Evidence Update Worksheet

Prearrest Care of the Infant or Child With Dilated Cardiomyopathy or Myocarditis
PLS 4.030.19

Worksheet author(s): Joseph Rossano

Task Force: PLS

PICOST / Research Question:

• Population: Infants and children with myocarditis or dilated cardiomyopathy (DCM) and impending cardiac arrest

• Intervention: A specific approach

• Comparator: The usual management of shock or cardiac arrest

• Outcome: Survival with favorable neurological/ functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; cardiac arrest frequency; ROSC

Year of last full review: 2020

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

2020 Document: No new data to change current recommendations from 2018 Scientific Statement on 'Cardiopulmonary Resuscitation in Infants and Children with Cardiac Disease'

2018 AHA recommendations from 'Cardiopulmonary Resuscitation in Infants and Children with Cardiac Disease'

1. Given the high risk of cardiac arrest in children with acute myocarditis who demonstrate high-risk ECG changes (arrhythmias, heart block, ST-segment changes) and/or low cardiac output, early consideration of transfer for ICU monitoring and therapy is recommended *(Class I; Level of Evidence C)*.

2. For children with cardiomyopathy or myocarditis and refractory low cardiac output, prearrest use of ECLS can be beneficial to provide end-organ support and prevent cardiac arrest *(Class IIa; Level of Evidence B)*.

3. Given the challenges to successful resuscitation of children with cardiomyopathy and myocarditis, once cardiac arrest occurs, early consideration of ECLS can be beneficial *(Class IIa; Level of Evidence B)*.

Current Search Strategy (for an existing PICOST) included in the attached approved PICOST

("Cardiomyopathy, Dilated"[Mesh] OR "dilated cardiomyopathy"[TIAB] OR "Myocarditis"[Mesh] OR "Myocarditis"[TIAB] OR "Shock"[Mesh:noexp] OR "Shock, Cardiogenic"[Mesh] OR "circulatory failure"[TIAB] OR "Heart Failure"[Mesh] OR "heart failure"[TIAB] OR "Acute Decompensated Heart Failure"[Mesh] OR "acute decompensated heart failure"[TIAB]) AND ("Pre-arrest"[TIAB] OR "'Pre arrest"[TIAB] OR "prearrest"[TIAB] OR "Heart Arrest"[Mesh] OR "heart arrest"[TIAB] OR "heart arrests"[TIAB] OR "heart arrests"[TIAB] OR "cardiac arrest"[TIAB] OR "cardiac arrests"[TIAB] OR "cardiovascular arrest"[TIAB] OR "cardiovascular arrests"[TIAB] OR "cardiopulmonary arrest"[TIAB] OR "cardiopulmonary arrests"[TIAB]) AND ("Emergency Treatment"[Mesh] OR "Emergency

Medicine"[Mesh] OR "Intubation, Intratracheal"[Mesh] OR Intubat*[TIAB] OR medication*[TI] OR drug*[TIAB] OR "Pharmaceutical management"[TIAB] OR "Atropine"[Mesh] OR Atropine[TIAB] OR "Ketamine"[Mesh] OR Ketamine[TIAB] OR Vasopressor*[TIAB] OR Vasoconstrictor*[TIAB] OR "Cardiovascular Agents"[Mesh] OR "Cardiotonic Agents"[Mesh] OR anti-arrhythmic*[TIAB] OR "Bicarbonates"[Mesh] OR bicarbonate*[TIAB] OR bolus[TIAB] OR "Hyperventilation"[Mesh:noexp] OR Hyperventilation[TIAB] OR "Hypoventilation"[Mesh:noexp] OR hypoventilation[TIAB] OR "Nitric Oxide"[Mesh] OR "nitric oxide"[TIAB] OR “Chest Compression”[Mesh] OR “chest compression”[TIAB] OR “chest compressions”[Mesh] OR “chest compressions”[TIAB] OR “Cardiopulmonary resuscitation"[Mesh] or “cardiopulmonary resuscitation”[TIAB] OR "Extracorporeal Membrane Oxygenation"[Mesh] OR "extracorporeal life support"[TIAB] OR "Heart-Assist Devices"[Mesh]) AND (infant*[TIAB] OR "Infant"[Mesh] OR "Child"[Mesh] OR "Pediatrics"[Mesh] OR "child*"[TIAB] OR "paediatric*"[TIAB] OR pediatric))) AND ("observational study"[Publication Type] OR "randomized control trial"[Publication Type])) AND ("2019/01/01"[Date - Publication] : "2023/05/28"[Date - Publication])

New Search strategy: Used prior search, with updated dates

Database searched: eg Medline Embase Cochrane - Pubmed

Time Frame: (existing PICOST) – updated from end of last search (1/1/2019 to 5/28/2023)

Time Frame: (new PICOST) – at the discretion of the Task Force (please specify) Used prior PICOST

Date Search Completed: 5/28/23

Search Results (Number of articles identified and number identified as relevant):

5 new articles identified.

2 excluded for being out of scope.

Ellouze O, Lamirel J, Perrot J, Missaoui A, Daily T, Aho S, Petrosyan A, Guinot PG, Bouchot O, Bouhemad B. Extubation of patients undergoing extracorporeal life support. A retrospective study. *Perfusion*. 2019;34:50-57. https://www.ncbi.nlm.nih.gov/pubmed/30044174

Tonna, J.E., et al., *Patient and Institutional Characteristics Influence the Decision to Use Extracorporeal Cardiopulmonary Resuscitation for In-Hospital Cardiac Arrest.* J Am Heart Assoc, 2020. **9**(9): p. e015522.

https://www.ncbi.nlm.nih.gov/pubmed/32347147

3 included articles are listed below

Summary of Evidence Update:

Relevant Guidelines or Systematic Reviews

Organization (if relevant); **Author;** **Year Published**	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**

RCT:

Study Acronym; **Author;** **Year Published**	**Aim of Study; Study Type;** **Study Size (N)**	**Patient Population**	**Study Intervention** **(# patients) /** **Study Comparator** **(# patients)**	**Endpoint Results** **(Absolute Event Rates, P value; OR or RR; & 95% CI)**	**Relevant 2° Endpoint (if any);** **Study Limitations; Adverse Events**
	Study Aim: **Study Type:**	**Inclusion Criteria:**	**Intervention:** **Comparison:**	**1° endpoint:**	**Study Limitations:**

Nonrandomized Trials, Observational Studies

Study Acronym; **Author;** **Year Published**	**Study Type/Design; Study Size (N)**	**Patient Population**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI)**	**Summary/Conclusion Comment(s)**
Conway JA, et al. 2020[1]	**Study Type:** Observational study. Retrospective review of National Emergency Airway Registry for Children (NEAR4KIDS);	**Inclusion Criteria:** Critically ill children aged 0-17 years who underwent tracheal intubation in a PICU	**1° endpoint:** Occurrence of adverse hemodynamic events during tracheal intubation including dysrhythmia, hypotension, and cardiac arrest	**Summary/Conclusion:** 32% of tracheal intubations included ketamine as an induction agent The most common diagnosis associated with ketamine use was sepsis / shock (49.7%)

	Multicenter registry. Data are prospectively obtained N=10,750 tracheal intubations	Only first encounter as included and endotracheal tube exchanges were excluded	The aim was to assess the association of ketamine exposure with the primary endpoint	Use of ketamine was associated with fewer adverse events (aOR 0.74, 95% CI, 0.58-0.95) Myocarditis or DCM not analyzed separately so it cannot be ascertained whether the association of ketamine and the primary outcome would also be observed in this population.
Holmbert MJ, et al. 2019[2]	**Study Type:** Observational study. Retrospective review of the multicenter AHA Get with Guidelines – Resuscitation (GWTG-R) registry N= 13, 184 patients (7,433 pulseless cardiac arrests, 5,751 nonpulseless cardiac event)	**Inclusion Criteria:** Patients ≤ 18 years with an index in-hospital cardiac arrest at site participating in the GWTG-R registry	**1° endpoint:** Survival to hospital discharge Secondary endpoint was ROSC Generalized estimation equations were used to assess for tends over time Separate analyses were performed pulseless and nonpulseless events and shockable vs nonshockable rhythms in pulseless cardiac arrests	**Summary/Conclusion:** For pulseless cardiac arrest, survival to hospital discharge improved from 19% (95% CI, 11%-29%) in 2000 and 38% in 2018 (95% CI, 34% - 43%). Improved survival appeared to plateau after 2010 For nonpulseless events, survival improved from 57% (95% CI, 39% - 75%) in 2000 to 66% (95% CI, 61% - 72%). There was no association of initial rhythm on survival. This study was did not analyze myocarditis or DCM separately and had no data on management strategies for this population.
Menendez JJ, et al. 2023[3]	**Study Type:** Observational. Retrospective study of all pediatric patients undergoing treatment with a ventricular assist device (VAD) in Spain	**Inclusion Criteria:** Pediatric patients (< 18 years) with VAD implant at one of 6 VAD centers in Spain.	**1° endpoint:** Hospital mortality Secondary endpoints included competing outcomes leading to VAD explantation and VAD-related complications	**Summary/Conclusion:** Patients with DCM (n=59) and myocarditis (n=11) were more likely to survive on with VAD treatment (78% and 72% respectively). On multivariable analysis, a diagnosis of congenital heart disease was associated with a greater

	from 2006 to 2020			likelihood of mortality (aOR 3.4, 95% CI 1.2 – 10.2) While this study has shown that VADs can be used effectively in patients with DCM or myocarditis, there is no group of DCM / myocarditis patients that did not undergo VAD placement to help to assess in what patients this therapy should be considered.

Reviewer Comments: *(including whether this PICOST should have a systematic or scoping review*)

There are few data on which to base specific recommendations. Given the lack of information, a systematic or scoping review is not needed at this time.

There are important areas of gaps in research including the following:

1. Fluid and inotropic management
2. Management and location for intubation
3. Stabilization prior to transfer to higher level of care
4. Monitoring for patient with myocarditis and dilated cardiomyopathy and low cardiac output
5. Timing and indications ECLS

<u>Conclusion</u>

1. Given the high risk of cardiac arrest in children with acute myocarditis who demonstrate high-risk ECG changes (arrhythmias, heart block, ST-segment changes) and/or low cardiac output, consider early transfer to higher level of care for monitoring and therapy is recommended.

2. For children with cardiomyopathy or myocarditis and refractory low cardiac output, where resources permit, pre-arrest use of ECLS can be beneficial to provide end-organ support and prevent cardiac arrest.

3. Given the challenges to successful resuscitation of children with cardiomyopathy and myocarditis, once cardiac arrest occurs, ECLS can be beneficial in settings where resources permit.

Reference list: ***(List by ILCOR ref standard (last name first author, year of publication, first page number) and insert hyperlink to all articles identified as relevant (if available on PubMed)***

1. Conway, J.A., et al., *Ketamine Use for Tracheal Intubation in Critically Ill Children Is Associated With a Lower Occurrence of Adverse Hemodynamic Events.* Crit Care Med, 2020. **48**(6): p. e489-e497.
2. Holmberg, M.J., et al., *Trends in Survival After Pediatric In-Hospital Cardiac Arrest in the United States.* Circulation, 2019. **140**(17): p. 1398-1408.
3. Menendez, J.J., et al., *Short- and long-term survival of children treated with ventricular assist devices in Spain, based on 15 years' experience.* Eur J Cardiothorac Surg, 2023. **63**(2).

Links to articles:

1. Conway, et al.: https://www.ncbi.nlm.nih.gov/pubmed/32317603
2. Holmberg, et al: https://www.ncbi.nlm.nih.gov/pubmed/31542952
3. Menendez, et al: https://www.ncbi.nlm.nih.gov/pubmed/36759938

Evidence Update Worksheet

Ventilation Rate When a Perfusing Rhythm Is Present

PLS 4.120.01

Worksheet author(s): Michelle Myburgh

Task Force: Pediatric

Date Submitted to SAC rep for peer review and approval: 30 Nov 2023

PICOST / Research Question:

Population	Infants and children (excluding newborn infants) with a perfusing rhythm but absent or inadequate respiratory effort
Intervention	Use of a any specific respiratory rate
Comparison	Compared with ventilation rate of 20-30 per minute
Outcomes	Clinical outcomes, including - short-term survival and neurological outcomes (e.g. survival to hospital discharge, survival at 30-days), - long-term survival and neurological outcomes (e.g. PCPC at 6-months, and 1-year).
Study Design	STEP 1: Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) that directly concern the population and intervention described above are eligible for inclusion. If it is anticipated that there will be insufficient studies from which to draw a conclusion, case series may be included in the initial search. The minimum number of cases for a case series to be included was set by the taskforce at 5. Systematic Reviews and guideline publications are eligible for inclusion. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded. STEP 2: The same study designs and/or existing systematic or scoping reviews not directly concerning the population or intervention defined above but considered informative as additional evidence (taking into account severe indirectness) for the development of the final taskforce insights.
Timeframe	For STEP 1: All studies published since last search (December 2, 2019) and all languages are included as long as there is an English abstract. For STEP 2, if a systematic or scoping review of high quality (as per AMSTAR 2 tool) is identified, search can be limited to beyond data and/or scope of that review.

Year of last full review :2020

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

Ventilation Rate When a Perfusing Rhythm Is Present (PLS 3103A and PLS 382: EvUp) This EvUp was undertaken to determine if there was published evidence to support the recommendation to deliver 1 breath every 3 seconds or any other specific ventilation rate for infants and children who require bag-mask ventilation but have a pulse and perfusing rhythm. The 2000 CoSTR on pediatric basic life support noted, “the goal of ventilation with a bag and mask should be to approximate normal ventilation and achieve physiological oxygen and carbon dioxide concentration while minimizing risk of iatrogenic injury.” The recommendation was based on expert consensus rather than a formal review of the evidence on the subject. The PLS Task Force has not made any previous recommendations for specific ventilation rate for the infant or child with respiratory arrest and a perfusing rhythm. Such recommendations have been included in council guidelines rather than in the ILCOR CoSTRs. The search conducted in December 2019 for this EvUp did not reveal any relevant evidence, and the task force concluded that there was no need to consider a recommendation for a SysRev.

Current Search Strategy (for an existing PICOST) included in the attached approved PICOST
PubMed 62 results - Includes MeSH ((((((("perfusing"[Text Word] OR "perfusion"[Text Word]) AND "rhythm"[Text Word]) OR "perfusing rhythm"[All Fields] OR "heart arrest/therapy"[MeSH Major Topic] OR "cardiopulmonary resuscitation/therapy"[MeSH Major Topic]) AND (("ventilat*"[Text Word] OR "breaths per minute"[All Fields] OR "breath per minute"[All Fields] OR ("apnea"[MeSH Terms] OR "respiratory rate"[MeSH Terms])) AND ("infan*"[Text Word] OR "child*"[Text Word] OR "adolescen*"[Text Word] OR "pediatric*"[Text Word] OR "paediatric*"[Text Word] OR "pube*"[Text Word] OR "juvenil*"[Text Word] OR "school*"[Text Word] OR "newborn*"[Title/Abstract] OR "newborn*"[Title/Abstract] OR "neonat*"[Title/Abstract] OR "neonat*"[Title/Abstract] OR "premature*"[Title/Abstract] OR "postmature*"[Title/Abstract] OR "premature*"[Title/Abstract] OR "post mature*"[Title/Abstract] OR "preterm*"[Title/Abstract] OR "preterm*"[Title/Abstract] OR "baby"[Title/Abstract] OR "babies"[Title/Abstract] OR "toddler*"[Title/Abstract] OR "youngster*"[Title/Abstract] OR "preschool*"[Title/Abstract] OR "kindergart*"[Title/Abstract] OR "kid"[Title/Abstract] OR "kids"[Title/Abstract] OR "playgroup*"[Title/Abstract] OR "play group*"[Title/Abstract] OR "playschool*"[Title/Abstract] OR "prepube*"[Title/Abstract] OR "preadolescen*"[Title/Abstract] OR "junior high*"[Title/Abstract] OR "highschool*"[Title/Abstract] OR "senior high"[Title/Abstract] OR "young people*"[Title/Abstract] OR "minors"[Title/Abstract])))) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) NOT ("Letter"[Publication Type] OR "Editorial"[Publication Type] OR "Comment"[Publication Type])) AND 2019/09/01:2023/12/31[Date - Publication]

New Search strategy: (for a new PICOST should be outlined here as per Evidence Update Process)

Database searched: Pubmed

Time Frame: (existing PICOST) – updated from end of last search

Time Frame: (new PICOST) – at the discretion of the Task Force

Date Search Completed: 15 Aug 2023

Search Results (Number of articles identified and number identified as relevant): 62 results on pubmed , 62 had title and abstract screening with 3 full text screens. Included studies: 1

Summary of Evidence Update:

Relevant Guidelines or Systematic Reviews

Organization (if relevant); **Author;** **Year Published**	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**
Holmberg et al., 2020	SR and meta-analysis including adults and children	Oxygenation and ventilation targets after cardiac arrest.	6 pediatric observational studies included		<u>Oxygenation:</u> None of the observational studies rated as having less than critical risk of bias found any association between hyperoxia and survival to hospital discharge or survival with favorable neurological outcome. Similar results were reported for hypoxia and survival to hospital discharge. <u>Carbon dioxide:</u> One observational study rated as having less than critical risk of bias found both hypocapnia (OR, 2.71; 95% CI, 1.04-7.05) and hypercapnia (OR, 3.27; 95% CI, 1.62-6.61) to be associated with worse survival to hospital discharge compared to normocapnia.

RCT:

Study Acronym; **Author;** **Year Published**	**Aim of Study; Study Type;** **Study Size (N)**	**Patient Population**	**Study Intervention** **(# patients) /** **Study Comparator**	**Endpoint Results** **(Absolute Event Rates, P value; OR or RR; & 95% CI)**	**Relevant 2° Endpoint (if any);** **Study Limitations; Adverse Events**

			(# patients)		
	Study Aim: **Study Type:**	**Inclusion Criteria:**	**Intervention:** **Comparison:**	**1° endpoint:**	**Study Limitations:**

Nonrandomized Trials, Observational Studies

Study Acronym; **Author;** **Year Published**	**Study Type/Design; Study Size (N)**	**Patient Population**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI)**	**Summary/Conclusion Comment(s)**
	Study Type:	**Inclusion Criteria:**	**1° endpoint:**	

Reviewer Comments: ***(including whether this PICOST should have a systematic or scoping review*****)**

The systematic review identified in the search only contained 6 observational studies related to paediatric patients with no RCTs included. The conclusions of the paper were related to oxygenation and ventilation targets and not to specific ventilation rates. There is insufficient evidence to make a recommendation on ventilation rates, but good practices related to post-cardiac arrest care in pediatric patients should involve titrating ventilation rates to maintain normoxaemia and normocapnoea in the post-arrest phase. It is not currently recommended to conduct a scoping or systematic review.

Reference list: ***(List by ILCOR ref standard (last name first author, year of publication, first page number) and insert hyperlink to all articles identified as relevant (if available on PubMed)***

Holmberg, Mathias J. et al. "Oxygenation and Ventilation Targets after Cardiac Arrest: A Systematic Review and Meta-Analysis." *Resuscitation* 152 (2020): 107–115. Web.

Links to article:

Holmberg et al. https://pubmed.ncbi.nlm.nih.gov/32389599/