2018 American Heart Association Focused Update on Pediatric Advanced Life Support

An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

ABSTRACT: This 2018 American Heart Association focused update on pediatric advanced life support guidelines for cardiopulmonary resuscitation and emergency cardiovascular care follows the 2018 evidence review performed by the Pediatric Task Force of the International Liaison Committee on Resuscitation. It aligns with the International Liaison Committee on Resuscitation's continuous evidence review process, and updates are published when the group completes a literature review based on new published evidence. This update provides the evidence review and treatment recommendation for antiarrhythmic drug therapy in pediatric shock-refractory ventricular fibrillation/pulseless ventricular tachycardia cardiac arrest. As was the case in the pediatric advanced life support section of the "2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care," only 1 pediatric study was identified. This study reported a statistically significant improvement in return of spontaneous circulation when lidocaine administration was compared with amiodarone for pediatric ventricular fibrillation/pulseless ventricular tachycardia cardiac arrest. However, no difference in survival to hospital discharge was observed among patients who received amiodarone, lidocaine, or no antiarrhythmic medication. The writing group reaffirmed the 2015 pediatric advanced life support guideline recommendation that either lidocaine or amiodarone may be used to treat pediatric patients with shock-refractory ventricular fibrillation or pulseless ventricular tachycardia.

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This 2018 American Heart Association (AHA) focused update on the pediatric advanced life support (PALS) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) is based on the systematic review of antiarrhythmic drugs for cardiac arrest and the resulting "2018 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations" (CoSTR) from the Pediatric Task Force of the International Liaison Committee on Resuscitation (ILCOR). The draft pediatric CoSTR was posted online for public comment,[1] and a summary containing the final wording of the CoSTR has been published simultaneously with this focused update.[2]

AHA guidelines for CPR and ECC are developed in concert with the ILCOR systematic review process. In 2015, the ILCOR evidence evaluation process transitioned to a continuous one, with systematic reviews performed as new published evidence warrants them or when the ILCOR Pediatric Task Force prioritizes a topic. The AHA science experts then review the evidence and update the AHA's guidelines as needed, typically on an annual basis. A description of the evidence review process is available in the 2017 CoSTR summary.[3]

The ILCOR systematic review process uses the Grading of Recommendations Assessment, Development, and Evaluation methodology and its associated nomenclature to determine the quality of evidence and strength of recommendations for the CoSTR. The expert writing group for this 2018 PALS guidelines focused update reviewed the studies and analysis of the 2018 CoSTR summary[2] and carefully considered the ILCOR Pediatric Task Force consensus recommendations in light of the structure and resources of the out-of-hospital and in-hospital resuscitation systems and providers who use AHA guidelines. In addition, the writing group determined the Classes of Recommendation and Levels of Evidence according to the recommendations of the American College of Cardiology/AHA Task Force on Clinical Practice Guidelines[4] (Table) by using the process detailed in the "2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care."[5]

It is important to note that this 2018 PALS guidelines focused update reevaluates only the recommendations for the use of antiarrhythmic drugs during ventricular fibrillation (VF)/pulseless ventricular tachycardia (pVT) cardiac arrest. All other recommendations and algo-rithms published in "Part 12: Pediatric Advanced Life Support" in the 2015 guidelines update[6] and "Part 14: Pediatric Advanced Life Support" in the "2010 Ameri-can Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care"[7] remain the official recommendations of the AHA ECC Science Subcommittee and writing groups. The recommendations contained in the "2017 American Heart Association Focused Update on Pediatric Basic Life Support and Cardiopulmonary Resuscitation Quality: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" continue to apply to CPR delivered to pediatric patients in cardiac arrest.[8]

BACKGROUND

Shock-refractory VF/pVT refers to VF or pVT that persists or recurs after ≥1 shocks. Two antiarrhythmic medications are currently discussed in the AHA guidelines: lidocaine, a fast sodium channel blocker (Class IB) that acts in part by accelerating repolarization, and amiodarone, a multiple ion channel blocker (Class III) that is believed to act predominantly by prolonging repolarization. An antiarrhythmic drug alone is unlikely to pharmacologically convert VF/pVT to an organized perfusing rhythm. Rather, the primary objective of antiarrhythmic drug therapy in shock-refractory VF/pVT is to facilitate successful defibrillation and to reduce the risk of recurrent arrhythmias. In concert with shock delivery, antiarrhythmic drugs can facilitate the restoration and maintenance of a spontaneous perfusing rhythm. Some antiarrhythmic drugs have been associated with increased rates of return of spontaneous circulation (ROSC) and survival to hospital admission,[9,10] but none have yet been demonstrated to increase long-term survival or survival with good neurological outcome. Thus, establishing vascular access to enable drug administration should not compromise the quality of CPR or delay timely defibrillation, both of which are associated with improved long-term survival. The optimal sequence of PALS interventions, including administration of antiarrhythmic drugs during resuscitation, and the preferred manner and timing of drug administration in relation to shock delivery are still not known.

The 2018 ILCOR Pediatric Task Force review addressed the use of antiarrhythmic drugs during pediatric cardiac arrest (in infants, children, and adolescents <18 years of age) with a shockable rhythm in any setting (in hospital and out of hospital), during CPR or immediately after ROSC. This review was triggered by the publication of 2 adult studies examining the use of antiarrhythmic medications in adult cardiac arrest.[11,12] However, unlike previous ILCOR reviews and several earlier AHA PALS guidelines, the ILCOR Pediatric Task Force review and this 2018 PALS guidelines focused update are based only on pediatric studies and did not consider evidence extrapolated from adult studies. The writing group agreed that pediatric patients with VF/pVT cardiac arrest differ substantially from adult patients in ways that could influence presentation, treatment, and response to antiarrhythmic drugs. We did not address the use of antiarrhythmic medications after ROSC.

Table. ACC/AHA Recommendation System: Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R — **(Randomized)**
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR — **(Nonrandomized)**
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD — **(Limited Data)**
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO — **(Expert Opinion)**

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

USE OF ANTIARRHYTHMIC DRUGS DURING RESUSCITATION FROM PEDIATRIC VF/pVT CARDIAC ARREST

2018 Evidence Summary

Amiodarone and Lidocaine

Only 1 pediatric study was identified in the 2018 ILCOR systematic review of the literature.[13] This same pediatric study was included in the 2015 guidelines update but was reviewed to determine whether any modification of AHA guidelines was warranted. The observational study is derived from the AHA Get With The Guidelines–Resuscitation registry. It evaluated a cohort of children enrolled from 2000 to 2008 who had an in-hospital cardiac arrest requiring CPR for at least 2 minutes, with a rhythm of VF/pVT at any time during the cardiac arrest.[13] Of the 9280 eligible patients with cardiac arrest, 1099

(12%) had VF/pVT documented at some time during the cardiac arrest; after those who received prearrest lidocaine or amiodarone were excluded, 889 patients were available for evaluation. Patients receiving lidocaine had statistically higher rates of ROSC compared with patients receiving amiodarone or no antiarrhythmic medication. There was no significant difference in ROSC for patients receiving amiodarone compared with those receiving no antiarrhythmic medication. There was no difference in survival to hospital discharge across the 3 groups. On multivariate analysis, lidocaine was independently associated with ROSC (odds ratio, 2.02; 95% CI, 1.36–3.00). Neither lidocaine nor amiodarone was found to have a significant independent association with survival to hospital discharge.

The raw data were used to calculate a relative risk of each outcome. There was a statistically significant improvement in ROSC in patients who received lidocaine compared with amiodarone (64% versus 44%; *P*=0.004; relative risk, 1.46; 95% CI, 1.13–1.88). There was no statistical difference in survival to hospital discharge in patients who received lidocaine compared with those receiving amiodarone (25% versus 17%; *P*=NS; relative risk, 1.50; 95% CI, 0.90–2.52) or when those who received lidocaine, amiodarone, or no antiarrhythmic medication were compared.

The results of this study were not reported by year of cardiac arrest. The study did not report adverse events, making it impossible to balance the risk and benefit of administration of antiarrhythmic medication in this population.

2018 Recommendation

Amiodarone and Lidocaine—Unchanged

1. **For shock-refractory VF/pVT, either amiodarone or lidocaine may be used (*Class IIb; Level of Evidence C-LD*). This is unchanged from the 2015 recommendation.[6]**

The Pediatric Cardiac Arrest Algorithm—2018 Update (Figure) is unchanged in the depiction of sequences and therapies from the version published in 2015.[6] To clarify the use of antiarrhythmic medications for shock-refractory VF/pVT, under Drug Therapy in the box on the right, the doses of amiodarone and lidocaine are clearly separated with the word "or." The writing group also took the opportunity to review the complete text of the algorithm and to eliminate minor wording differences between the adult and pediatric cardiac arrest algorithms. Under Asystole/PEA (pulseless electrical activity), in Box 10, the writing group added the word "capnography" to the last bullet after "Consider advanced airway" and made minor edits to Box 12, eliminating the bulleted phrase "Organized rhythm→check pulse." In the CPR Quality box on the right, in the fourth bullet, the word "rotate" was changed to "change." These changes will make the wording identical to that in the boxes located in the same position in the Adult Cardiac Arrest Algorithm—2018 Update. All other parts of the Pediatric Cardiac Arrest Algorithm are unchanged.

Discussion

Past ILCOR pediatric evidence reviews, CoSTRs, and AHA PALS guidelines on the topic of antiarrhythmic therapy in pediatric cardiac arrest have incorporated data extrapolated from adult studies. For this update, the consensus of the ILCOR Pediatric Task Force was to consider only pediatric studies because the experts agreed that the pediatric cardiac arrest population differs significantly from the adult cardiac arrest population. The most recent adult studies examining the effect of antiarrhythmic medication for shock-refractory VF/pVT had an average patient age of >60 years and specifically excluded patients <18 years of age.[11,12,14] Pediatric cardiac arrests typically occur in patients with progressive respiratory failure or shock, and most are preceded by a period of hypoxia and hypotension, with a terminal rhythm of bradycardia or asystole. Ventricular arrhythmias are more common in certain subpopulations, such as children with congenital heart disease or channelopathies. However, in general, VF/pVT is uncommon, occurring as the first documented rhythm in 10% to 14% of pediatric in-hospital cardiac arrests[13,15–18] and in 7% of pediatric out-of-hospital cardiac arrests.[19,20] Subsequent VF/pVT (ie, VF/pVT that develops during resuscitation from an arrest with a non–VF/pVT initial arrest rhythm such as pulseless electrical activity or asystole) occurs in 15% of pediatric in-hospital cardiac arrests.[15] In the Valdes et al[13] study, subsequent VF/pVT was associated with lower rates of ROSC and survival to hospital discharge than initial VF/pVT was; this outcome is consistent with other pediatric[16,17] and adult[21] reports.

Unlike pediatric cardiopulmonary arrest, cardiac arrest in adults is often secondary to a sudden ventricular arrhythmia. Coronary occlusion with subsequent myocardial ischemia serves as a common trigger for these arrhythmias, typically with no preceding hypoxia or hypotension. The most common arrest rhythm in adult cardiac arrest is VF/pVT, present in up to 44% of adult cardiac arrests.[21,22] Because it is unclear how differences between pediatric and adult cardiac arrest may influence the effect of antiarrhythmic therapy, the writing group agreed with the ILCOR Pediatric Task Force to analyze evidence from only pediatric cardiac arrest studies.

The indication for the use of amiodarone or lidocaine in this 2018 PALS guidelines focused update is shock-refractory VF/pVT, defined as VF or pVT that per-

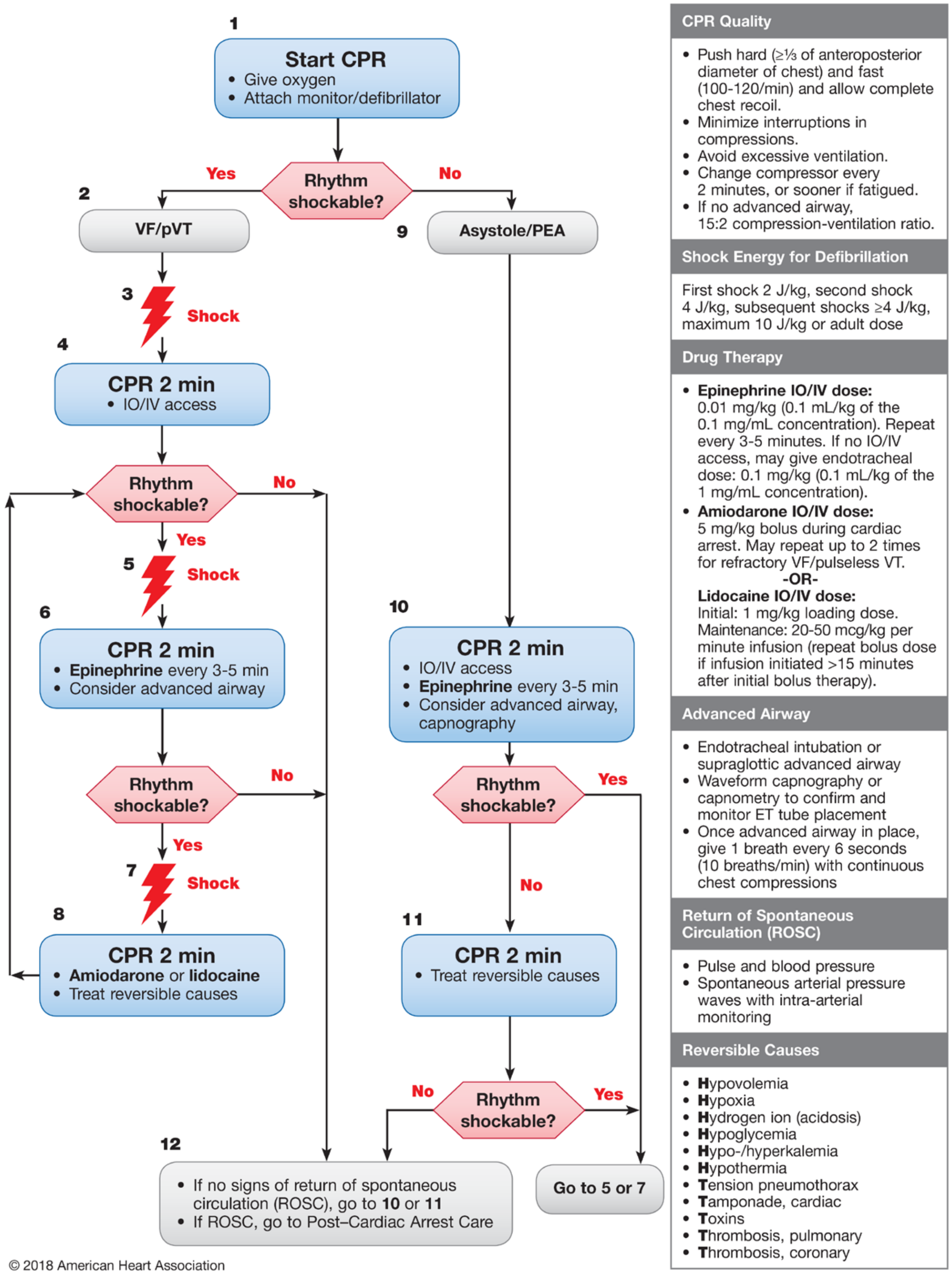

Figure. Pediatric Cardiac Arrest Algorithm—2018 Update.
CPR indicates cardiopulmonary resuscitation; ET, endotracheal; IO, intraosseous; IV, intravenous; PEA, pulseless electrical activity; pVT, pulseless ventricular tachycardia; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

sists or recurs after the delivery of at least 1 shock. In the Valdes et al[13] study, the mean number of shocks administered is 3, but the number of subjects who required >1 shock is not reported, so it is impossible to determine with certainty how many of the patients in the study had shock-refractory VF/pVT. In the absence of evidence to the contrary, the writing group assumed that enrolled patients received at least 1 shock before antiarrhythmic therapy and could therefore be considered to have shock-refractory VF/pVT.

Another potential limitation of the Valdes et al[13] study is the period during which patients were enrolled in the study. The study included patients who had in-hospital cardiac arrest between 2000 and 2008, spanning the years during which the "2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care" were introduced.[23] These 2005 guidelines emphasized the importance of high-quality CPR, including emphasis on minimizing interruptions in chest compressions by using a new compression-to-ventilation ratio and a new defibrillation sequence (1 shock followed by immediate resumption of CPR instead of 3 "stacked" shocks). Because recommended resuscitation sequences and interventions differed substantially before and after the implementation of the 2005 guidelines, the Valdes et al study was downgraded in the ILCOR systematic review for indirectness (ie, many patients in the study were treated in a manner inconsistent with current resuscitation practice). This issue highlights a challenge of resuscitation research: As guidelines are updated, research protocols become outdated and comparisons challenging. In the future, authors are encouraged to provide subgroup analyses of patients enrolled in studies after major guideline changes.

SUMMARY

A review of the peer-reviewed publications on antiarrhythmic therapy in pediatric shock-refractory VF/pVT cardiac arrest resulted in no change in PALS guideline recommendations but has identified several gaps in our knowledge. As noted in the 2010 guidelines,[7] high-quality CPR and defibrillation are the only therapies proven to increase survival in patients with VF/pVT. The optimal sequence of PALS interventions for VF/pVT cardiac arrest, including administration of a vasopressor or antiarrhythmic medication, and the timing of medication administration in relation to shock delivery are not known. The sequence of interventions recommended in the current PALS algorithm should consider the individual patient and the environment of care.

Future updates will address new research such as targeted temperature management after ROSC[24] and hemodynamic monitoring to guide CPR quality[25–27] to integrate new published evidence into resuscitation recommendations.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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Disclosures

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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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