

WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)

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Clinical question.

In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use intravenous fluids (I) compared with not using fluids (or standard resuscitation) (C), improve outcomes (eg. ROSC, survival of event, survival to hospital discharge, intact neurological survival) (O).

Is this question addressing an intervention/therapy, prognosis or diagnosis? INTERVENTION
State if this is a proposed new topic or revision of existing worksheet: REVISION C2005

Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No relevant conflicts

Search strategy (including electronic databases searched).

Search strategies were tailored to the databases searched, allowing for variation in MeSH terms and updated based on WSE feedback.

1) Medline (28th September 2009):

Infusions, intravenous OR blood transfusion OR plasma substitutes OR colloids

AND

Cardiopulmonary resuscitation OR heart arrest (exploded) OR ventricular fibrillation

Results:

352 Results

87 Results since January 1 2004

6 for inclusion

2) Embase (28th September 2009):

Plasma substitute (exploded) OR Hartmann solution OR Ringer solution OR hypertonic solution OR fluid resuscitation (exploded)

AND

Heart arrest (exploded) OR cardiopulmonary arrest (exploded) OR asystole (exploded) OR heart ventricle fibrillation

332 Results

161 Results since January 1 2004

6 for inclusion

3) AHA Endnote Library (Last updated March 2008):

Arrest
AND
Fluid OR infusion
195 Results
21 Results since January 1 2004
3 for inclusion

4) Cochrane systemic reviews and central register of controlled trials (22nd May 2009)

Cardiopulmonary resuscitation OR heart arrest
AND
Infusions, intravenous
331 Results
Results since July 1 2004:
7 Cochrane Reviews
15 Other Reviews
0 Method Study
8 Technology Assessments
10 Economic assessments
310 Clinical Trials
2 for inclusion

} No studies for inclusion

5) Google Scholar (28th September 2009)

Fluid
AND
Cardiopulmonary arrest OR ventricular fibrillation
AND
(at least one of) Colloid OR blood OR saline
Results
4,390 results since July 1 2004
9 included

The reference lists of relevant papers identified were also hand-searched for additional sources, and abstracts from relevant resuscitation conferences were also searched.

Several papers were identified by more than one search strategy.

- State inclusion and exclusion criteria

Include studies looking at adults ≥ 18 years in human studies

Include studies with English language abstracts

Include animal studies

Include studies with fluids administered to induce hypothermia

Include studies that do not have a control group that receive no fluid

Include studies identified by worksheet with the same clinical question from 2005, unless exclusion criteria are met

Exclude single cases, but include case series

Exclude papers that focus on trauma-related resuscitation

Exclude post-ROSC fluid administration (the subject of worksheet ALS-PA-043)

- **Following removal of duplicates, number of articles/sources meeting criteria for further review: 22**

12 from 2005 worksheet, 10 additional.

Relevant papers were selected using inclusion and exclusion criteria and abstracts were reviewed to ensure that they were appropriate to address the PICO question. Trials of either animal models or adult patients that included the use of intravenous fluid during cardiopulmonary arrest were eligible for further review, whether or not they compare fluid use to no fluid.

Four of the papers that were included in the previous worksheet (WS 105, c2005: *Does the routine use of fluids during resuscitation improve outcome from cardiac arrest?*) have been excluded as three focus on resuscitation following trauma or haemorrhage, and one on haemoconcentration occurring during cardiac arrest.

22 papers were eligible for further review.

Summary of evidence

Evidence Supporting Use of fluids during cardiac arrest

Good					
Fair					
Poor					
	1	2	3	4	5
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 use of fluids during cardiac arrest

Good					*Bruel et al, 2008 ^{ABD} <i>Miclescu et al</i> ∇, 2006 ^{A, B, E1, E2} *Nozari et al, 2006 ^{A, B, E3, E4} *Nordmark et al, 2005 ^{A, E1, E2} <i>Krep et al</i> ∇, 2004 ^{A, B, E1} <i>Frenneaux</i> , 2003 ^{E2} <i>Breil et al</i> ∇, 2003 ^{A, B, E2} <i>Fischer et al</i> ∇, 2002 ^{A, B, E2} <i>Ujhelyi</i> , 1996 ^{E5} <i>Jameson et al</i> , 1993 ^{A, B, E2}
Fair					Bender et al ∇, 2007 ^{AB} Longstreth et al, 1993 ^{A, B, C} Paradis et al, 1990 ^{A, E2} <i>D'Alecy et al</i> , 1986 ^{A, B, E3}
Poor					*Kamarainen et al, 2008 ^{ABC} *Kamarainen et al, 2008 ^{ABC}
	1	2	3	4	5
Level of evidence					

* Fluids used for therapeutic hypothermia

∇ Study looking primarily at efficacy of hypertonic infusions

Italics = Animal studies

A = Return of spontaneous circulation

C = Survival to hospital discharge

B = Survival of event

D = Intact neurological survival

E = Other

E1= cerebral cortical blood flow

E2 = haemodynamic variables (including coronary perfusion pressure)

E3 = neurological function up to 96hrs post-ROSC

E4 = histological brain damage

E5 = defibrillation threshold

Evidence Opposing use of fluids during cardiac arrest

Good					<i>* Riter et al, 2009^{A, E2}</i> <i>Yannopoulos, 2009^{A, E2}</i> <i>Steen, 2003^A</i> <i>Gentile et al, 1991^{E2}</i>
Fair					<i>Vorhees, 1987^{E1, E2}</i> <i>Ditchey et al, 1984^{E2}</i>
Poor					
	1	2	3	4	5

* Fluids used for therapeutic hypothermia

A = Return of spontaneous circulation
endpoint

C = Survival to hospital discharge

E = Other

B = Survival of event

D = Intact neurological survival

Italics = Animal studies

E1= cerebral cortical blood flow

E2 = haemodynamic variables (including coronary perfusion pressure)

REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

C2005 Consensus on Science:

There are no human studies of routine fluid use compared to no fluids during cardiac arrest.

Evidence from four animal studies (Ditchey 1984, Gentile 1991, Jameson 1993, Voorhees 1987, LOE 5) of experimental ventricular fibrillation neither supports or refutes the use of routine intravenous fluids in ventricular fibrillation cardiac arrest in any clinical setting.

C2005 Treatment recommendation:

There is insufficient evidence to support any recommendation regarding routine use of fluids for cardiac arrest.

There is no guidance regarding the routine use of intravenous fluid during cardiac arrest. We have therefore defined standard care as no fluids.

This updated WS identified 9 new studies about the use of fluids during cardiopulmonary resuscitation (CPR). The previous WS included mainly animal studies [Breil, 2003, 307-17, Fischer, 2002, 269-80, Frenneaux, 2003, 259-65, Gentile, 1991, 55-63, Jameson, 1993, 243-50, Steen, 2003, 249-58, Ujhelyi, 1996, 784-90, Voorhees, 1987, 113-23, Yannopoulos, 2009,120:1426-35]. All of these studies look at fluids during VF arrest.

All papers are LOE 5 as they are either animal studies or they do not directly address the PICO as they do not have control groups with no fluids or standard care.

Recent studies have looked at giving cold fluids during CPR to induce therapeutic hypothermia. Most of these hypothermia studies do not have a control group with no fluids [Bruel, 2008, R31, Kamarainen, 2008, 360-3, Nordmark, 2005, 357-65, Nozari, 2006, 2690-6]. These therefore are LOE 5 as they do not directly address the PICO question.

We have considered the evidence in three groups:

1. Studies giving cold fluids during CPR to induce hypothermia
 2. Studies comparing different intravenous fluids given during CPR
 3. Studies looking at the haemodynamic effects of fluids during CPR
1. The evidence for intra-arrest (post-arrest fluids is the subject of worksheet ALS-D- 043) intravenous fluid use has increased with the use of cold fluids to induce hypothermia. Five studies are included in this WS that used fluids for induction of hypothermia. Two studies (LOE5) of cold IV fluids during CPR had a control group that did not receive fluids [Yannopoulos, 2009, 1426-35, Riter, 2009, 561]. One good quality animal study [Riter, 2009, 561] showed a decreased coronary perfusion pressure (CPP) within the first 3 minutes of CPR with cold normal saline compared to no fluids. A further good quality animal study had control groups with both normothermic fluid and no fluid [Yannopoulos, 2009, 1426-35], which found a statistically significant difference in ROSC between normothermic fluid and no fluid – ROSC was better without volume. It also found that LV function was better preserved without volume loading. Other animal studies of normothermic IV fluids also show this fall in CPP [Gentile, 1991, 55-63, Voorhees, 1987, 113-23, Ditchey, 1984, 181] Physiological studies show that there is a better outcome with improved CPP [Paradis, 1990, 1106-13]. One animal study [Nordmark, 2005, 357-65] found that there was no difference in haemodynamic variables or the cerebral cortical blood flow in a group receiving fluid at room temperature and another group receiving fluid at 4°C. [Kamarainen, 2008, 360-3] study only had 5 patients and no survivors. Further work by the same group [Kamarainen, 2008, 205-11] had 17 patients but only one survived to discharge and it is difficult to draw conclusions regarding the impact of fluid use.

Few adverse affects were reported with the use of cold fluids during CPR, with one case of pulmonary oedema in a study of 33 patients [Bruel, 2008, R31]. One study [Nozari, 2006, 2690] concluded that the incidence of adverse effects was related to the timing of the fluid infusion, with patients in the delayed infusion group experiencing higher rates of complications. These

studies fail to identify the true incidence of complications directly due to fluids during CPR as there is no control group receiving no fluids. They also only report complications in patients with ROSC.

2. Five papers using hypertonic solutions in cardiac arrest were reviewed [Bender, 2007, 74-81, Breil, 2003, 307-17, Fischer, 2002, 269-80, Krep, 2004, 73-83, Ujhelyi, 1996, 784-90], and a further study [Miclescu, 2006, 2806-13] with methylene blue added to the hypertonic infusion. Four of the five papers found a benefit of hypertonic saline over isotonic solutions with varying outcome measures. A RCT (LOE 5) of fair quality looked at fluid use in out of hospital arrests [Bender, 2007, 74-81] and found increased rates of ROSC and survival to hospital admission in the patient group that received hypertonic saline compared to hydroxyethyl starch, although this was not statistically significant (ROSC: HHS 66.7%, HES 51.5%, $p = 0.21$; admission: HHS 57.6%, HES 39.4%, $p = 0.14$). Animal studies also show a benefit of hypertonic fluids over isotonic fluids [Breil, 2003, 307-17, Fischer, 2002, 269-80, Krep, 2004, 73-83]. The use of methylene blue with hypertonic solution was found to improve ROSC and short-term survival compared to 0.9% saline [Miclescu, 2006, 2806-13]. Neither hypertonic saline nor 5% dextrose during CPR were found to lower the defibrillation threshold [Ujhelyi, 1996, 784-90]. Voorhees et al [Voorhees, 1987, 113-23] compared Ringer's lactate to whole blood, but ROSC and survival of event outcomes were not included and thus it is difficult to extrapolate data to draw useful, applicable conclusions from this paper. One human study [D'Alecy, 1986, 505-11] concluded that the use of dextrose-containing fluid is harmful in cardiac arrest compared to Ringer's lactate, with lower survival rates and increased neurological deficit.

[Longstreth, 1993, 2534] compared 5% dextrose in water with 0.45% NaCl. It found that type of fluid administered was not related to awakening (16.7% for D5W versus 14.6% for 0.45S), admission (38.0% for D5W versus 39.8% for 0.45S), or discharge (15.1% for D5W versus 13.3% for 0.45S).

Without definite proven benefit of intravenous fluid use, the value of knowing which fluid to give and whether it is beneficial is difficult to judge when there is no control group receiving no fluids.

3. Two animal studies examined the use of normothermic fluids with a no fluid group control [Gentile, 1991, 55-63, Jameson, 1993, 243-50]. Neither study found an improvement in coronary perfusion pressure during CPR with intravenous fluids. One animal study of good quality but small sample size [Jameson, 1993, 243-50] using hypertonic saline dextran found that the group receiving fluids had no benefit during CPR but superior haemodynamic parameters following ROSC than the group that did not (CPP, $P = <0.05$), although this did not equate to an improved rate of ROSC.

Gentile et al [Gentile, 1991, 55-63] concluded that volume expansion would lead to increased preload and afterload and thus may be detrimental during CPR. Interpretation of the Frank Starling law [Frenneaux, 2003, 259-65], suggests that normovolaemia is optimal, although this theory can only be applied with ROSC and thus a contracting heart. Paradis et al found that coronary perfusion pressure is associated with improved rates of ROSC. Two papers [Gentile, 1991, 55-63, Jameson, 1993, 243-50] did not find a difference in coronary perfusion pressure with the use of fluids in addition to epinephrine, while another [Ditchey, 1984, 181-9] found that volume expansion without epinephrine reduced coronary and cerebral perfusion pressures, thus making it detrimental. Voorhees et al [Voorhees, 1987, 113-23] describe an increase in cardiac output during CPR with the use of IV fluid, but also documents a fall in cerebral and coronary perfusion pressures.

One animal study (Yannopoulos, 2009) showed that volume loading during cardiac arrest whether normothermic or hypothermic, decreases CPP and ROSC when compared to no fluid or a cooling method not involving fluid loading. This study had relevant control groups – no fluids, room temperature fluids, cold fluid.

The animal studies suggest fluids during CPR cause a fall in CPP.

In summary, there is insufficient evidence to support routine use of fluids during CPR. The use of intravenous fluid for the inducing of therapeutic hypothermia during CPR does decrease patient temperature but it is not clear whether there is any benefit or harm in the rate of ROSC compared to the administration of no fluids.

Acknowledgements:

Raina Merchant and Terry Vanden Hoek contributed to the Guidelines 2005 worksheet on this topic

References

Bender, R., M. Breil, et al. (2007). "Hypertonic saline during CPR: Feasibility and safety of a new protocol of fluid management during resuscitation." Resuscitation 72(1): 74-81.

Level 5; RCT; Fair quality; Neutral.

No group that did not receive fluids. (if comparing with isotonic fluids would be Level 1)

Focus was to evaluate use of hypertonic saline.

Study supports safety of intra-CPR fluid use. It reports a high ROSC rate in both the hypertonic saline and the control group, although this cannot be attributed to the use of intravenous infusions as there was no control group receiving no fluid and it may be due to confounding factors. Better outcome was observed in the hypertonic saline patient group with both ROSC and survival to admission to hospital. This shows that different intravenous fluids are likely to have different outcomes and so should be considered separately in evaluation once further RCTs have been conducted.

Breil M, Krep H, Sinn D, Hagendorff A, Dahmen A, Eichelkraut W, et al. Hypertonic saline improves myocardial blood flow during CPR, but is not enhanced further by the addition of hydroxy ethyl starch. Resuscitation 2003;56(3):307-17.

Level 5; Animal study; RCT; Good quality;

No group that did not receive fluids.

Focus was to evaluate use of hypertonic saline.

CPR performed using open chest technique.

Improved short term survival with hypertonic fluids.

Bruel, C., J. J. Parienti, et al. (2008). "Mild hypothermia during advanced life support: a preliminary study in out-of-hospital cardiac arrest." Crit Care 12(1): R31.

Level 5; Case series – prospective, multi-centre, observational trial; Good quality; Neutral.

No group that did not receive fluids. Therefore Level 5 (if did answer question Level 4)

Use of fluids was for induction of therapeutic hypothermia.

One patient developed pulmonary oedema, otherwise no adverse effects of infusion of 2L of normal saline. Thus supports the safety of intravenous fluid use during CPR, but does not confer a benefit as this is outside the scope of the study.

D'Alecy, L. G., E. F. Lundy, et al. (1986). "Dextrose containing intravenous fluid impairs outcome and increases death after eight minutes of cardiac arrest and resuscitation in dogs." Surgery 100(3): 505-511.

Level 5; Animal study; ?RCT ?Quality

No group that did not receive fluid.

Comparison of Ringer's lactate or 5% dextrose in Ringer's lactate. Suggests that the use of dextrose-containing fluids is harmful in the peri-arrest period compared to Ringer's lactate. As no control without fluids has been included, we cannot conclude benefit of intravenous fluid from this study.

Ditchey, R. V. and J. Lindenfeld (1984). "Potential adverse effects of volume loading on perfusion of vital organs during closed-chest resuscitation." Circulation 69(1): 181-189.

Level 5; Animal study; Fair - case-control study (randomization not made clear in method); Opposing.

No group that did not receive fluid.

Results suggest that expansion of blood volume with intravenous fluids during CPR decrease both coronary and cerebral perfusion.

Fischer, M., A. Dahmen, et al. (2002). "Effects of hypertonic saline on myocardial blood flow in a porcine model of prolonged cardiac arrest." Resuscitation 54(3): 269-80.

Level 5; Animal study; RCT; Good quality; Neutral.

No group that did not receive fluid.

Evaluates use of hypertonic saline.

CPR performed using open chest technique.

Improved short term survival and haemodynamic variables during CPR with hypertonic fluids. No improvement in haemodynamic variables with increased volume of normal saline. Small sample size, therefore difficult to draw conclusions on survival, and no comparison without fluids to directly address PICO question.

Frenneaux, M. (2003). "Cardiopulmonary resuscitation; some physiological considerations." Resuscitation 58: 259-65.

Level 5, Good, Neutral [?relevance]. Review of physiology of LV function and Frank Starling Law. Suggests that with a normal circulating volume addition of fluids unlikely to add benefit and may be detrimental. Suggests with decreased circulating volume, fluids may be necessary to correct circulating volume.

Gentile, N. T., G. B. Martin, et al. (1991). "Effects of arterial and venous volume infusion on coronary perfusion pressures during canine CPR." Resuscitation 22(1): 55-63

Level 5; Animal study; Fair – case-control study, no evidence of randomization; Opposing

Epinephrine alone compared to epinephrine with a bolus of normal saline intravenously with a third group given normal saline via an aortic catheter. Suggests that volume loading does not add any benefit during experimental CPR during VF when vasopressors have been used. Fluids did not increase the coronary perfusion pressure. Discussion suggests volume loading may be harmful during CPR.

Jameson, S. J., J. R. Mateer, et al. (1993). "Early volume expansion during cardiopulmonary resuscitation." Resuscitation 26(3): 243-50.

Level 5; Animal study; RCT; Good quality; Neutral.

Intra-arterial infusion compared with intravenous hypertonic fluid, both with epinephrine, or epinephrine alone.

No improvement in CPP found with use of fluid with epinephrine in ROSC or survival of event, but improved haemodynamic variables were demonstrated, as well as improved tissue perfusion post-ROSC. Difficult to draw conclusions as no survival benefit demonstrated and small sample size.

Kamarainen, A., I. Virkkunen, et al. (2008). "Prehospital induction of therapeutic hypothermia during CPR: a pilot study." Resuscitation 76(3): 360-3.

Level 5; Case series; Poor quality; Neutral.

No group that did not receive fluids. Therefore Level 5 study

Use of fluids for induction of therapeutic hypothermia.

Small study size (N=5) with poor outcomes (ROSC in only 2/5, only 1 survived to hospital admission and then died within 24 hours), therefore difficult to draw conclusions aside from feasibility of initiation in a pre-hospital environment.

Kamarainen A, Virkkunen I, Tenhunen J, Yli-Hankala A, Silfvast T. Induction of therapeutic hypothermia during prehospital CPR using ice-cold intravenous fluid. Resuscitation. 2008;79(2):205-11.

Level 5; Case series; poor quality; neutral.

No group that did not have fluid.

Use of fluid for induction of therapeutic hypothermia.

N=17. Only 1 survived to hospital discharge.

Unable to draw conclusions of effects of fluid use.

Krep, H., M. Breil, et al. (2004). "Effects of hypertonic versus isotonic infusion therapy on regional cerebral blood flow after experimental cardiac arrest cardiopulmonary resuscitation in pigs." Resuscitation 63(1): 73-83.

Level 5; Animal study; RCT; Good quality.

No group that did not receive fluids.

Focus was to evaluate use of hypertonic saline.

CPR performed using open chest technique.

Higher proportions of ROSC in hypertonic groups, although small sample size therefore of questionable significance. Hypertonic saline and hypertonic/isotonic saline groups showed improved cerebral blood flow during and after CPR in comparison to normal saline and iso-oncotic saline, hypoperfusion was sustained in the isotonic/isooncotic groups but returned to baseline in the hypertonic groups. This shows that different intravenous fluids are likely to have different outcomes and so should be considered separately in evaluation once further RCTs have been conducted. However, as no control without fluids has been included, we cannot conclude benefit of intravenous fluid from this study.

Longstreth, W. T., Jr., M. K. Copass, et al. (1993). "Intravenous glucose after out-of-hospital cardiopulmonary arrest: a community-based randomized trial." Neurology 43(12): 2534-41

Level 5; RCT; Fair quality; Neutral.

No group that did not receive fluids.

5% dextrose in water compared to half normal saline. No benefit found in ROSC, survival of event or survival to discharge from hospital. Difficult to draw conclusions as no group receiving no fluids. Cannot say if any fluid had an adverse effect.

Miclescu, A., S. Basu, et al. (2006). "Methylene blue added to a hypertonic-hyperoncotic solution increases short-term survival in experimental cardiac arrest." Crit Care Med 34(11): 2806-13.

Level 5; Animal study; RCT; Good quality.

No group received no fluids.

Focus was to evaluate use of hypertonic-hyperoncotic solution with methylene blue added.

Pigs were randomised to receive saline(SAL), hypertonic saline with dextrose(HSD) or hypertonic saline with dextrose and methylene blue(MB). The MB was demonstrated to have a statistically significant benefit over SAL in terms of short-term survival. The MB group also showed more sustained improvements in haemodynamic variables that were measured than the other two groups, and a higher cerebral cortical blood flow. As there was no group receiving no fluids no firm conclusions can be drawn in terms of the PICO question of the worksheet.

This shows that different intravenous fluids are likely to have different outcomes and so should be considered separately in evaluation once further RCTs have been conducted.

Nordmark, J. and S. Rubertsson (2005). "Induction of mild hypothermia with infusion of cold (4 degrees C) fluid during ongoing experimental CPR." Resuscitation 66(3): 357-65.

Level 5; Animal study; RCT; Good quality.

No group that did not receive fluids.

Use of fluids was for induction of therapeutic hypothermia.

There was no significant difference in the haemodynamic variables or the cerebral cortical blood flow in the two groups, one of which received Ringer's lactate at room temperature and one at 4°C. As there is no group that did not receive fluids, the benefit of fluid administration is not demonstrated, but there were no adverse effects and further studies are required with a control group receiving no fluids to evaluate benefit/harm of fluids.

Nozari, A., P. Safar, et al. (2006). "Critical time window for intra-arrest cooling with cold saline flush in a dog model of cardiopulmonary resuscitation." Circulation 113(23): 2690-6.

Level 5; Animal study; RCT; Good quality; Neutral.

No group that did not receive fluids.

Use of fluids for induction of therapeutic hypothermia.

This study found more adverse effects secondary to fluid infusion when initiated 20 minutes into cardiac arrest as opposed to 10 minutes, including oedema, ascites, pleural effusion and vasopressor-resistant shock. While this study does not compare benefits of fluid use with no fluid use, it raises the question of timing of intravenous fluids within CPR related to benefit/risk of use – further studies would be required to draw conclusions.

Paradis, N. A., G. B. Martin, et al. (1990). "Coronary perfusion pressure and the return of spontaneous circulation in human cardiopulmonary resuscitation." JAMA 263(8): 1106-1113.

Level 5; Case-control not specific to patient group; Fair; Neutral.

Focus on coronary perfusion pressure, no fluids given therefore not directly applicable to PICO question.

This human study of all cardiac arrest rhythms demonstrates the importance of CPP for ROSC. Any intervention that decreases CPP is likely to be harmful. Intravascular volume expansion may lower CPP by increasing right atrial pressure.

Riter HG, Brooks LA, Pretorius AM, Ackermann LW, Kerber RE.

Intra-arrest hypothermia: Both cold liquid ventilation with perfluorocarbons and cold intravenous saline rapidly achieve hypothermia, but only cold liquid ventilation improves resumption of spontaneous circulation. Resuscitation. 2009 May;80(5):561-6. Epub 2009 Feb 2

Level 5; Animal study; RCT; Good quality; Opposing.

Control group that did not receive fluid.

No group that received fluid that was not cooled.

Use of fluids was for induction of therapeutic hypothermia.

CPP in the control group was not statistically significantly different from either of the two trial groups (TLV $p = 0.13$, Sp = 0.88) over the full experiment time. Graphical data shows CPP and right atrial pressure were higher in the control group than for the group that received cold fluid in the first 3 minutes.

Small study size. Useful to have control receiving no fluid, and it could be concluded that no fluid is better than fluid, however it is not possible to tell whether administering fluid that is not cooled would have different results.

Steen, S., Q Liao, L Pierre, A Paskevicius, T Sjoberg. (2003). " The critical importance of minimal delay between chest compressions and subsequent defibrillation: a haemodynamic explanation." Resuscitation 58: 249-58.

Level 5; Animal study; RCT; Good quality; Opposing.

Does not examine the use of fluids, but useful regarding physiology of volume during CPR.

Suggests that venous pooling occurs with emptying of the left ventricle after onset of VF, causing coronary perfusion pressure (CPP) to fall to zero over about 4 mins. Defibrillation is unlikely to be successful under these conditions unless the right/left ventricle volumes and CPP have been restored by chest compressions. The addition of an intravenous fluid bolus could worsen this right ventricular distension. Other studies show that fluids decrease CPP during CPR.

Ujhelyi, M. R., A. P. Winecoff, et al. (1996). "Influence of hypertonic saline solution infusion on defibrillation efficacy." Chest 110(3): 784-90.

Level 5; Animal study; RCT; Good quality; Neutral.

No group that did not receive fluid.

Focus was to evaluate use of hypertonic saline.

The study found that defibrillation threshold is not effected by 5% dextrose infusion or hypertonic saline infusion.

Voorhees, W. D., 3rd, S. H. Ralston, et al. (1987). "Fluid loading with whole blood or Ringer's lactate solution during CPR in dogs." Resuscitation 15(2): 113-23.

Level 5; Animal study; Fair – no evidence of randomization; Opposes.

No group that did not receive fluid.

Intravenous blood compared to Ringer's lactate. Fluid loading with blood or Ringers transiently improved cardiac output during CPR but coronary and cerebral blood flow fell. Survival and ROSC

not included and no comparison without fluid to address PICO, therefore difficult to draw firm conclusions.

Yannopoulos. Loading in an Ischemic Model of Cardiac Arrest IntraCardiopulmonary Resuscitation Hypothermia With and Without Volume Resuscitation. 2009;120:1426-35.

Level 5; Animal study;

Included a control group that did not receive fluids and a control group that received normothermic fluid.

ROSC rates were significantly lower in normothermic fluid group than in control groups that did not receive fluid ($p < 0.05$), and best in the group that was cooled externally but did not receive volume. LV function was better in the groups that did not receive volume. This study shows that fluid infusion in pigs with normal hearts during CPR can be harmful.