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Evidence-Based Medicine

CLINICAL DECISION RULES FOR TERMINATION OF RESUSCITATION IN OUT-OF-HOSPITAL CARDIAC ARREST

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☐ Abstract—Background: Out-of-hospital cardiac arrest (OHCA) has a low probability of survival to hospital discharge. Four clinical decision rules (CDRs) have been validated to identify patients with no probability of survival. Three of these rules focus on exclusive prehospital basic life support care for OHCA, and two of these rules focus on prehospital advanced life support care for OHCA. Clinical Question: Can a CDR for the termination of resuscitation identify a patient with no probability of survival in the setting of OHCA? Evidence Review: Six validation studies were selected from a PubMed search. A structured review of each of the studies is presented. Results: In OHCA receiving basic life support care, the BLS-TOR (basic life support termination of resuscitation) rule has a positive predictive value for death of 99.5% (95% confidence interval 98.9–99.8%), and decreases the transportation of all patients by 62.6%. This rule has been appropriately validated for widespread use. In OHCA receiving advanced life support care, no current rule has been appropriately validated for widespread use. Conclusions: The BLS-TOR rule is a simple rule that identifies patients who will not survive OHCA. Further research is required to identify similarly robust CDRs for patients receiving advanced life support care in the setting of OHCA. © 2010 Elsevier Inc.

☐ Keywords—termination of resuscitation; emergency medical services; cardiac arrest

CASE

A 72-year-old man is found by his daughter in his bedroom without vital signs. Upon emergency medical services (EMS) arrival, cardiopulmonary resuscitation (CPR) is initiated. The presenting rhythm is asystole and does not change during the course of his prehospital resuscitation. As a base hospital physician, you receive a radio patch from the paramedics requesting an order to terminate the resuscitation.

CLINICAL QUESTION

Can a clinical decision rule (CDR) for the termination of resuscitation identify a patient with no probability of survival in the setting of out-of-hospital cardiac arrest (OHCA) from a presumed cardiac etiology?

CONTEXT

OHCA has a very low survival rate to hospital discharge, with < 5% reported in one large study (1). Transporting all OHCA patients to the hospital therefore results in the inappropriate utilization of valuable resources, as well

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exposing EMS personnel and the public to the dangers of high-speed transport (2). A position paper on prehospital termination of resuscitation published by the National Association of EMS Physicians advocates for criteria to establish appropriate termination of resuscitation (3). In response, a number of CDRs have recently been published which provide an evidence-based approach to identify patients with no probability of survival to hospital discharge.

EVIDENCE SEARCH

Using PubMed clinical queries, category: clinical prediction guides, and scope: broad, sensitive search, the keywords "termination" and "resuscitation" were entered on November 20, 2008. Seventy-two articles were displayed, which were searched by title. Twelve titles were selected for further review of the abstract. Five articles were selected for appraisal. An additional title (accepted for publication) was indentified for appraisal by contacting the authors of selected articles. Each CDR was graded according to a published hierarchy of evidence (4).

EVIDENCE REVIEW

CDRs for Basic Life Support Prehospital Care
TOR Investigators, University of Toronto

Validation of a rule for termination of resuscitation in out-of-hospital cardiac arrest. *New England Journal of Medicine*, 2006 (5).

Population. Consecutively enrolled adults with OHCA who exclusively received basic life support (BLS), including automatic external defibrillation (AED), if required, in one of 24 EMS systems in Ontario, Canada. The region included communities with populations of 40,000 to 2.5 million persons. Of 1620 eligible patients, 1240 were enrolled (no data collection forms were available for 380 cases). The mean age was 69.2 years, 69.0% were male, 57.4% of cardiac arrests were witnessed, and the median time to EMS response was 8.0 min.

Study design. Prospective, observational validation study from January 1, 2002 to January 30, 2004. The previously derived BLS-TOR (basic life support termination of resuscitation) rule recommends termination of resuscitation when there is no return of spontaneous circulation (ROSC), no AED shocks are administered before transport, and the arrest is not witnessed by EMS personnel (Figure 1). Before patient transport to the hospital, the emergency medical technicians were asked to administer the rule to the patient. Regardless of the rule's decision to "terminate" or "transport," all patients were transported to the hospital.

Out-of-hospital Cardiac Arrest (OHCA) in field after EMT-D resuscitation attempt completed but prior to transport is eligible for BLS-TOR rule if:

1. No Return of Spontaneous Circulation has occurred and,
2. No Shock has been administered and,
3. The OHCA was not witnessed by EMS personnel.

All other patients require continued resuscitation and emergent transport to the nearest Emergency Department

Figure 1. BLS-Termination of Resuscitation Clinical Decision Rule. Adapted from (5): Morrison LJ, Visentin LM, Kiss A, et al.; TOR Investigators. Validation of a rule for termination of resuscitation in out-of-hospital cardiac arrest. N Engl J Med 2006;355:478–87. EMT-D = emergency medical technician defibrillation; BLS-TOR = basic life support termination of resuscitation; EMS = emergency medical services.

Primary outcome(s). Primary outcomes included: pronounced dead in the emergency department (ED); died after admission to the hospital; alive in the hospital at 6 months; or discharged from the hospital. The secondary outcome was cerebral performance categorical score of survivors at 6 months.

Exclusion criteria. Patients were excluded if they had a do-not-resuscitate order or an obvious non-cardiac arrest, such as trauma.

Main results. Of the 776 patients for whom the BLS-TOR rule recommended termination of resuscitation, 4 survived. Of these 4 patients, 3 were considered to have good cerebral performance. The positive predictive value (PPV) for death was 99.5% (95% confidence interval [CI] 98.9–99.8%). The BLS-TOR rule would decrease the transportation of all patients by 62.6%.

OPALS Sub-study

Comparison of termination-of-resuscitation guidelines for basic life support: defibrillator providers in out-of-hospital cardiac arrest. *Annals of Emergency Medicine*, 2006 (6).

Population. Consecutively enrolled adults with OHCA who exclusively received BLS care including AED, if required, in one of 21 EMS systems in Ontario, Canada. The region included communities with populations of 16,000 to 750,000, totaling 2.7 million persons. There were 13,684 patients enrolled. The mean age was 69.1 years, 67.3% were male, 52.2% of cardiac arrests were witnessed, and the mean time to EMS response was 8.5 min.

Study design. Retrospective validation using a cohort study from 1988 to 2003. Three previously derived guidelines were externally validated using cohort data from the previously described BLS-TOR rule; the Petrie et al. rule, which recommends termination of resuscitation if the initial rhythm is asystole and the EMS response time is > 8 min; and the Marsden et al. rule, which recommends termination of resuscitation if the initial rhythm is not shockable, there is no ROSC, and no evidence of CPR within the past 15 min (5,7,8).

Primary outcome(s). The primary outcome was survival to hospital discharge. The secondary outcome was cerebral performance of survivors, where available.

Exclusion criteria. Patients were excluded if they had obvious signs of death, such as decomposition, or a clearly non-cardiac arrest, such as trauma.

Main results. Of the 6908 patients for whom the BLS-TOR rule would recommend termination of resuscitation, 3 would survive. The negative predictive value (NPV) for survival was 100.0% (95% CI 99.9–100.0%). The transportation rate of all patients would decrease by 50.5%. Of the 1293 patients for whom the Petrie et al. rule would recommend termination of resuscitation, one would survive. The NPV was 99.9% (95% CI 99.8–100.0%). The transportation rate would decrease by 9.4%. Of the 2536 patients for whom the Marsden et al. rule would recommend termination of resuscitation, one would survive. The NPV was 100.0% (95% CI 99.9–100.0%). The transportation rate would decrease by 18.5%.

CARE Study Group (Singapore)

Comparison of termination-of-resuscitation guidelines for out-of-hospital cardiac arrest in Singapore EMS. *Resuscitation*, 2007 (9).

Population. Consecutively enrolled adults in OHCA who exclusively received BLS care including AED, if required, in Singapore, population 4.1 million. There were 2269 patients enrolled. The mean age was 61.1 years, 68.4% were male, 65.3% of cardiac arrests were witnessed, and the mean time to EMS response was 12.0 min.

Study design. Retrospective validation of a cohort study from October 2001 to October 2004. The BLS-TOR, Petrie et al., and Marsden et al. rules were validated (5,7,8).

Primary outcome(s). The primary outcome was survival to hospital discharge or survival to 30 days post cardiac arrest, whichever came first.

Exclusion criteria. Patients were excluded if they had obvious signs of death, such as decomposition.

Main results. Of the 1559 patients for whom the BLS-TOR rule would recommend termination of resuscitation, 6 would survive. The NPV for survival was 99.6% (95% CI 99.2–99.8%). The transportation rate of all patients would decrease by 68.7%. Of the 718 patients for whom the Petrie et al. rule would recommend termination of resuscitation, 2 would survive. The NPV was 99.7% (95% CI 99.0–100.0%). The transportation rate would decrease by 31.6%. Of the 1450 patients for whom the Marsden et al. rule would recommend termination of resuscitation, 3 would survive. The NPV was 99.8% (95% CI 99.4–99.9%). The transportation rate would decrease by 63.9%.

In the setting of exclusive basic life support with AED care for OHCA, the BLS-TOR rule meets Level 2 criteria for CDRs. The Petrie et al. and Marsden et al. rules meet Level 4 criteria (Table 1, Figure 2).

CDRs for Advanced Life Support Prehospital Care
CARES Surveillance Group (USA)

Prehospital termination of resuscitation in cases of refractory out-of-hospital cardiac arrest. *Journal of the American Medical Association*, 2008 (10).

Table 1. Levels of Evidence for CDRs*

Level 1	Rules that can be used in a wide variety of settings with confidence that can change clinician behavior and improve patient outcomes. Prospectively validated in at least one different population and also one impact analysis, demonstrating change in clinician behavior with beneficial consequences.
Level 2	Rules that can be used in various settings with confidence in their accuracy. Validated by a demonstration of accuracy in either one large prospective study (including a broad spectrum of patients and clinicians) or in several smaller settings that differ from one another.
Level 3	Rules that clinicians may consider using with caution if patients in the study are similar to those in the clinician's clinical setting. Validated in only one narrow prospective sample.
Level 4	Rules that need further evaluation before they can be applied clinically. Derived but not validated or validated only in split samples, large retrospective databases, or by statistical techniques.

* Adapted from (4): McGinn TG, Guyatt GH, Wyer PC, Naylor CD, Stiell IG, Richardson WS. Users' guides to the medical literature: XXII: how to use articles about clinical decision rules. Evidence-Based Medicine Working Group. JAMA 2000;284:79–84.
CDR = clinical decision rule.

Negative Predictive Value (NPV)
The probability of a negative outcome in those individuals that have a negative test or prediction rule result. In the context of a Clinical Decision Rule such as the TOR-BLS, the NPV for survival would therefore be the probability of survival if the prediction rule is negative, i.e., does not suggest termination of the resuscitation. This could also be thought of as the probability that the rule suggests termination of resuscitation in a patient that would be a survivor. Predictive values are susceptible to changes in prevalence of the disease.

Positive Predictive Value (PPV)
The probability of a positive outcome in those individuals that have a positive test or prediction rule result. In the context of a Clinical Decision Rule such as the TOR-BLS, the PPV for death would therefore be the probability of death if the prediction rule is positive, i.e., suggests termination of the resuscitation. Predictive values are susceptible to changes in prevalence of the disease.

Clinical Decision Rule (CDR)
A clinical decision rule is derived from original research and is defined as a decision-making tool that incorporates 3 or more variables from the history, examination, or simple tests to promote effective and efficient diagnosis, management and/or risk stratification.

Hierarchy of Evidence – Clinical Decision Rules (4)
Clinical Decision Rules should be assessed according the strength of their scientific merit (see Table 1). CDRs that have been proven to have high performance and clinical impact in new clinical settings to their original derivations and validations are appropriate for widespread implementation.

Confidence Interval (CI)
The CI is an indicator of the precision of a study result or estimate. It is a range between two values within which it is probable that the true value lies for the whole population of patients from which the study patients were selected. With a 95% CI the true value can be expected to be within that interval with 95% confidence.

Figure 2. Evidence-based medicine teaching points.

Population. Prospectively enrolled adults in OHCA in one of 19 EMS systems in Anchorage, AL; Atlanta, GA; Boston, MA; Raleigh, NC; Cincinnati and Columbus, OH; and Austin and Houston, TX. Atlanta submitted 50.5% of cases. There were 5556 patients enrolled (51 were excluded due to lost data). The mean age was 64.4 years, 60.0% were male, and 49.5% of cardiac arrests were witnessed.

Study design. Retrospective validation using a registry database from October 1, 2005 to April 30, 2008. The previously described BLS-TOR rule and the ALS-TOR rule were externally validated (11). The ALS-TOR rule recommends termination of resuscitation when there is no ROSC, no shock before transport, the arrest is not witnessed by either bystanders or EMS personnel, and no bystander CPR is administered. All patients received advanced life support (ALS) care.

Primary outcome(s). The primary outcome was survival to hospital discharge. The secondary outcome was cerebral performance of survivors.

Exclusion criteria. Patients were excluded if they had obvious signs of death, such as decomposition, or a clearly non-cardiac arrest, such as trauma.

Main results. Of the 2592 patients for whom the BLS-TOR rule would recommend termination of resuscitation, 5 would survive. Of these 5 patients, 4 were considered to have good cerebral performance. The PPV for death was 99.8% (95% CI 99.6–99.9%). The transportation rate of all patients would decrease by 47.1%. Of the 1192 patients for whom the ALS-TOR rule would recommend termination of resuscitation, none would survive. The PPV for death was 100.0% (95% CI 99.7–100.0%). The transportation rate would decrease by 21.7%.

In the setting of advanced life support care for OHCA, the ALS-TOR rule and the BLS-TOR rule meet Level 4 criteria for CDRs (Table 1, Figure 2).

Universal CDRs Arizona Group

Independent evaluation of an out-of-hospital termination of resuscitation (TOR) clinical decision rule. *Academic Emergency Medicine*, 2008 (12).

Population. Consecutively enrolled adults in OHCA in one of 30 EMS systems in Arizona. The study region included 67% of the state population. There were 2180 of 2239 eligible patients enrolled; no data were available for 59 patients. The mean age was 64 years, 65% were male, and the median time to EMS response was 5.5 min.

Study design. Retrospective cohort analysis from October 2004 to October 2006. The BLS-TOR rule described above was evaluated. The majority of patients received ALS care, although some patients may have received BLS with AED care.

Primary outcome(s). The primary outcome was survival to hospital discharge. The secondary outcome was cerebral performance of survivors at discharge.

Exclusion criteria. Patients were excluded if they had obvious signs of death (e.g., lividity) or had suffered a traumatic arrest.

Main results. Of the 1160 patients for whom the BLS-TOR rule recommended termination of resuscitation, one survived with a good neurological outcome. The BLS-TOR rule would decrease the transportation of all patients by 69%.

Validation of a universal prehospital termination of resuscitation clinical prediction rule for advanced and basic life support providers. *Resuscitation*, 2009 (13).

Population. Consecutively enrolled adults with OHCA who were treated by either paramedics or defibrillation-only emergency medical technicians in one of 6 EMS systems including Toronto, Canada and five adjacent municipalities serving 6.7 million people by land and 11 million by air. There were 2415 OHCA patients included, of which 1992 (82.5%) were attended to by paramedics. The mean age was 69.4 years, 63.0% were male, 38% of cardiac arrests were witnessed by a bystander, and 28% received bystander CPR.

Study design. Retrospective validation using registry data from a single research site from April 1, 2006 to April 1, 2007. The previously described BLS-TOR rule and the ALS-TOR rule were validated.

Primary outcome(s). The primary outcome was survival to hospital discharge but had met either the ALS-TOR or BLS-TOR criteria.

Exclusion criteria. Patients were excluded if they had: a do-not-resuscitate order; a non-cardiac etiology; obvious signs of death as defined by local legislation; or were < 18 years old.

Main results. Of the 1302 patients for whom the BLS-TOR rule recommended termination of resuscitation, none survived. The PPV for deaths was 100% (95% CI 99.8–100). The BLS-TOR rule would decrease the transportation of all patients by 54.4%. Of the 743 patients for whom the BLS-TOR rule recommended termination of resuscitation, none survived. The PPV for death was 100% (94% CI 99.8–100). The ALS-TOR rule would decrease transportation by 31%.

In a mixed clinical setting, where either ALS care or BLS with AED care for OHCA may be applied, the BLS-TOR and ALS-TOR rules meet Level 4 criteria for CDRs (Table 1, Figure 2).

CONCLUSION

OHCA presents emergency physicians and EMS systems with the challenge to identify potential survivors among the vast majority of patients who will not survive a cardiac arrest, while efficiently and safely utilizing prehospital resources. In response to the calls for evidence to guide OHCA resuscitation, four CDRs have been derived and subsequently validated in various fashions. In the setting of OHCA receiving exclusive basic life support with AED, only the BLS-TOR rule has been prospectively validated in a rigorous fashion to warrant widespread use. In the setting of OHCA receiving only advanced life support or in a mixed environment of either advanced life support or basic life support with AED, neither the BLS-TOR nor the ALS-TOR rule have been appropriately validated to warrant widespread use. However, the robust preliminary findings of the retrospective data suggest that the ALS-TOR rule holds promise in these settings. Future large, prospective trials are required before the external generalizability of this rule can be established.

COMMENTARY BY DANIEL DAVIS, MD

The issue of termination of resuscitation in out-of-hospital cardiac arrest (OHCA) is critically important, requiring that we balance the need to provide each patient with the opportunity to achieve return of spontaneous circulation (ROSC) and meaningful survival on one hand against the unnecessary allocation of valuable EMS resources and exposure of providers to a potentially dangerous "lights-and-sirens" transport on the other. Multiple high-quality research efforts have been made on this topic, demonstrating that high negative predictive value (NPV) is achievable and that a substantial number of emergency transports can be avoided. Particularly with the BLS-TOR rule, which has maintained excellent predictive ability with prospective validation in large datasets, it is justifiable for a Medical Director to apply these criteria for clinical use. It even seems reasonable to integrate the ALS-TOR rules into clinical practice, given their excellent performance using data from the Resuscitation Outcomes Consortium Epistry database. However, there are several issues that should be considered when evaluating these rules for application in an individual EMS system.

First, one must consider the configuration of the EMS system with regard to the presence of ALS vs. BLS providers, as well as the potential input of online medical control. The BLS-TOR rule was designed for application without the presence of ALS providers, which is relatively unusual except in rural areas. Thus, the use of rhythm interpretation, administration of ALS medications, advanced airway insertion, or capnometry are not incorporated into the guidelines. Although decision rules that incorporate some of these components have been derived, including the ALS-TOR guidelines, they have not been subject to the same rigorous scrutiny as the BLS-TOR guidelines. Although it is difficult to improve upon the NPV reported for the various rules discussed here, it may be worthwhile to consider some of these tools in future guidelines regarding termination of resuscitative efforts. Limiting the decision regarding continued resuscitation to the elements of the BLS-TOR rule is certainly an option. However, it would be somewhat ridiculous to ask an ALS-level provider to ignore certain information or withhold certain available treatments solely to fulfill the BLS-TOR requirements. The predictive ability of either the BLS-TOR or ALS-TOR guidelines in a tiered-response system remains unclear.

This introduces a second consideration—the role of online medical control. Although one might assume that the additional experience and clinical insight from an emergency nurse or physician would enhance the precision of decisions regarding termination of resuscitation, this has not been demonstrated scientifically. In fact, I would not be surprised if practice variability and challenges with radio communication and remote medical control do not result in substantial inconsistencies and, ultimately, diminished performance with regard to both NPV and the avoidance of unnecessary transports. That said, the value of online medical control may lie in the perceived mitigation of liability issues with real-time physician input. This is clearly an area ripe for investigation.

The final consideration is perhaps the most nebulous, although equally important given the consequences of misclassification for a patient with OHCA. The resuscitation world seems to be dividing the history of cardiac arrest investigation into the period before and after the 2005 International Liaison Committee on Resuscitation guidelines. The level of interest within the scientific and EMS communities, the attention given to resuscitation training and monitoring, and outcomes in several systems seem to be undergoing a renaissance previously unseen in this area of medicine. It remains unclear how this might affect "dogma" established in the "Pre-2005" era, but investigators in resuscitation science are openly questioning whether a lack of effectiveness for certain therapies might be due to suboptimal performance of CPR. Experimental data suggest that the window of opportunity for resuscitation may be wider than previously thought, and we have observed an increase in survival for patients arriving to the ED in cardiopulmonary arrest from 0% to over 10% since adopting a more aggressive protocol and training strategy. Thus, it is conceivable that advancements in our understanding of resuscitation physiology and therapeutics will change the definitions for futility, and continuing refinement and re-evaluation of standard guidelines will be important in the future.

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ARTICLE SUMMARY

1. Why is this topic important?

Termination of resuscitation clinical prediction rules may minimize costs and better focus emergency medical services resources.

2. What is the clinical question?

Can a clinical decision rule (CDR) for the termination of resuscitation identify a patient with no probability of survival in the setting of out-of-hospital cardiac arrest (OHCA) from a presumed cardiac etiology?

Search Strategy: PubMed clinical queries, category: clinical prediction guides, and scope: broad, sensitive search.

Citations Appraised: Validation of a rule for termination of resuscitation in out-of-hospital cardiac arrest. *New England Journal of Medicine*, 2006 (5).

Comparison of termination-of-resuscitation guidelines for basic life support: defibrillator providers in out-of-hospital cardiac arrest. *Annals of Emergency Medicine*, 2006 (6).

Comparison of termination-of-resuscitation guidelines for out-of-hospital cardiac arrest in Singapore EMS. Resuscitation, 2007 (9).

Independent evaluation of an out-of-hospital termination of resuscitation (TOR) clinical decision rule. *Academic Emergency Medicine*, 2008 (10).

Prehospital termination of resuscitation in cases of refractory out-of-hospital cardiac arrest. *Journal of the American Medical Association*, 2008 (11).

Validation of a universal prehospital termination of resuscitation clinical prediction rule for advanced and basic life support providers. *Resuscitation*, 2009 (13).

3. Are the results valid?

Yes—in the setting of OHCA receiving exclusive basic life support (BLS) with automatic external defibrillation (AED).

4. What are the results?

The BLS-TOR rule is a simple rule that identifies patients who will not survive OHCA. Further research is required to identify similarly robust CDRs for patients receiving advanced life support care in the setting of OHCA.

5. Can I apply the results to my practice?

Yes—in the setting of OHCA receiving exclusive basic life support with AED.