary and secondary analysis included those patients presenting with an initially observed cardiac arrest rhythm of VF.

The study was approved by the institutional review boards of the University of Iowa and Children's Hospital and Regional Medical Center, Seattle, WA.

Results

A total of 57 patients with VF were identified and their characteristics are shown in Table 1. Thirty-

Table 1 Age, gender, and event characteristics of pediatric patients receiving out of hospital shocks for ventricular fibrillation in Seattle and King County, Washington and Eastern Iowa, 1986–2002

Patient characteristics	No. (%), *N* = 57
Sex	
Male	31 (54)
Female	26 (46)
Age (years)	
0–1	8 (14)
2–5	4 (7)
6–12	13 (23)
13–17	32 (56)
Preexisting condition	
None or unknown	31 (54)
Cardiac	15 (26)
Congenital heart disease	6 (11)
Arrhythmia	5 (9)
Other heart disease	4 (7)
Neurological	7 (12)
Psychiatric	3 (5)
Pulmonary	1 (2)
Location	
Home	27 (47)
Public indoors	3 (5)
Public outdoors	18 (32)
School	5 (9)
Physician office or other patient care facility (non-hospital)	4 (7)
Event variables	
CPR	
CPR/assisted ventilation	57 (100)
Bystander CPR	34 (60)
Witnessed arrest	36 (63)
Initial rhythm	
VF	43 (80)
Asystole	3 (5)
PEA	3 (5)
VT	2 (4)
Sinus	2 (4)
SVT	1 (2)
Cumulative energy/kilogram delivered	
1–4.9 J/kg	16 (28)
5–10.9 J/kg	12 (21)
≥11 J/kg	29 (51)
Number of shocks	
Mean 3, range 1–11	
1–2	28 (49)
3–5	19 (33)
≥5	10 (18)

Table 2 Year of arrest, age, estimated weight at 50th percentile weight for age, cumulative energy dose/kg, and survival status

Patient number	Event year	Age (years)	Estimated weight (kg)	Cumulative energy (J/kg)	Survival
1	1981	4	16	18	No
2	1986	16	60	14	No
3	1986	16	60	8	No
4	1986	11	36	24	No
5	1986	16	60	8	No
6	1987	1	10	40	Yes
7	1987	16	60	28	Yes
8	1987	17	55	33	Yes
9	1988	9	28	14	Yes
10	1988	0.17	5	4	No
11	1988	15	56	50	No
12	1989	9	28	53	No
13	1990	12	40	1	No
14	1990	1.5	11	11	Yes
15	1990	13	45	4	No
16	1991	16	53	11	Yes
17	1991	14	49	30	No
18	1991	2	12	4	No
19	1991	15	56	26	No
20	1991	16	60	13	No
21	1991	17	65	11	Yes
22	1991	15	56	4	Yes
23	1991	17	65	3	No
24	1992	0.5	8	10	No
25	1992	15	52	73	Yes
26	1993	9	28	7	Unknown
27	1993	12	40	13	No
28	1993	1	10	20	No
29	1993	17	55	7	Yes
30	1994	16	53	34	Yes
31	1994	14	50	4	Yes
32	1995	16	60	19	No
33	1996	9	28	3	Yes
34	1996	15	56	14	No
35	1996	13	45	65	Yes
36	1996	15	56	11	Unknown
37	1996	13	45	4	No
38	1996	15	52	8	Yes
39	1997	12	40	19	No
40	1997	17	65	6	No
41	1997	10	32	6	No
42	1998	3	12	6	Yes
43	1998	1	10	6	Yes
44	1998	0.75	10	4	No
45	1998	8	25	59	Yes
46	1998	16	53	4	No
47	1998	10	32	2	No
48	1998	8	25	48	No
49	1999	0.25	5	1	No
50	1999	16	60	43	No
51	1999	13	45	4	Yes
52	2000	0.25	5	8	No
53	2000	16	53	28	No
54	2000	17	55	4	No
55	2001	13	45	4	No
56	2001	7	23	43	No
57	2002	17	65	17	No

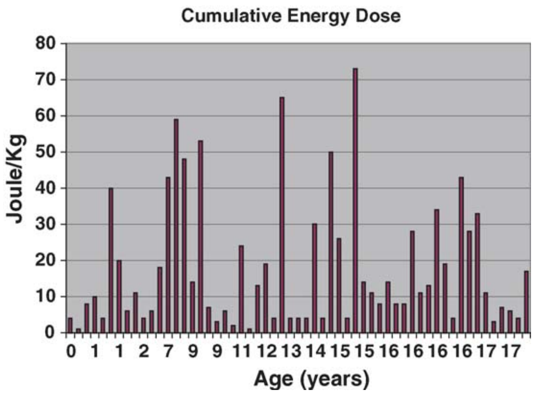

Figure 1 Patient age and cumulative energy dose per kilogram (based on estimated 50th percentile weight) received.

one (54%) were male. Median age was 13 years, range 2 months to 17 years. A preexisting medical condition was documented in 26 (46%). Of these, cardiac disease was the most common, found in 15 (58%). The medical problem that led to cardiac arrest was cardiac disease in 13 (23%), ingestion in 5 (9%), drowning in 5 (9%), trauma in 2 (4%), neurological disease in 2 (4%), respiratory disease in 3 (5%), electrocution in 1 (2%), and unknown in 21 (37%). The majority of arrests were witnessed and received bystander CPR prior to EMS arrival. In 54 patients for whom the initial rhythm was recorded, ventricular fibrillation was the initial cardiac arrest rhythm assessed by the EMS in most cases ($n = 43$, 80%) (Table 1).

Individual patients age at arrest, estimated weight at 50th percentile weight for age, cumulative energy in J/kg, and survival status are listed in Table 2. Patient age and cumulative energy dose in J/kg are displayed in Figure 1.

Most patients were treated with multiple shocks until defibrillation was achieved or resuscitation was terminated. The mean number of shocks delivered was 3, with $\leq$2 shocks delivered to 28 (49%) and $\geq$5 shocks delivered to 10 (18%) patients. Using the 50th percentile weight for age, the median dose for the first shock was 3.6 J/kg, range 0.67—14.3 J/kg. Evaluation of all 185 shocks showed, using the 50th percentile estimated weight, 45 (24%) shocks were at recommended doses, 56 (30%) were at moderately high energy doses, and 84 (45%) high energy doses. Evaluation of weight-based dose by shock sequence showed elevated energy dose was associated with increasing shock sequence. (Figure 2) For example, for the first shock, 9 (16%) received the recommended dose, 29 (51%) received moderately high energy dosing, and 19 (33%) received high energy dosing. More patients received the recommended energy dose for the second shock, ($n = 26$, 65%). However, for patients receiving more than two

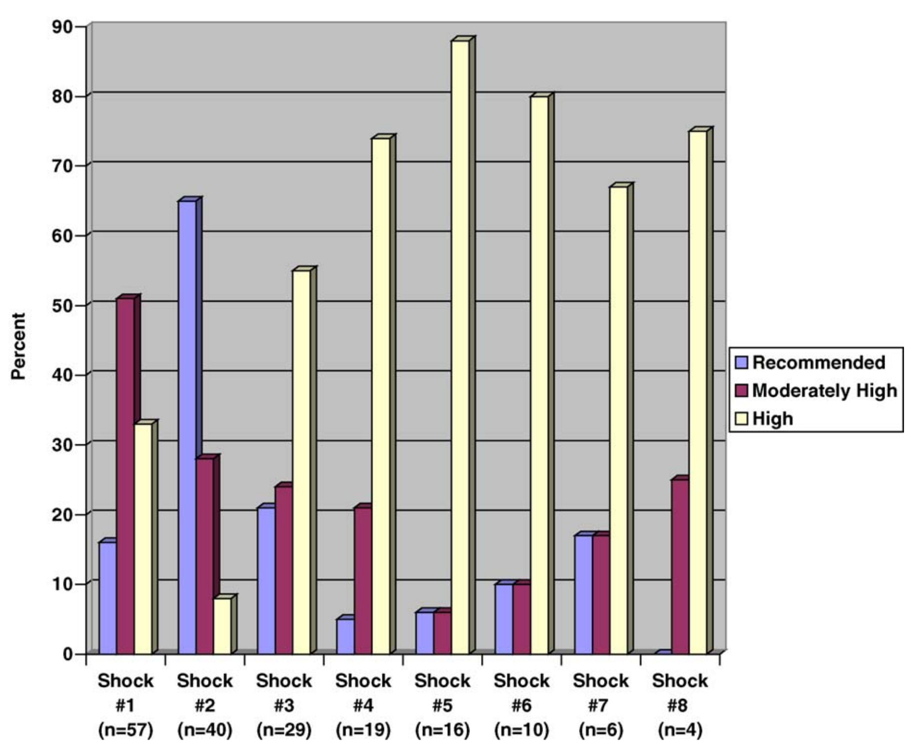

Figure 2 Energy dosing (per kilogram of 50th percentile weight for age) for each shock delivered to pediatric patients receiving out of hospital defibrillation.

Table 3 Patient and event characteristics according to 50th percentile weight-based shock group for 185 total shocks

Characteristic	Recommended, $n = 45$ shocks, 24%	Moderately high, $n = 56$ shocks, 30%	High energy, $n = 84$ shocks, 45%
Age (years), median (25th, 75th %)	12 (4, 16)	16 (13, 16)	13 (8, 15)
Male, *n* (%)	20 (44)	35 (62)	38 (45)
Preexisting clinical cardiac condition, *n* (%)	19 (42)	29 (52)	32 (38)
Home location, *n* (%)	18 (40)	32 (57)	35 (42)
Seattle—King County, *n* (%)	35 (78)	35 (62)	63 (75)
Witnessed arrest, *n* (%)	35 (78)	41 (73)	46 (55)
Bystander CPR, *n* (%)*	36 (80)	36 (64)	41 (49)
Initial rhythm VF, *n* (%)	38 (84)	49 (87)	67 (80)

* $p < .05$.

shocks, the majority (55—85%) received energy in the high energy dosing range (>6 J/kg) ($p < .05$). Results were similar when the dose group was based on the 95th percentile weight for age. In addition to shock sequence, lack of bystander CPR was associated with increasing energy dose group. Results were similar when dose group was based on the 95% weight estimate and when the analyses were restricted to the subgroup that presented initially with ventricular fibrillation (Table 3).

Evaluation of the doses by patient, using the 50th percentile weight for age, showed only 8 (14%) of patients received the recommended energy dosing for all of their shocks, 22 (39%) received at least one shock of moderately high energy dose, and 27 (47%) received at least one shock of high energy dose. Using 95th percentile weight for age, 9 (16%) patients received the recommended energy dose for all of their shocks, 38 (67%) received at least one shock of moderately high energy dose, and 10

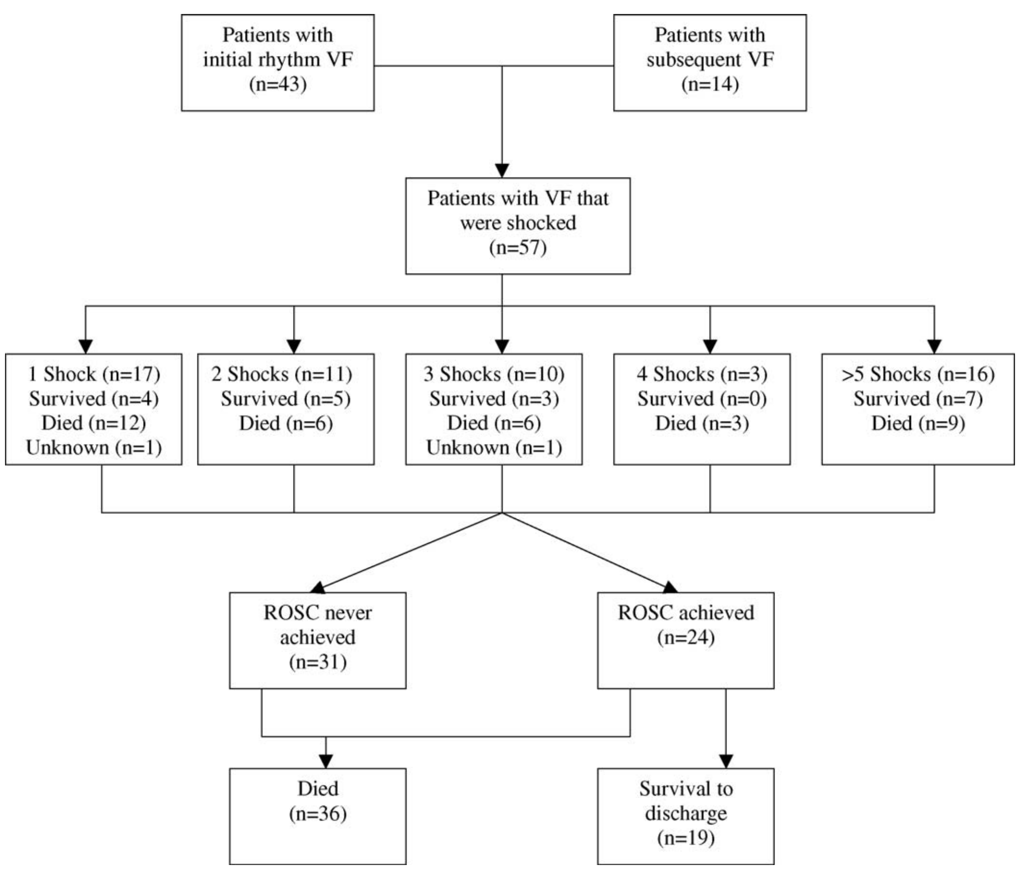

Figure 3 Outcome of pediatric patients receiving out of hospital shocks for ventricular fibrillation using the pediatric Utstein resuscitation template.

Table 4 Patient and event characteristics according to survival status from out of hospital ventricular fibrillation

Categories	Non-survivors ($n = 36$)	Survivors ($n = 19$)
Age (years) median (25th, 75th %)	13 (7, 16)	14 (8, 16)
Male, *n* (%)	23 (64)	6 (32)
Witnessed, *n* (%)	21 (58)	13 (68)
Home location, *n*, (%)	19 (53)	7 (37)
Bystander CPR, *n* (%)	23 (64)	11 (58)
Estimated weight (kg), median (25th, 75th %)	45 (24, 60)	52 (25, 55)
Initial rhythm VF—VT, *n*, (%)	31 (86)	13 (68)
Number of shocks (25th, 75th)	2.5 (1, 5)	3 (2, 6)
Cumulative energy dose (J/kg), median (25th, 75th %)	10 (4, 23)	11 (4, 34)
Dose group, *n* (%)		
Recommended	5 (14)	3 (16)
Moderately high	14 (39)	6 (32)
High	17 (47)	10 (53)
Resuscitation duration*, median (25th, 75th %)	51 (37, 74)	20 (11, 30)

All weights and weight-based dosing use the 50% percentile for age.
* $p < 0.05$.

(18%) received at least one shock of high energy dose.

Overall, 24 (42%) were admitted to the hospital and 19 (33%) survived to discharge (Figure 3). Thirty-one patients (54%) did not survive to be admitted to the hospital. Of these, 23 (74%) died in the emergency department, 6 (19%) died in the field, and 2 (6%) died at unknown locations. The survival status of 2 patients (4%) patients was unknown. A shorter duration of CPR was the only factor associated with survival; survivors had a shorter median resuscitation duration, 20 min (25th, 75th % 11, 30), compared with non-survivors, 51 min (25th, 75th % 37, 74) ($p = 0.0001$). Using the 50th percentile for weight, no dose group was associated with survival (Table 4). Dose group was also not associated with survival when the 95th percentile for weight was used. Survival occurred with total doses as low as 3 J/kg and up to 73 J/kg (50th percentile weight for age). Cumulative dose per kilogram did not differ between those who survived and died (10 and 11 J/kg, respectively).

Discussion

As one of the largest case series of pediatric VF arrests, this multi-community study reports the treatment and outcome of resuscitation for VF in children and adolescents. Arrests were observed among children as young as 2 months, were a consequence of a variety of etiologies, and occurred among children with and without preexisting clinical illness. The majority of children received three or more shocks. Energy dose often exceeded the guideline recommended dose. Approximately 30% survived, which is similar to previous pediatric and adult prehospital cardiac arrest outcome studies from Seattle and King County where the initial rhythm was ventricular fibrillation.[1,11]

Early defibrillation is a critical component of the chain of survival. Approaches that incorporate early defibrillation can improve survival.[19] Thus strategies that incorporate AED defibrillation for pediatric VF could provide earlier defibrillation and potentially improve outcome in this age group. The challenge is that conventional AEDs are designed to deliver adult energy doses. Since many AEDs could only deliver fixed adult doses, 150—200 J for the initial shock, which would be approximately 15—20 J/kg for a 10 kg child, the 50th percentile weight for a 1-year old, energy dose has been one of the deterrents to the use of AEDs in children.

For pediatric VF arrest, one important question is whether the benefit of earlier AED defibrillation with higher adult doses might be preferable to the risk of toxicity related to the higher dose. The magnitude of high energy toxicity is not clear. In a pediatric animal study, the pediatric heart tolerated substantial monophasic defibrillation dosing, up to over ten times higher than the recommended doses high dose delivered into sinus rhythm or short duration ventricular fibrillation.[9] Biphasic shocks are promising as they require lower energy to achieve defibrillation, produce less myocardial dysfunction, and improve short term outcome in pediatric animal studies.[20—22] However, even biphasic defibrillation with standard adult doses in a pediatric swine model produced more troponin T release, poorer ventricular function and lower 24 h survival than attenuated pediatric doses.[23]

With these considerations in mind, the 2003 revised guidelines recommend the use of AEDs in children 1 year of age and older but advise the use of the energy attenuating pads and cable systems.[24] Currently four manufacturers have received FDA clearance to market these attachments and human data on their use is limited.[25] The vast majority of EMS agencies however do not have these specialized pads or the devices with which they can be used. The current cost of special equipment and the training required to use them are considerable for an uncommon event.

Within this context, we evaluated the actual energy doses used for pediatric out-of-hospital VF arrest. Most children received more than the recommended 2—4 J/kg energy dose. Indeed, the majority of patients in the current study received energy doses similar to those provided in adult arrests by standard AEDs. Even when the analysis used the 95th percentile weight for age, 84% of patients received greater than the recommended energy dose and 18% received ≥4—6 J/kg (1.5—2 times the recommended dose). The results of this study suggest that some pediatric patients can be treated successfully with higher doses. While the use of attenuated energy in pediatric ventricular fibrillation appears to be preferable and should be encouraged, our findings suggest that it is reasonable to attempt defibrillation with higher doses if this is the only option available.

Many factors may have influenced why children received higher than recommended energy doses. Increasing number of shocks was associated with higher dose group. Current and past pediatric defibrillation guidelines support escalating energy for initial sequenced shocks. Along these lines, the expectation may have been that even higher doses may provide additional benefit so that increasing the dose beyond guideline recommendations might be the tendency in an arrest that requires several shocks. In addition, the lack of bystander CPR was independently associated with the increasing dose group. The reason for this is unclear and pure chance should be considered. Individual paramedics may have limited experience with pediatric cardiac arrests and have a lack of training in estimating the weight of children.[26] This study spans 16 years during which EMS equipment options were limited. If defibrillators with the ability to reduce the dose were not always available, paramedics may have elected to shock at a higher dose as opposed to not shocking at all.

In this small series of patients, only a shorter duration of resuscitation correlated with greater likelihood of survival. This is consistent with several other studies showing short resuscitation duration is associated with improved survival and improved neurologically intact survival.[27—32] In our study, only one patient who received CPR for >45 min survived.

Limitations

This study has several limitations. Although the study examined multiple variables that might be predictors of energy dose, the analysis had limited power to detect associations. Similarly, the study lacked power to clearly evaluate the relationship between survival and energy doses clearly and did not allow for adjustment for confounding factors that might have influenced patient survival. Differences in survival may be apparent in larger studies. This will be very difficult to establish because of the infrequency of the out of hospital pediatric cardiac arrest.[33] As an alternative, one approach to improve the understanding might be to evaluate whether the energy dose is associated with intermediate measures of successful resuscitation such as defibrillation, organized rhythm, and/or spontaneous circulation after each shock.

The weights used to calculate energy dose per kilogram were estimated, and thus the energy dose could have been an over or under estimate of the true weight-based dose delivered. However the range of the dosages delivered typically exceeded the weight ranges of children of these ages. We chose only to estimate weights at the 50th and 95th percentiles. However many of the children with preexisting conditions, especially cardiac, may have been smaller, with weights below the 25th percentile. Therefore, it is possible that the estimated weight-based doses were actually even larger than what we calculated.

Only out-of-hospital arrests were evaluated, and the findings may not be applicable to in-hospital ventricular fibrillation where patient weights are usually known. The patients were treated primarily with monophasic waveforms. The findings may be different with different waveforms. Additionally, the only outcome data collected was survival status. Other important outcomes, such as neurologically intact survival, were not collected in all of the databases sampled.

The study illustrates the challenges of undertaking evidence-based research in pediatric out-of-hospital VF arrest. One approach to address this challenge is a collaborative and systematic data collection of pediatric cardiac arrest across multiple communities as created for other uncommon pediatric disease states, such as cancer.

Conclusion

In this observational study, children received a wide range of defibrillation doses in the out of hospital setting that often exceeded recommended doses especially with the third and subsequent shocks. While these data do not allow us to evaluate optimal energy dose levels, children survived energy doses equivalent to adult energy levels. Additional study is needed to determine whether the energy dose influences survival in pediatric ventricular fibrillation. Such an evaluation will require an organized approach to data collection so that a database of sufficient size and detail may be assembled.

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