



TITLE: Normothermia versus Therapeutic Hypothermia for Adult Patients after Cardiac Arrest: Clinical Evidence

DATE: 26 August 2014

RESEARCH QUESTION

What is the clinical evidence for neurological benefits or harms of maintaining normothermia versus induction of therapeutic hypothermia in adult patients following cardiac arrest?

KEY FINDINGS

Six systematic reviews and one randomized controlled trial were identified regarding the comparative neurological benefits and harms of maintaining normothermia versus induction of therapeutic hypothermia in adult patients following cardiac arrest.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 8), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and August 14, 2014. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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SELECTION CRITERIA

Table 1: Selection Criteria	
Population	Adult patients, following cardiac arrest. Pre- or in-hospital setting
Intervention	Maintaining normothermia (36°C)
Comparator	Therapeutic hypothermia (33°C)
Outcomes	Neurological recovery
Study Designs	Health technology assessments, systematic reviews/meta-analyses, and randomized controlled trials

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials (RCTs). Six systematic reviews and one RCT were identified regarding the comparative neurological benefits and harms of maintaining normothermia versus induction of therapeutic hypothermia in adult patients following cardiac arrest. No health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

The summary of study findings is presented in Table 2. Results from the systematic reviews were mixed and some indicated that the quality of evidence was low. The randomized controlled trial, which had a follow-up of 180 days, found that therapeutic hypothermia did not confer a benefit for neurological function compared with maintaining normothermia, in adults with out-of-hospital cardiac arrest.

Table 2: Summary of Findings			
Authors, publication date	Comparators	Study Sizes	Authors' Conclusions
<i>Systematic Reviews/Meta-analyses</i>			
Hunter et al., 2014 ¹	Pre-hospital initiation of TH versus No TH	Six RCTs included; N = 715	<ul style="list-style-type: none"> No difference in good neurologic outcomes between the 2 groups No important benefit to pre-hospital initiation of hypothermia
Diao et al., 2013 ²	Pre-hospital initiation of TH versus In-hospital initiation of TH or no initiation of TH	Five RCTs included; N = 633	<ul style="list-style-type: none"> No significant differences in neurological outcomes at hospital discharge between any of the interventions Quality of evidence was very low
Wang et al., 2013 ³	Standard care with normothermia versus Induction of TH	Four RCTs included; N = 417	<ul style="list-style-type: none"> Statistically significant improved neurological outcomes for patients receiving TH No significant difference in adverse events between the two groups

Table 2: Summary of Findings

Authors, publication date	Comparators	Study Sizes	Authors' Conclusions
Arrich et al., 2012 ⁴	Induction of TH versus No induction of TH	Four RCTs included; N = 481	<ul style="list-style-type: none"> • TH seemed to improve neurological outcome, but statistical significance was not indicated in the abstract
Kim et al., 2012 ⁵	Induction of TH versus Normothermia	Two RCTs and 12 non-randomized studies included; N not reported	<ul style="list-style-type: none"> • TH was associated with reduced risk for poor neurological outcome; • Most studies had substantial risks of bias and quality of evidence was very low
Nielsen et al., 2011 ⁶	Induction of TH versus Comparator not specified, but abstract seems to indicate that it is no induction of TH	Five RCTs; N = 478	<ul style="list-style-type: none"> • Evidence was inconclusive • Quality of evidence was low
<i>Randomized Controlled Trial</i>			
Nielsen et al., 2013 ⁷	Induction of TH versus Normothermia	N = 950	TH did not confer a benefit for neurological function compared with normothermia, after 180 days follow-up

REFERENCES SUMMARIZED

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Hunter BR, O'Donnell DP, Allgood KL, Seupaul RA. No benefit to prehospital initiation of therapeutic hypothermia in out-of-hospital cardiac arrest: a systematic review and meta-analysis. *Acad Emerg Med*. 2014 Apr;21(4):355-64.
[PubMed: PM24730397](#)
2. Diao M, Huang F, Guan J, Zhang Z, Xiao Y, Shan Y, et al. Prehospital therapeutic hypothermia after cardiac arrest: a systematic review and meta-analysis of randomized controlled trials. *Resuscitation*. 2013 Aug;84(8):1021-8.
[PubMed: PM23454259](#)
3. Wang XP, Lin QM, Zhao S, Lin SR, Chen F. Therapeutic benefits of mild hypothermia in patients successfully resuscitated from cardiac arrest: a meta-analysis. *World J Emerg Med [Internet]*. 2013 [cited 2014 Aug 22];4(4):260-65. Available from:
<http://www.wjem.org/upload/admin/201311/1eca1643541e536d96aa292530a16ea1.pdf>
4. Arrich J, Holzer M, Havel C, Mullner M, Herkner H. Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation. *Cochrane Database Syst Rev*. 2012;9:CD004128.
[PubMed: PM22972067](#)
5. Kim YM, Yim HW, Jeong SH, Klem ML, Callaway CW. Does therapeutic hypothermia benefit adult cardiac arrest patients presenting with non-shockable initial rhythms?: A systematic review and meta-analysis of randomized and non-randomized studies. *Resuscitation*. 2012 Feb;83(2):188-96.
[PubMed: PM21835145](#)
6. Nielsen N, Friberg H, Gluud C, Herlitz J, Wetterslev J. Hypothermia after cardiac arrest should be further evaluated--a systematic review of randomised trials with meta-analysis and trial sequential analysis. *Int J Cardiol*. 2011 Sep 15;151(3):333-41.
[PubMed: PM20591514](#)

Randomized Controlled Trials

7. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, et al. Targeted temperature management at 33 degrees C versus 36 degrees C after cardiac arrest. *N Engl J Med*. 2013 Dec 5;369(23):2197-206.
[PubMed: PM24237006](#)

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APPENDIX – FURTHER INFORMATION:

Systematic Reviews – Predictive value of tests for neurological outcomes

8. Golan E, Barrett K, Alali AS, Duggal A, Jichici D, Pinto R, et al. Predicting neurologic outcome after targeted temperature management for cardiac arrest: systematic review and meta-analysis*. Crit Care Med. 2014 Aug;42(8):1919-30.
[PubMed: PM24717465](#)

Non-Randomized Studies

9. Vaahersalo J, Hiltunen P, Tiainen M, Oksanen T, Kaukonen KM, Kurola J, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest in Finnish intensive care units: the FINNRESUSCI study. Intensive Care Med. 2013 May;39(5):826-37.
[PubMed: PM23417209](#)

Review Articles

10. Friberg H, Rundgren M, Westhall E, Nielsen N, Cronberg T. Continuous evaluation of neurological prognosis after cardiac arrest. Acta Anaesthesiol Scand. 2013 Jan;57(1):6-15.
[PubMed: PM22834632](#)
11. Tice JA. Therapeutic hypothermia following cardiac arrest [Internet]. San Francisco (CA): California Technology Assessment Forum; 2011 Feb 16. [cited 2014 Aug 22]. Available from:
http://www.ctaf.org/sites/default/files/assessments/1249_file_Hypothermia_final_W.pdf