QUESTION

Should ECPR or CPR be used for pediatric patients with cardiac arrest?	
POPULATION:	Children with cardiac arrest
INTERVENTION:	Patients/cases with ECPR
COMPARISON:	Patients/ cases where manual or mechanical CPR is provided
MAIN OUTCOMES:	Survival to hospital discharge, long-term survival, neurological outcome at hospital discharge, and long-term neurological outcome.
SETTING:	Out of hospital or in hospital cardiac arrest (OHCA or IHCA)
PERSPECTIVE:	Patient perspective
BACKGROUND:	ECPR is used in pediatrics with in-hospital cardiac arrest. The evidence is largely limited to observational single-center studies.
CONFLICT OF INTERESTS:	None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	This problem is a high priority for select children who may not survive without ECPR intervention in organizations with systems of care with access to this resource. Applying ECPR is a complex intervention compared to providing conventional CPR. There is uncertainty about the optimal ECPR approach (timing and technique) and wide variability (Lasa 2017 125) compared to conventional CPR to achieve highest survival and favourable functional outcomes in survivors.	Significant resources are required to maintain systems of care that can effectively deliver ECPR as an intervention, and to support patients and their families during post cardiac arrest care.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	ECPR may be associated with increased probability of survival and among survivors, improved early functional outcomes (Lasa 2016 165).	The rationale for ECPR is that it may provide better organ reperfusion than conventional CPR (Lasa 2016 165); as such the desirable effects would be a decrease in risk of hypoxic ischemic encephalopathy, myocardial ischemia, and multi-organ dysfunction in the post cardiac arrest syndrome in select populations where standard CPR may have limited value (Marino 2018 e691).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ○ Trivial ● Varies ○ Don't know	The un-desirable or potential effects associated with ECPR compared to conventional CPR are the following: decrease in the quality of conventional CPR during the cannulation procedure (Taeb 2018 831), potential risk of neurologic and/or limb and/or myocardial ischemia and reperfusion injury (associated with the anatomical site of cannulation),(Joffe 2012 297, Larovere 2017 64) the consequences of exposure to anticoagulation and hemorrhagic complications, and to blood products administration (Conrad 2017 4).	The un-desirable effects associated with ECPR may be to re-establish perfusion in patients without preventing irreversible end-organ damage and severe morbidities.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Overall, very low certainty of the evidence of effects with wide confidence intervals in the systematic review (Holmerg 2018 91).	Longer-term functional outcomes and quality of life outcomes in survivors and in non-survivors and their families would greatly inform the field.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	The outcomes evaluated and published in the literature focused on short-term survival and early survival with favorable functional outcome.	The studies are relatively small and may not be representative of broad population of pediatric cardiac arrest, its multiples causes or outcomes.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ●Varies ○ Don't know	The heterogeneity of the studies evaluated, the observational nature of available data, and the wide confidence intervals do not allow for a precise analysis of the balance between desirable and undesirable effects. The studies could not be pooled into a meta-analysis.	The delivery of ECPR in the in-hospital or out-of-hospital settings increases the complexity of resuscitation systems and the resources required to sustain these systems. ECPR and subsequent ECMO post cardiac arrest management involve direct and indirect costs. These resources may only be available in very select emergency departments, or emergency response regional systems, or in-hospitals settings.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	Comparative cost analyses were not included in the systematic review.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Very low ○ Low ○ Moderate ○ High ● No included studies	There was no formal cost analysis undertaken for this summary of the evidence but the intervention is known to involve added costs, is resource intensive, requires specialist teams, and as well as supportive infrastructure to launch ECPR and to support patients and their families during post cardiac arrest syndrome.	Cost effectiveness and health care resource utilization studies are not available; these may be best suited to understand the tradeoffs involved in implementation of ECPR compared to conventional CPR. Economic analyses of other populations with ECMO are emerging (Peek 2010 1) and of cardiac arrest suggest increased costs with the use of technology (Damluji 2018 1)

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No studies were identified in cardiac arrest literature.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ● Don't know	No relevant studies were identified.	

Acceptability

Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	The acceptability of this intervention to key stakeholders would likely depend on their expectations and on the healthcare system being able to deliver this service.	Centers require additional resources to implement and sustain a program.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ●Yes ○ Varies ○ Don't know	ECPR is feasible to implement in select in-hospital cardiac arrest settings.	

SUMMARY OF JUDGEMENTS

Summary of judgements for pediatric recommendations:

	JUDGEMENT							IMPLICATIONS
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know	Setting
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know	
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know	
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies	
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know	
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	

	JUDGEMENT							IMPLICATIONS
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			No included studies	
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	No included studies	
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know	
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know	

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
O	O	O	O	

CONCLUSIONS

Recommendation

We suggest ECPR may be considered as an intervention for selected children with in-hospital cardiac arrest refractory to conventional CPR in settings where resuscitation systems allow ECPR to be implemented (weak recommendation, very-low-certainty evidence).

Justification

Centers that apply this intervention for select patients justify its use by suggesting that conventional CPR alone is insufficient to ensure return of circulation for optimal perfusion to optimize functional outcomes.

Subgroup considerations

There is a need to better identify select patients for whom ECPR is beneficial over conventional CPR alone, and to identify the optimal timing and technique to apply the intervention in order to increase the risk of survival and the risk of favorable functional outcomes in survivors.

Implementation considerations

Highly resource intensive across the broad system of care.

Monitoring and evaluation

Requires ongoing performance evaluation of favorable and unfavorable outcomes.

Research priorities

- The majority of studies published in the literature do not include comparisons (ECPR vs conventional CPR), and therefore could not be included in the systematic review in 2018.
- Published studies in children all use observational designs.
- There is a serious risk of bias.
- The risk of heterogeneity within and between studies is high.
- There is a need for comparative studies, including but not exclusively randomized controlled trials.
- There are gaps in the literature about the following in paediatrics:

- Timing of cannulation for ECPR following conventional CPR
- Technique of cannulation to ensure quality CPR and optimal reperfusion
- Delivery of co-interventions for ongoing CPR such as inotropes (e.g., epinephrine), vasoactive agents (e.g., constrictors or dilators), or for the extracorporeal technique: type of crystalloid vs blood primed circuits, fraction of device oxygen (FdO_2) delivery in membrane lung and target oxygenation, circuit target blood flow rate, de-carboxylation rate i.e., management of CO_2, temperature target and management.
- Post cardiac arrest care goals and co-interventions.

- Post cardiac arrest assessment and timing of prognostication.