Question
Should ECPR vs. no ECPR be used for adult patients with cardiac arrest

Problem:	Cardiac arrest	**Background:**	ECPR may be used to support circulation in patients with cardiac arrest. The evidence is largely limited to observational single-center studies.
Option:	ECPR		
Comparison:	Manual or mechanical CPR		
Main outcomes:	Survival to hospital discharge, long-term survival, neurological outcome at hospital discharge, and long-term neurological outcome		
Setting:	OHCA/IHCA		
Perspective:	Patient perspective		

Assessment

	Judgement	**Research evidence**	**Additional considerations**
Problem	**Is the problem a priority?** ○ No ○ Probably no ○ Probably yes ○ **Yes** ○ Varies ○ Don't know	This problem is a high priority as many potential candidates for ECPR may not survive without the intervention. Consideration of the timing of implementation is also a high priority, given the overall low survival and neurologically intact survival rates in cardiac arrest.	Significant resources are required to both establish and maintain systems of care that can effectively deliver this therapy.
Desirable Effects	**How substantial are the desirable anticipated effects?** ○ Trivial ○ Small ○ Moderate ○ **Large** ○ Varies ○ Don't know	The risk of harm with the provision of ECPR remains unknown and is likely dependent on the scenario in which the intervention is applied. The risk of harm would be minimal or negligible if ECPR is provided to obtain ROSC/survival in a patient who already received prolonged advanced life support management and where no other treatment options are available, Conversely, if ECPR is provided early in the course of the cardiac arrest, then the risk of harm would include the possibility that ROSC and survival could have occurred without requiring ECPR since ECPR is known to have complications including but not limited to hemorrhage and death. From a resource-allocation standpoint, the risks in applying ECPR to a non-selected population may be the provision of extraordinary life support to patients who will inevitably not survive (e.g. elderly patient with severe comorbidities). The studies evaluated are heterogenous with respect to timing, approach, population, and setting.	The Task Force discussed the potential that ECPR could disadvantage individuals if ECPR increases probability of survival without good neurological recovery. Conversely, the Task Force discussed the potential that ECPR could provide societal benefit by allowing initial survivors who subsequently meet criteria for brain death or withdrawal of life sustaining treatment to be considered as potential organ donors. The ethics of these situations will need future discussion, particularly if future trials find that ECPR increases numbers of neurologically injured and/or brain dead subjects.
Undesirable Effects	**How substantial are the undesirable anticipated effects?** ○ Large ○ **Moderate** ○ Small ○ Trivial ○ Varies ○ Don't know		
Certainty of evidence	**What is the overall certainty of the evidence of effects?** ○ **Very low** ○ Low ○ Moderate ○ High ○ No included	Overall, very low certainty with inconsistent effects and wide confidence intervals.	

	studies		
Values	**Is there important uncertainty about or variability in how much people value the main outcomes?** ○ Important uncertainty or variability ○ **Possibly important uncertainty or variability** ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Since ROSC cannot be easily defined with this intervention, the outcomes evaluated focused on short-term and long-term survival and survival with good neurological function. The importance of neurologically intact survival is generally agreed upon with recognition that survival without neurological recovery is an undesirable outcome for most patients.	
Balance of effects	**Does the balance between desirable and undesirable effects favor the intervention or the comparison?** ○ 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 all available data, and the wide confidence intervals do not allow for a precise analysis of the balance between desirable and undesirable effects. Specifically, these studies were unable to be pooled into a meta-analysis.	
Resources required	**How large are the resource requirements (costs)?** ○ **Large costs** ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	There is no formal cost analysis so this remains unknown. The provision of ECPR followed by management with ongoing ECMO is resource intensive and costly. This intervention is currently unavailable for most OHCA settings and only available in select emergency departments and in-hospitals settings.	
Certainty of	**What is the certainty of the evidence of resource requirements (costs)?**		

Certainty of evidence of required resources	**(costs)?** ○ Very low ○ Low ○ Moderate ○ High ○ **No included studies**	There was no formal cost analysis but the intervention is well-known to be costly and resource intensive.	
Cost effectiveness	**Does the cost-effectiveness of the intervention favor the intervention or the comparison?** ○ 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 relevant studies identified.	
Equity	**What would be the impact on health equity?** ○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ **Don't know**	No relevant studies identified.	No relevant studies have been identified, however logic would dictate that resource poor areas may not have local centers capable of providing this intervention.
Acceptability	**Is the intervention acceptable to key stakeholders?** ○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ **Don't know**	This is not formally known, but the acceptability of this intervention to key stakeholders would likely depend on their available resources.	
Feasibility	**Is the intervention feasible to implement?** ○ No ○ Probably no ○ Probably yes ○ Yes ○ **Varies** ○ Don't know	Some are already poised to provide ECPR, but most centers and hospitals would require substantial additional resources and training to be capable of performing it.	

Summary of judgements

Problem	No	Probably no	Probably yes	Yes		Varies	Don't know	
Desirable Effects	Trivial	Small	Moderate	Large		Varies	Don't know	
Undesirable Effects	Large	Moderate	Moderate	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	
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	

Conclusions:

Type of recommendation	Strong recommendation against the option: ○ | Conditional recommendation against the option: ○ | Conditional recommendation for either the option or the comparison: ○ | Conditional recommendation for the option: ○ | Strong recommendation for the option: ○
Recommendation	We suggest ECPR may be considered as a rescue therapy for select patients with cardiac arrest when conventional CPR is failing in settings where this therapy can be implemented (weak recommendation, very-low-certainty evidence).
Justification	Currently, some centers apply this therapy as a rescue therapy for select patients who would likely have been pronounced dead without the intervention. Therefore, the use of ECPR seems justified in select centers and with select populations. The evidence for using ECPR early in resuscitation efforts remains less clear.
Subgroup considerations	Need to identify select populations for whom this would be beneficial
Implementation considerations	Highly resource intensive
Monitoring and evaluation	
Research priorities	Discussions included: ● There were many studies without control groups that were not included in the systematic review since quantification of these studies is not possible ● Current studies are all observational ● Current studies have considerable heterogeneity and very serious risk of bias ● There is a need for randomized trials with considerable attention to design of the study and populations evaluated ● Importance of timing of the intervention – is this a rescue intervention or something to be applied early after cardiac arrest? Interpreting future study results will likely depend highly on the design around timing