Clinical question.

In pediatric patients in cardiac arrest (prehospital [OHCA] or in-hospital [IHCA]) (P) does the use of rapid deployment ECMO or emergency cardiopulmonary bypass (I), compared with standard treatment (C), improve outcome (ROSC, survival to hospital discharge, survival with favorable neurologic outcomes) (O)?

Is this question addressing an intervention/therapy, prognosis or diagnosis? Intervention/therapy

State if this is a proposed new topic or revision of existing worksheet: revision of existing worksheet

Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? M Morris is an author on one paper cited in this worksheet (Morris 2004).

Search strategy (including electronic databases searched).

Literature search included Medline, Embase, and the Cochrane Library.

Terms searched include:
“ECMO and cardiac arrest,”
“ECMO and heart arrest,” ECPR, and
“extracorporeal cardiopulmonary resuscitation.”

Search methodology also included review of the references cited in that literature, and review of the ECC EndNote database. Last search: November 2009.

State inclusion and exclusion criteria

Inclusion Criteria: Peer reviewed articles reporting on ECMO initiated during cardiac arrest.

Excluded: Case series with 3 or fewer patients, articles in which it was not clear whether ECMO was initiated during active CPR, and case series that included only a subset of subjects where the larger group was reported in other published literature. Consensus articles, letters to the editor, and editorials were excluded. Case series published prior to 1990 were excluded.

Number of articles/sources meeting criteria for further review: 31 studies were included for review.
### Summary of evidence

#### Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th></th>
<th>Good</th>
<th>Evidence Supporting Clinical Question</th>
<th>Fair</th>
<th>Poor</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Alsoufi 2007 (D)</td>
<td>Duncan, 1998 (D)</td>
<td>Walpoth 1997 (E)</td>
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<td>Huang 2008 (E)</td>
<td>Prodhan 2009 (D)</td>
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<tr>
<td>Good</td>
<td>DeMos 2006 (C)</td>
<td>Aharon, 2001 (C)</td>
<td>Barrett 2009 (D)</td>
<td>Chen, 2003 (D)</td>
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<tr>
<td></td>
<td>Morris 2004 (C)</td>
<td>Chan 2008 (D)</td>
<td>del Nido, 1992 (D)</td>
<td>Gazmuri, 1991 (B)</td>
</tr>
<tr>
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<td></td>
<td>del Nido, 1996 (D)</td>
<td>Parra, 2000 (D)</td>
<td>Gazmuri, 1992 (B)</td>
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<td>Parra, 2000 (D)</td>
<td>Shah 2005 (C)</td>
<td>Willms, 1997 (C)</td>
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<td>Thourani 2006 (C)</td>
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<tr>
<td>Fair</td>
<td></td>
<td>Cochran, 1999 (D)</td>
<td>Dalton 1993 (C)</td>
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<td>3</td>
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<td>4</td>
<td>5</td>
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**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italics = Animal studies*
**Evidence Neutral to Clinical question**

<table>
<thead>
<tr>
<th>Good</th>
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<td>Fair</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>Wu 2009 (CD)</td>
<td></td>
<td>Yamamoto 2007 (D)</td>
<td></td>
</tr>
</tbody>
</table>

| 1 | 2 | 3 | 4 | 5 |

**Level of evidence**

A = Return of spontaneous circulation  
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*Italics = Animal studies*

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**Evidence Opposing Clinical Question**

<table>
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<tbody>
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<td>Fair</td>
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<tr>
<td>Poor</td>
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| 1 | 2 | 3 | 4 | 5 |

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A = Return of spontaneous circulation  
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D = Intact neurological survival  
E = Other endpoint  

*Italics = Animal studies*
REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

Very little human pediatric data specifically demonstrates a positive effect of ECPR specifically compared to conventional CPR. However, animal models strongly support a physiologic advantage of ECPR over conventional CPR, and the outcomes following pediatric ECPR seem considerably better than one might expect for a group of children with cardiac arrest refractory to tens of minutes of conventional resuscitative efforts. Several reports find better outcomes for children with primary cardiac disease than for children with other etiologies of cardiac arrest.

Studies conflict regarding the duration of conventional CPR following which ECPR may still be successful, but reports exist of favourable neurologic outcome in children who received over an hour of conventional CPR before ECPR. Neurologic impairment is fairly common in children managed with ECPR, though the incidence of neurologic impairment following ECPR may not differ from that following VA ECMO for other indications, and in both cases, it can not be determined how much of the neurologic impairment if ECMO/CPR related and how much is related to the children’s underlying conditions.

Summary of outcomes in pediatric ECPR case series

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Patient population</th>
<th>Number of patients successfully cannulated*</th>
<th>Number of patients decannulated to sustained spontaneous circulation</th>
<th>Number of long term survivors</th>
<th>Duration of CPR in minutes: median (range) or mean +/- SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aharon, 2001</td>
<td>Pediatric post-cardiotomy</td>
<td>10</td>
<td>8 (80%)</td>
<td></td>
<td>42 (5-110)</td>
</tr>
<tr>
<td>Alsoufi, 2007</td>
<td>Pediatric, largely cardiac</td>
<td>80</td>
<td>42 (54%)</td>
<td>27 (34%)</td>
<td>Favorable 46 (14-45) Unfavorable 41 (19-110)</td>
</tr>
<tr>
<td>Cochran</td>
<td>Pediatric cardiac catheterization lab</td>
<td>3</td>
<td>3 (100%)</td>
<td>2 (67%)</td>
<td></td>
</tr>
<tr>
<td>Dalton, 1993</td>
<td>Pediatric cardiac</td>
<td>17</td>
<td>3 (100%)</td>
<td>11 (65%)</td>
<td></td>
</tr>
<tr>
<td>del Nido, 1996</td>
<td>Pediatric post-cardiotomy</td>
<td>11</td>
<td>7 (64%)</td>
<td>6 (55%)</td>
<td>65 +/- 9</td>
</tr>
<tr>
<td>Duncan, 1998</td>
<td>Pediatric Cardiac</td>
<td>11</td>
<td>9 (82%)</td>
<td>6 (55%)</td>
<td>55 (20-103)</td>
</tr>
<tr>
<td>Eich, 2007</td>
<td>Pediatric drowning</td>
<td>12</td>
<td></td>
<td>5 (42%)</td>
<td></td>
</tr>
<tr>
<td>Huang, 2008</td>
<td>Pediatric</td>
<td>27</td>
<td></td>
<td>11 (41%)</td>
<td>Non-survivors 60 (37-81) Survivors 45 (25-50)</td>
</tr>
<tr>
<td>Morris, 2004</td>
<td>Pediatric, largely cardiac</td>
<td>64</td>
<td>31 (48%)</td>
<td>21 (33%)</td>
<td>48 (5-105)</td>
</tr>
<tr>
<td>Parra DA 2000</td>
<td>Pediatric cardiac</td>
<td>4</td>
<td>4 (100%)</td>
<td>4 (100%)</td>
<td>16 (12-20)</td>
</tr>
<tr>
<td>Prodhain, 2009</td>
<td>Pediatric ICU</td>
<td>34</td>
<td></td>
<td>24 (75%)</td>
<td></td>
</tr>
<tr>
<td>Thourani, 2006</td>
<td>Pediatric cardiac</td>
<td>15</td>
<td></td>
<td>11 (73%)</td>
<td></td>
</tr>
<tr>
<td>Trittenwein, 2001</td>
<td>Pediatric in-hospital</td>
<td>10</td>
<td></td>
<td>3 (30%)</td>
<td></td>
</tr>
</tbody>
</table>

*The number of attempted cannulations is inconsistently reported and hence is not included in this table
Citation List


LOE: 4 Quality: Fair Supportive
This is a case series of children who underwent ECMO following heart surgery, including 10 ECPR patients. 8/10 survived to discharge. Limited, early neurologic evaluation only. Sample is small and detail for the ECPR cohort is limited.


LOE: 4 Quality: Good Supportive
This is a retrospective cohort study of children undergoing ECPR (2000-2005). Outcomes reported include mortality and gross neurologic outcome at 1 and 3 years after ECPR. 1/9 children with a non-cardiac etiology survived, while 34% of those with a cardiac indication survived, 30% with a favorable neurologic outcome. Strengths of the study include the large consecutive sample size and the relative richness of patient information. The study supports ECPR for children with primary cardiac disease, and does not specifically support ECPR for children with other etiologies of cardiac arrest, though the numbers are small.


LOE: 4 Quality: Fair Supportive
This study represents an attempt to identify risk factors for acute neurologic injury following/during ECPR, using the ELSO Registry. The authors report a 22% incidence of neurologic injury and find less neurologic injury in patients with less severe metabolic acidosis, primary cardiac disease, and an uncomplicated ECMO course. As ELSO reporting is voluntary, the sample is not necessarily representative. Further, it is not possible with this type of registry to be certain that ascertainment of neurologic injury is complete.


LOE: 4 Quality: Fair Supportive
This is an analysis of the ELSO registry, with the aim of identifying risk factors for mortality among children with heart disease undergoing ECPR (1992-2005). The authors report single ventricle physiology, a history of a phase I palliation, and extreme acidosis as pre-ECMO factors associated with mortality. The study is subject to all of the limitations of registry studies, including the limitations on available data and the voluntary nature of reporting.


LOE: 5 Quality: Fair Supportive
This is a single center case series of 57 adult ECPR patients. The mean duration of conventional CPR was 48 minutes, with a 32% early survival and 29% long term survival. Among late survivors,
the incidence of neurologic injury was 5.6%. Quality of the study is good overall, but only fair for this purpose, as the patients were all adults.


LOE: 4  Quality: Poor  Supportive
This is a case series of three children who underwent ECPR in the cardiac catheterization lab. Two survived grossly intact. The sample is small and adds only incrementally to the literature.


LOE 4  Quality poor  Supportive
This is a single center case series of children with heart disease who were managed with ECMO, including 11 ECPR patients. Neurologic outcome is provided for the parent group but not for the ECPR subgroup.


LOE: 4  Quality: Fair  Supportive
This is a case series of 11 children who underwent ECPR following cardiac surgery 1981-1991. There were 7 survivors to discharge and 6 long-term, grossly intact survivors. Strengths include the richness of resuscitation data presented. Limitations include the relatively long-ago nature of the series.


LOE: 4  Quality: Fair  Supportive
This is a retrospective description of children managed with ECMO, including 11 ECPR patients at a single institution from 1981-1996. There is considerable overlap with DelNido 1992.


LOE: 3  Quality: Fair  Supportive
This is a retrospective cohort study of children with in-ICU cardiac arrest. The report includes 5 ECPR patients, and an additional 23 who had ECMO initiated within 24 hours following resuscitation. The authors report better outcome among the ECMO patients than the non-ECMO patients, though this comparison is subject to bias as not all patients are deemed ECMO candidates, based on co-morbidities. Limited data specific to the ECPR patients is available.


LOE: 4  Quality: Good  Supportive
This is a case series of 11 children with heart disease and ECPR. Seven survived to discharge and 6 survived long term. Strengths of the study include detail provided about resuscitation and ECMO course. Gross neurologic outcome was reported. Efforts were made to compare to historic controls, though this comparison is inherently subject to bias as the decision to employ ECPR depends on comorbidities.


LOE: 4 Quality: Fair Neutral

This is a retrospective series of children with drowning associated with cardiac arrest and ECPR, 1987-2005. 5/12 survived to discharge, two neurologically intact. The authors were not able to identify predictors of mortality.


LOE: 5 Quality: Fair Supportive

This is an animal model comparing ECPR to open-chest cardiac massage in pigs, demonstrating significantly better hemodynamics and survival in the pigs managed with ECPR. Strengths include the head to head, randomized comparison. Weaknesses include the fact that the pigs were pre-instrumented, possibly biasing in favor of ECPR compared to a clinical situation.


LOE: 5 Quality: Fair Supportive

This is an animal model comparing conventional CPR to ECPR in pigs, demonstrating significantly better survival in the ECPR animals. Strengths include the head to head, randomized comparison. Weaknesses include the fact that the pigs were pre-instrumented, possibly biasing in favor of ECPR compared to a clinical situation.


LOE: 4 Quality: Fair Opposing

This is a single center follow-up study of children managed with ECMO following cardiac surgery 1009-2001. This study represents the most detailed and thorough neurologic evaluation of ECMO patients published to date. Of 55 original patients, 16 survived short term, and 14 were alive at the time of the study, plus one who was lost to follow-up. 7/14 patients evaluated demonstrated no neurologic deficit. Only 1 of 12 ECPR patients survived, making it impossible to draw conclusions about the neurologic outcome of this subpopulation.


LOE: 4 Quality: Good Supportive
This is a case series of pediatric ECPR patients with gross neurologic follow-up. 11/27 patients survived. 10/11 survivors had a good gross neurologic outcome, but 4 were noted to have deficits at later follow-up. Longer duration of conventional CPR was associated with worse outcome. Strengths of the study include the neurologic outcome and the detail provided regarding ECPR deployment and clinical details of the resuscitation.


LOE: 4 Quality: Fair Neutral
This is a long-term evaluation of children with heart disease who were managed with ECMO, including ECPR patients. The ECPR patients were not separately discussed. 59% of ECMO patients had neurologic impairment.


LOE: 4 Quality: Fair Neutral
This is a long-term neurologic evaluation of children who were managed with ECMO at an age less than five years, including 12 ECPR patients. There was a very high incidence of neurologic and behavioral problems. The ECPR patients are not separately described but are reported to not differ from the parent population. The major weakness is the limited discussion of the ECPR cohort.


LOE: 5 Quality: Poor Supportive
This is a single center retrospective case series of seven adult ECMO patients, including 5 ECPR patients and two with intractable cardiogenic shock. Three survived, two neurologically intact. The authors emphasize that patient selection should be limited to those with rapidly correctable underlying cardiopulmonary pathology. The study is limited by small size and co-analysis of ECPR and non-ECPR patients.


LOE: 5 Quality: Fair Neutral
This is a single center report of 10 adult patients managed with femoro-femoral ECPR in the emergency room. While the authors cite the “feasibility” of performing ECPR in this setting, none of the patients survived. The study includes rich detail about the resuscitations and the ECMO initiation, but is limited by small size.


LOE: 2 Quality: Fair Supportive
This is a single center retrospective cohort study of 64 pediatric ECPR patients from 1995-2002. Outcome was found to be better in children with isolated heart disease when compared to those with other medical conditions. Limited neurologic follow-up is provided and is favorable, though incomplete.

LOE: 4  Quality: Fair  Supportive  
This is a retrospective cohort study of children with in-ICU cardiac arrest from 1995-1997, including 4 ECPR patients. 4/4 ECPR patients survived. The median duration of conventional CPR was only 16 minutes in these ECPR patients, shorter than is reported elsewhere. Limited information available about this small subset of patients. The study is valuable overall, but adds only incrementally to the ECPR literature.


LOE: 4  Quality: Good  Supportive  
This is a single center, relatively large case series of PICU patients undergoing ECPR from 2001-2006. 24/32 deployments resulted in survival to hospital discharge (two patients had two deployments). 18/24 survivors were grossly neurologically intact. Strengths of the study include rich detail and the fairly current cohort. Survival and intact neurologic outcome were better than many other reports, though the reasons for this difference are not clear.


LOE: 4  Quality: Fair  Supportive  
This is a single center case series of children managed with ECMO following heart surgery 2001-2004, including 27 ECPR patients. Strengths include discussion of the ECMO process, but a major weakness is the limited data specific to the ECPR patients (e.g. duration of conventional CPR). Patients undergoing ECPR did not differ immortality from the parent cohort.

**Schwarz** B, et al., Experience with percutaneous venoarterial cardiopulmonary bypass for emergency circulatory support. Critical Care Medicine, 2003. 31(3): p. 758-64.

LOE: 5  Quality: Fair  Neutral  
This study is a retrospective report of 46 adult ECMO patients, including 21 ECPR patients. Most of the analyses are conducted on the entire population rather than on the ECPR population alone.


LOE: 4  Quality: Fair  Supportive  
This is a retrospective cohort of children with cardiac disease managed with ECMO 2002-2004, including 15 ECPR patients. 11/15 survived, but neurologic outcome is not reported.


LOE: 5  Quality: Good  Supportive  
This study reports an evaluation of adults who survived following ECPR associated with accidental hypothermia. 15/42 initial patients survived, and while some had early neurologic deficits, virtually
all neurologic defecits resolved completely. This data support the use of ECPR for adults with deep hypothermia associated cardiac arrest.


LOE: 5  Quality: Fair  Supportive
This is a retrospective, single center cohort study of adults managed with ECMO, including 68 ECPR patients. 17 survived to hospital discharge. Limited ECPR data is provided, but it is a comparatively large series.


LOE: 2  Quality: Poor  Neutral
This is a single center retrospective study designed to identify correlates with survival for children with in-hospital cardiac arrest. The series contains 64 patients managed with ECPR or ECMO soon after ROSC. 18% of ECMO patient survived a year with a good neurologic outcome. Major weakness as pertains to this question is the lack of separate analysis of ECPR patients. Further, the authors attempt to compare ECMO “cases” to non-ECMO “controls,” which is inherently biased given that selection criteria for ECMO candidacy (though not delineated) make the groups fundamentally non-comparable.


LOE: 4  Quality: Poor  Neutral
This is a report of only two children both with fulminant myocarditis, both of whom survived following ECPR initiated in the emergency room at a single center. It is not at all clear that the experience with these two patients should be extrapolated to suppot ED use of ECPR, as significant selection bias exists. It is unclear whether both or either child was in full cardiac arrest.


LOE: 5  Quality: Fair  Neutral
This is a mixed adult-pediatric, single center case series of 25 patients with ECPR or ECMO attempted immediately after resuscitation from cardiac arrest. Initiation of ECMO was successful in 21, and 9 survived. Mortality was associated with longer duration of conventional CPR. Five patients had ECPR initiated in the ED, with no survivors. Series includes only three children.