Clinical question.
"In adult patients who are comatose after cardiac arrest (prehospital or in-hospital) (P), does the use of imaging studies (I) as opposed to standard care (C), allow accurate prediction of outcome (O) (eg. survival)?"

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

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

Search strategy (including electronic databases searched).
Database: Ovid MEDLINE(R) 1950 to January 2009
Search Strategy:
1 Heart Arrest/ (17456)
2 cardiac arrest.ti. (5245)
3 Cardiopulmonary Resuscitation/ (6869)
4 cpr.ti. (1331)
5 resuscitation/ or advanced cardiac life support/ (19052)
6 exp Brain/ (778276)
7 exp Anoxia/ (45351)
8 hypoxia, brain/ or hypoxia-ischemia, brain/ (7649)
9 Hypoxia-Ischemia, Brain/ (1943)
10 Brain Injuries/ or Nervous System Diseases/et [Etiology] (38474)
11 or/1-10 (887611)
12 diagnostic imaging/ or tomography, emission-computed/ or positron-emission tomography/ or tomography, emission-computed, single-photon/ or tomography, x-ray computed/ or tomography, spiral computed/ or magnetic resonance imaging/ or diffusion magnetic resonance imaging/ or echo-planar imaging/ or magnetic resonance angiography/ or ultrasonography, doppler/ or ultrasonography, doppler, duplex/ or ultrasonography, doppler, color/ or ultrasonography, doppler, pulsed/ or ultrasonography, doppler, transcranial/ or neuroimag$3.ti,ab. (438289)
13 11 and 12 (94922)
14 or/1-5 (37475)
15 or/6-10 (853052)
16 14 and 15 (2791)
17 12 and 16 (159)

Database: EBM Reviews - Cochrane Database of Systematic Reviews <1st Quarter 2009>
Search Strategy:
1 ((cardiac or heart) adj1 arrest).ti,ab. (9)
2 ((cardiac or cardiopulmonary) adj1 resuscitation$).ti,ab. (3)
3 (brain adj1 (anoxia or anoxic or hypoxia or hypoxic or ischemic or ischemic)).ti,ab. (0)
4 or/1-3 (9)
5 neuroimag$3.ti,ab. (1)
6 imag$3.ti,ab. (36)
7 5 or 6 (37)
8 4 and 7 (0)

EMBASE.com Search Queries
1974 - April 2009

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#1. brain/exp 748,609
#2. brain ischemia/exp 58,545
#3. brain hypoxia/exp 7,970
#4. #1 OR #2 OR #3 790,890
#5. heart arrest/exp 25,727
#6. resuscitation/exp 40,338
#7. #5 OR #6 57,558
#8. nuclear magnetic resonance imaging/exp 279,480
#9. tomography/exp 419,130
#10. doppler flowmetry/exp 18,755
#11. #8 OR #9 OR #10 625,447
#12. #4 AND #7 2,917
#13 #11 and #12 277 27 Apr 2009

**State inclusion and exclusion criteria**

The following studies were excluded: Non-cardiac arrest models (22); studies not including neuroimaging (6); trials involving monitoring but not neuroimaging (2); trials involving therapeutics but not neuroimaging (2); trials involving cardiac imaging, not neuroimaging (1). Pediatric and animal studies were excluded, and trials not addressing prognosis were excluded. Non-English language studies were NOT excluded.

**Number of articles/sources meeting criteria for further review:**

60
## Summary of evidence

### Evidence Supporting Clinical Question

<table>
<thead>
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### Level of evidence

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- A = Return of spontaneous circulation
- B = Survival of event
- * = MRI study
- ** = CT study
- x = PET study
- Italic = Animal study
- y = SPECT study
- z = other study
### Evidence Neutral to Clinical question

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**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
* = MRI study  
** = CT study  
\( y \) = SPECT study  
* = Animal studies  
\( \times \) = PET study  
\( z \) = Other study

### Evidence Opposing Clinical Question

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**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
* = MRI study  
** = CT study  
\( y \) = SPECT study  
* = Animal studies  
\( \times \) = PET study  
\( z \) = Other study
Human studies regarding the use of neuroimaging to predict outcome in comatose cardiac arrest patients are quite limited. The most rigorous and well-structured studies have been performed outside of the acute setting, which is not the most important to clinicians and families interested in prognosis. Studies that have taken place in the acute setting are all relatively small and underpowered to show a significant result. Furthermore, they are most commonly retrospective studies, not prospectively testing a hypothesis. Many are single case reports or small case series, which add very little to our scientific knowledge of this disease. Perhaps most importantly, very few have compared neuroimaging with another modality, such as the clinical exam or electrophysiology, which are the current standards of care for prediction of outcome following cardiac arrest (although these are also flawed). Finally, nearly all of the studies are biased by a likely self-fulfilling prophesy – withdrawal of care in this population may lead to a poor outcome, and if done early in the clinical course, the true ultimate outcome can never be known.

No LOE P1 trials exist. Two LOE P2 trials were evaluated. The first (Roine 1991, 625) used Positron Emission Tomography (PET) as the modality to evaluate association with outcome, and has the benefit of a control group of healthy age-matched controls, but is limited by the fact that patients were evaluated in the chronic setting, and PET itself is not widely available as a diagnostic tool, thus limiting the study’s generalizability. The second LOE P2 trial (Roine 1993, 1005) used magnetic resonance imaging (MRI), and benefited from using a control group of community volunteers. However, the patients in this study were also studied in the chronic setting, and did not use more modern and sensitive MRI techniques, such as diffusion-weighted imaging (DWI) or fluid-attenuated inversion-recovery (FLAIR).

The types of studies are best separated by modality: PET, computed tomography (CT) and MRI, in order of increasing usefulness.

PET: The LOE P4 study by Edgren et al (Edgren 2003, 161) evaluated PET in 7 comatose cardiac arrest patients, comparing this with the clinical examination on days 1, 3 and 7 post-arrest. Patients with a progressive depression in the cerebral metabolic rate (3 of 7 patients) appeared to have a worse outcome compared with those who did not, and this appeared to be more informative than the clinical exam. However, this study is limited by the small number of patients, and PET is expensive and not uniformly available, limiting its usefulness in the general population. Rudolf et al (Rudolf 1999, 81) performed a similar LOE P4 study in 28 patients, evaluating PET 3-5 weeks after the cardiac arrest in comparison to electroencephalography (EEG), and suggested the superiority of PET in comparison for prediction. However, the usefulness of prediction at this later phase in the illness is of questionable value.

CT: The LOE P4 study by Hollerbach et al (Hollerbach 1995, 215) evaluated 20 comatose cardiac arrest patients with the Glasgow Coma Scale (GCS), evoked potentials (EP) and computed tomography (CT). They suggested that CT was inferior at predicting outcome, but only 12 of the 20 patients underwent CT imaging, and the size of this study makes it of quite limited significance. Furthermore, there was no control group. The LOE P4 study by Torbey et al (Torbey 2004, 55) investigated the combined approach of using the information from CT, the duration of cardiac arrest, and the clinical examination (GCS) to suggest the superiority of PET in comparison for prediction. However, the usefulness of prediction at this later phase in the illness is of questionable value.

MRI: More recent studies have focused on the use of MRI, but are limited by: 1) small numbers; 2) the self-fulfilling prophesy of early withdrawal of care; 3) frequent lack of control for confounders; and most importantly, 4) a lack of comparison to a more standard method of predicting outcome. Currently, the most standard methods of predicting outcome in clinical practice include the clinical examination and electrophysiology (EEG and EP).

Two important relatively larger MRI series were published this year (2009), which add greatly to literature. However, both are LOE P4 studies (Wijman 2009, 394; Wu 2009, page number not available at present). Wijman et al evaluated at total of 51 patients with diffusion-weighted MRI, and the study had the added benefit of at least attempting to avoid a self-fulfilling prophesy by encouraging the treating physicians to not withdraw care by using the 2006 AAN guidelines as a guide. The authors propose that using diffusion-weighted imaging improved the sensitivity for predicting poor outcome by 38%, while maintaining 100% specificity. The study is limited however, but a lack of control for confounders, a lack of a comparison group, and its retrospective design. Wu et al evaluated 80 comatose cardiac arrest patients with diffusion-weighted imaging in the acute setting, and found a strong correlation between the amount of apparent diffusion coefficient depression and outcome, as measured by the 6-month modified Rankin Scale score and early eye opening. This study, however, is also limited by a lack of a control group, the bias introduced by early withdrawal of care, and a lack of comparison with another method of predicting outcome.

Although neuroimaging has not been validated for use in prediction of outcome after cardiac arrest, in actuality, clinicians frequent use the results of neuroimaging (typically CT and MRI) to help in prognostication. But the use of neuroimaging cannot be said to be valid at this time. Further studies are essential, and should include comparison groups, and more importantly, a comparison with a validated method of prognostication.
David Greer – Neurologist, specialist in neurocritical care and stroke. No intellectual or commercial conflicts as pertain to this project.

Acknowledgements:
None

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Citation List


Level 3 (compared EEG with CT in same patients, retrospective), opposing. Poor (outcomes measured objectively (GOS), but unclear if confounders identified and controlled for, and unclear follow up period)


Level 5 (single case report), opposing. Poor quality.


Level 3 (case-control), supportive. Good (Comparison group clearly defined, outcomes measured objectively, confounders identified and controlled for, sufficient follow up time allowed).


Level 4 (retrospective case series), supportive. Poor (outcomes not reported, confounders not identified or controlled, and follow up period not clear)


Level 5, supportive. Fair (outcome assessed (PVS), and adequate follow up time, but unclear if confounders controlled) Have not been able to retrieve this article, but have entered into worksheet above based on abstract.


Level 4 (retrospective case series), supportive. Poor (outcome well defined by CPC, confounders not well controlled (included isolated respiratory arrest patients), and unclear length of time before w/d of care for dead patients).


Level 4 (retrospective case series), supportive. Poor (outcomes measured by CPC, but confounders not identified or appropriately controlled for, and unclear follow up time for those who died).


Level 3 (case series, but measured two modalities), opposing. Poor (outcome measured only in comparison to another modality, confounders not well controlled, follow up period not applicable, only an acute period study)


Level 3 (case vs. normal controls), supportive. Fair (comparison groups clearly defined, outcome measured by GOS), confounders identified and controlled, but unclear follow up time, many patients who died may have done so due to w/d of care)


Level 4 (retrospective case series), supportive. Good (outcomes measured in an objective way, confounders identified and controlled for, follow up time sufficiently long).


Level 4 (12 chronic cases, compared with normal values), supportive. Good (outcome appears objectively measured (functional status in 4, others PVS), no possible confounders at the time point, and sufficient survival time). Have not been able to retrieve this article, but have entered into worksheet above based on abstract.


11 patients comatose following cardiac arrest. All studied with xenon CT. Level 4 (retrospective case series), supportive. Poor (outcome measured by GOS, but confounders not controlled (barbiturates given), and unclear duration of survival)


Level 4 (Case series, but comparison of clinical exam on days 1,3 and 7 with PET imaging), supportive. Good (outcomes measured objectively (recovery at 1 week), confounders controlled for, postulated adequate follow up time (7 days at minimum?)).


Level 5 (single case of CA of 6 reported), supportive. Fair (unclear how outcomes measured, but confounders not possible, and follow up period sufficient) Have not been able to retrieve this article, has not been entered into worksheet above.

Level 4, supportive. Fair (outcomes measured on an objective 5-point scale of independence, follow up excellent (6 months, including PVS pts – no w/d), but confounders not clearly controlled).


Level 5, supportive. Good (outcome measured objectively, no possible confounders at 3 months, and adequate time).


Level 5 (single case report), supportive. Poor


Level 4 (retrospective case series), supportive. Poor (outcomes measured as mortality, but confounders not identified or appropriately controlled for, and follow up time not sufficient).


Level 3 (retrospective cohort study), supportive. Good (comparison groups clearly defined, confounders controlled, follow up time sufficient, outcomes all PVS or death)


Level 4 (case series), supportive. Poor (unclear how outcomes measured, confounders identified or follow up period) Have not been able to retrieve this article, has not been entered into worksheet above.


Level 5 (single case report), supportive. Good (outcome measured objectively, confounders appropriately controlled for, follow up time sufficient).


Level 4 (retrospective case series), supportive. Good (outcomes measured by neuropsych testing, confounders identified and controlled for, and follow up period sufficient).


Level 4 (case series, but comparing 2 modalities – neuropsych testing or MRI), supportive), supportive. Good (outcomes assessed with neuropsych testing, confounders not possible, late subacute or chronic patients) Have not been able to retrieve this article, but have entered into worksheet above based on abstract.


Level 5 (single case report), supportive. Good (outcomes measured objectively, confounders controlled, sufficient follow up time).

Level 4 (case series, compared multiple modalities. Only 12 of 20 patients received CT), neutral. Fair (Outcomes measured by GOS, confounders unlikely, follow up period likely adequate, but modality not sufficiently compared to clinical exam or SSEPs).


Level 5, supportive. Poor (unclear outcome, confounders, follow up period)


Level 4 (case series), supportive. Poor (outcome assessed by level of recovery (functional status), confounders not controlled several patients received barbiturates), follow up period unclear)


Level 5 (case report), supportive. Fair (outcome measured objectively, sufficient follow up time, but unclear if confounders controlled) Have not been able to retrieve this article, but entered information into worksheet based on the abstract.


Level 4 (case series), supportive. Fair (outcomes measured objectively (GOS), adequate follow up time (6 months), but unclear if confounders controlled).


Level 5 (single case report), supportive. Poor


Level 4 (retrospective case series), supportive. Fair (outcomes measured objectively (survival, functional recovery), follow up sufficiently long (the patient who died on day 3 was from herniation, the other 2 survived to PVS or functional recovery), but confounders not identified or appropriately controlled for).


Level 5 (single case report), supportive. Poor (outcome assessed objectively, but confounders not controlled, and insufficient follow up time).


Level 4 (retrospective case series, only 4/10 were CA patients), supportive. Poor (outcomes measured as survival, but confounders not sufficiently identified or controlled for, and follow up time not sufficient (all died within 5 days)


Level 5 (single case report), supportive. Fair (unclear how outcomes measured, but confounders not possible, and long enough time to assess outcome). Have not been able to retrieve this article, has not been entered into worksheet above.

Level 5 (single case report), supportive. Poor


Level 5 (2 case reports), supportive. Good (outcomes measured objectively, confounders controlled, follow up sufficient).


Level 3 (case series, many of whom may have had circulatory arrest, compared with normal controls), supportive. Fair (outcomes all good, confounder of possible alternative reason for cerebellar atrophy in one patient, good long-term f/u)


Level 4 (prospective case series, in which 5 were CA patients), supportive. Poor (unclear outcome measured, confounders controlled, or follow up period) Have not been able to retrieve this article, has not been entered into worksheet above.


Have not been able to retrieve this article, has not been entered into worksheet above.


Level 4 (retrospective case series), supportive. Poor (outcome assessed as wakefulness and survival, but confounders not identified or appropriately controlled for, and follow up time only 1 week).


Level 4 (retrospective case series), supportive. Fair (outcomes appear to have been measured objectively (GOS), unclear if confounders controlled or length of follow up)


Level 4 (retrospective case series), supportive. Fair (outcome measured by CPC as well as detailed cognitive testing, and follow up time excellent (6 months), but confounders not identified or appropriately controlled for).


Level 3 (case vs. age-matched controls), supportive. Poor (outcomes measured objectively (survival), but confounders not clearly identified and controlled for, and unclear follow up period for those who died).

Level 2 (cases from randomized nimodipine trial) vs. age-matched controls), opposing. Fair (outcomes measured objectively (recovery of consciousness and GOS), confounders adequately controlled, but follow up time insufficient (many only survived 2-4 days in the poor recovery group).


Level 2 (cases from a RCT, compared with age-matched community controls), opposing. Good (comparison groups clearly defined, outcomes measured the same objective way in both groups, known confounders identified and appropriately controlled for, follow-up sufficiently long and complete).


Level 3 (case vs. age-matched controls, CA part of the group of cases), opposing. Poor (comparison groups clearly defined, but outcomes were not assessed, confounders were not controlled for, and not mention of follow up)


Level 4 (case series), supportive. Good (outcomes measured objectively, confounders identified and controlled for, follow up sufficiently long)


Level 4 (case series, but comparing SSEP, EEG and PET), opposing. Good (appears to have stratified into recovery of function vs. PVS or death, confounders not possible 3-5 weeks post arrest, and adequate time)


Level 4, opposing. Fair (outcomes measured by GOS (but all had poor outcome), confounders adequately controlled for, but survival only 1-9 days in 7/10 patients)


Level 5 (single case report), supportive. Poor (patient died, but unclear if confounders or survival time)


Level 5 (single case of CA among 3 different cases), supportive. Poor (Outcomes measured in an objective way, but confounders not appropriately identified or controlled for, and follow up time not sufficient).


Level 4 (retrospective case series, but compared electrophysiology and TCD), unclear if supportive or not. Poor (outcomes measured by GOS, but unclear if confounders identified and controlled for, and unclear follow up time) Have not been able to retrieve this article, has not been entered into worksheet above.

Level 5 (case report), supportive. Poor (patient died after 25 days, confounders not clearly controlled, but had long enough survival)


Level 3 (case vs. age-matched controls), supportive. Good (outcomes measured objectively, confounders unlikely at this later time point, and length of follow up period adequate, even for coma cases)


Level 4 (retrospective case series), supportive. Poor (outcome measured by alive or dead or GOS, but confounders not identified or appropriately controlled for, and follow up of only 5 +/- 1 day in the dead group, vs. 20 +/- day in the survival group).


Level 4 (retrospective case series), supportive. Poor (outcomes measured by survival, GOS and Rankin, but confounders not identified or appropriately controlled for, and unclear how long patients survived for – only 24% survived to discharge, unclear how many of the dead had early w/d of care).


Level 5 (single case report), supportive. Fair (outcome was good, sufficient follow up time, but possible confounders given it was in the setting of drug abuse)


Level 5 (single case report), supportive. Poor


Level 4 (retrospective case series), supportive. Fair (outcomes measured in an objective way (survival or PVS vs normal), confounders identified and controlled for, but follow up period potentially not long enough (“six patients died within several weeks from withdrawal of support or systemic complications.”)).


Level 4 (retrospective case series), supportive. Fair (outcomes measured in an objective way (GOS), but confounders not clearly identified or controlled for, and follow up period potentially not long enough, although treating physicians were encouraged not to withdraw care early unless the patients fit into the poor outcome categories from the AAN guidelines in 2006).


Level 4 (retrospective case series), supportive. Fair (outcomes measured in an objective way (mRS and eye opening), but confounders not controlled for, and follow up period potentially not long enough).


Level 5 (single case report), supportive. Good (outcome measured objectively, no confounders, sufficient follow up time.)

Level 4 (retrospective case series), supportive. Fair (outcomes measured by CPC, but confounders not identified and appropriately controlled for, follow up probably long enough (31.0 +/- 18.3 days in the poor recovery group)


Level 5 (case reports), supportive. Poor (outcomes not measured objectively, confounders not controlled, but follow up complete)