Critical Review Form
Clinical Prediction or Decision Rule

Validation of a Rule for Termination of Resuscitation in
Out-of-Hospital Cardiac Arrest, *NEJM* 2006; 355: 478-487

Objectives: **To "used methods of prospective validation to test the predictive value of this (BLS TOR) rule". Also, "to evaluate whether a response interval of more than eight minutes … would increase the predictive power of the rule". (p. 479)**

Methods: **Using a region of Ontario consisting of 24 EMS Systems consecutive adults treated by EMT-D (AED, CPR but no ACLS intubation or IV drugs) for presumed out-of-hospital cardiac arrest from Jan 2002 through Jan 2004 were eligible. Exclusion criteria include trauma or asphyxia related arrest, written or oral DNR orders, or prior receipt of advanced cardiac life support for the current arrest situation. All patients had an AED placed and up to three cycles of a protocol (AED shock or no shock, followed by CPR) before transport to a hospital. EMT's received *a priori* instruction on the use of AED and the BLS TOR prediction rule. After transport to the hospital they completed a data collection form. Study coordinators at each site reviewed the EMS forms before sending to a central coordinating office where four trained assistants abstracted the data using a standardized form.**

Site coordinators obtained patient outcome data from the receiving hospital at six to eight months post-arrest. Outcomes were classified as pre-hospital death, post-hospital admission death, alive and hospitalized at 6-months or alive and discharged at 6-months. Cerebral performance was also evaluated among survivors (1 = good cerebral performance, 5 = death). (p.480)

Based upon a survival rate less than 1%, a one-tailed $\alpha < 0.05$ significance, and 80% power the *a priori* sample size was 773 subjects.

Guide		Comments
I.	***Is this a newly derived instrument* (Level IV)?**	
A.	Was validation restricted to the retrospective use of statistical techniques on the original database? (If so, this is a Level IV rule & is not ready for clinical application).	No, validation was prospective. Therefore, the BLS TOR rule is at least a Level III CDR.
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	See the PGY-I derivation papers.
1a	Were all important predictors included in the derivation process?	No, only five candidate variables were considered neglecting such features as age and pre-arrest function status.
1b	Were all important predictors present in significant proportion of the study population?	Yes. "There was no return of spontaneous circulation in 1172 cases (94.5%), no shocks were delivered in 868 (70.0%), and the cardiac arrest was not witnessed by EMS personnel in 1120 cases (90.3%)". (p. 481). Additionally, 654 (53.2%) had EMS response time ≤ 8 minutes (Table 2, p. 482).
1c	Does the rule make clinical sense?	Yes, each variable has content and face validity.
2	Did validation include prospective studies on several different populations from that used to derive it (II) or was it restricted to a single population (III)?	This derivation occurred in one large province with two-dozen distinct EMS systems, although the same population from which BLS TOR was derived. Therefore a Level III CDR.
3	*How well did the validation study meet the following criteria?*	

3a	Did the patients represent a wide spectrum of severity of disease?	Uncertain since scant demographic information is provided, though one urban adult cardiac arrest population is probably much like another. This study had mean age 69 years with male predominance (69%) and incomplete data collection in 379 cases (23%) without any attempt to compare demographics between incomplete and complete data collection subsets. However, investigators note that "data on 89 to 100 percent of all eligible patients were available to the four largest sites, and the demographic characteristics of the patients and the survival rates were similar at all 12 sites. We, therefore, suggest that the missed cases were probably similar to those included in the study". (p. 485)
3b	Was there a blinded assessment of the gold standard?	Uncertain. "Study coordinators at each site obtained information on patients' outcomes from the receiving hospitals six to eight months after the cardiac arrest". (p. 480) Whether these study coordinators were blinded to the BLS TOR variables is not clearly stated.
3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	Yes. "After a patient was transferred to the hospital, the EMTs completed a data collection form that included all relevant clinical characteristics of the cardiac arrest as well as the elements of the prediction rule". (p. 480) Paramedics undoubtedly knew the outcome of some of these patients, but there is no way to blind them in this clinical scenario.
3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	No – all patients were transported to the ED where their ultimate outcome was determined independent of the EMS personnel or BLS TOR variable results. In other words, the BLS TOR was <u>not</u> used to determine which patients were transported to the ED or how aggressive ED resuscitation efforts would be.

4	How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?	• 1240/1620 eligible subjects were included in this validation trial. • The 12 participating sites had enrollment rates ranging from 21 – 100% (overall 76.5%). • In total 1140/1240 (91.9%) were declared dead on ED arrival, 59/1240 (4.8%) died after ED admission, 2/1240 (0.2%) were still hospitalized at 6-months and 39/1240 (3.1%) survived to hospital discharge. • Among survivors BLS TOR recommended transport in 37/41. On the other hand, for non-survivors BLS TOR recommended no transport in 772/1199 as represented by the following 2x2 table Sen 64 (64 65) Spec 90 (77- 97) LR+ 6.6 (2.9 – 17) LR- 0.4 (0.37 – 0.46) NPV 8 (7 – 8.5) PPV 99.5 (98.8 – 99.8) Death Survival Terminate BLS 772 **4** Transport to ED (Continue BLS) 427 37 • Among the four (0.5% survival rate) subjects mislabeled by BLS TOR as "terminate resuscitation" who subsequently survived, 3 had category 1 good cerebral performance. • Addition of response time ≥ 8 minutes further reduced survival rate to 0.3% but increased ED transports from 37% to 68%. • Addition of post hoc variable "cardiac arrest not witnessed by bystander" reduced survival rate to 0%, but increased ED transport rates from 37% to 62%.

III.	**Has an impact analysis demonstrated change in clinical behavior or patient outcomes as a result of using the instrument? (Level I). If so, consider the following:**	
1	How well did the study guard against bias in terms of differences at the start (concealed randomization, adjustment in analysis) or as the study proceeded (blinding, co-intervention, loss to follow-up)?	No impact analysis performed and well-designed trial minimizes the likelihood of systematic error (bias).
2	What was the impact on clinician behavior and patient-important outcomes?	No impact analysis was performed but investigators project that appropriate use of BLS TOR would reduced ED transports from 100% to 37% while only missing 0.5% (0.1 -0.9%) of survivors. While the definition of futility and its EMS applicability are debated, clinicians and policy makers should note that the BLS TOR in combination with no bystander witness reduces survival rates to 0% (with tight confidence intervals) which might be acceptable to EMS personnel, EMS directors, ED staff, and society given the expense and danger of often meaningless transfers of pre-hospital cardiac arrest patients.

Limitations:

1) **Validation in the same population as the derivation set. Therefore a Level III CDR not yet proven to accurately identify cardiac-arrest non-survivors in settings outside of Toronto.**

2) **No assessment of inter rater reliability for the elements of BLS TOR.**

3) **No clear statement of blinding for outcomes assessors. If not blinded to BLS TOR results, ascertainment bias possible.**

4) **EMT's could not be blinded to every subjects outcome so possible bias in completing their data collection sheets upon ED arrival.**

Bottom Line:

Ontario-based adult cardiac arrest patients lacking any pre-hospital BLS TOR findings (see below) are extremely unlikely to survive hospital discharge (0.5%, 95 CI

0.1 – 0.9%) with AED-trained, non-ALS pre-hospital providers. If validated in other populations, these findings produce an ethical dilemma for pre-hospital and EM since these scene-to-ED transports are expensive, dangerous, and deprive more viable patients access to EMS in many settings where only one team may be available. Currently, pre-hospital resuscitation decisions are heterogeneous; use of a well-validated, societal-accepted BLS TOR CDR may offer distributive justice. Nonetheless, "prediction rules for the termination of resuscitation efforts should remain advisory and they should be tempered by the full clinical picture, taking into account the very small possibility of successful resuscitation when the prediction rule suggests termination". (p. 483)

BLS TOR

Transport to the ED if any of the following pre-hospital Findings are noted in suspected cardiac arrest:

1) AED shock delivered;
2) Return of spontaneous circulation;
3) EMS-provider witnessed arrest.

Otherwise consider termination of resuscitation efforts.