Critical Review Form
Clinical Prediction or Decision Rule

Prehospital Termination of Resuscitation in Cases of Refractory Out-of-Hospital Cardiac Arrest, *JAMA* 2008; 30: 142-1438

Objective: **"To independently assess the validity of the BLS and ALS rules for identifying individuals with refractory OHCA (out of hospital cardiac arrest) who likely will not benefit from rapid transport to a hospital for further attempts at resuscitation." (p. 1433)**

Methods: **Investigators performed a retrospective validation of the two rules using data from the Cardiac Arrest Registry to Enhance Survival (CARES) network of eight US cities collected from Oct 2005 until April 2008. CARES is designed to capture all cardiac arrest events in a defined geographic area or which 911 is activated. As a quality improvement project CARES is exempt from consent by their IRB's. CARES subjects are excluded if EMS personnel determine a non-cardiac etiology (trauma, electrocution, drowning or respiratory), out-of-hospital resuscitation not attempted due to obvious decomposition or rigor mortis, or if subjects were under 16 years old.**

CARES receives web-based reports from hospitals on patient cerebral performance score-based outcomes at discharge and length of stay in compliance with the Utstein criteria. After data-quality review at the central study site, data is entered into the registry data base permanently devoid of any identifiers. Based upon a 1% or less misclassification error rate, the *a priori* power calculation for the more conservative ALS rule was 192 subjects for 80% power and 1-sided $\alpha = 0.05$. Additionally, a sensitivity analysis was performed to reassess the rule accounting for those not transported to the ED and those who had termination of pre-hospital resuscitation.

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).	Retrospective validation of the two rules on a population distinct from that upon which they were derived so still a Level IV CDR.
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	
1a	Were all important predictors included in the derivation process?	Yes, see PGY-I and PGY-III papers.
1b	Were all important predictors present in significant proportion of the study population?	Yes. Arrest not witnessed by EMS (88%), no AED used or shock applied (61%), no out-of-hospital ROSC (47%), no bystander witnessed arrest (32%), and no bystander initiated CPR (22%). (Figure, p.1436)
1c	Does the rule make clinical sense?	Yes, each component of the ALS and BLS TOR 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)?	Different population but still retrospective so a Level IV CDR.
3	*How well did the validation study meet the following criteria?*	
3a	Did the patients represent a wide spectrum of severity of disease?	Very little patient demographics are provided (Table 1, p. 1435) but given large sample size, multiple stats included, and consistently bleak prognosis for OHCA regardless of age, locale, or EMS response, these results probably reflect reality for most US or Canadian systems.
3b	Was there a blinded assessment of the gold standard?	"The gold standard in this study was survival to hospital discharge as documented by hospital records". (p. 1434). The authors do not state whether data analysts or outcome assessors were blinded to survival.
3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	Unknown since variables were determined by retrospective review without reliability analysis.
3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	No, patients were assessed for life or death regardless of the presence or absence of individual variables.

4	How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?	• From 7235 cases involving 19 EMS agencies and 111 hospitals, 5505 cardiac arrests met inclusion criteria. • 947/5505 (1.2%) were pronounced dead in the out-of-hospital setting based on local protocols. • The following prognostic test characteristics were identified: **BLS TOR** Sen 50.6 (50.5 – 50.7) Spec 98.7 (97.1 – 99.5) PPV 99.8 LR+ 39.7 (17 – 93) BLS Rule / Died / Survived Met 3/3 criteria 2587 **5** Did not meet criteria 2526 387 **ALS TOR** Sen 23.3 (23.2 – 23.3) Spec 100 (99 - 100) PPV 100 (99.7 – 100) LR+ ∞ ALS TOR / Died / Survived Met 3/3 criteria 1192 **0** Did not meet criteria 3921 392 • BLS TOR misclassified 5 patients, 4 of whom left the hospital with a good CPC score, while 1 had severe disability. (p. 144) • BLS TOR would have increased pre-hospital pronouncements from 17% to 47%. • ALS TOR would have increased pre-hospital pronouncements from 17% to 22% while not misclassifying a single individual. • Results were robust to sensitivity analysis for the 51 (0.2%) lost to follow-up when assuming that the18 and 9 who met BLS and ALS TOR criteria all survived. In such a case BLS TOR would have misclassified 23 patients (0.4%) and ALS TOR 9 (0.2%). • Results were also unaltered when excluding from analysis the 947 upon who resuscitation efforts were stopped by local protocol.

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 was performed, but future prospective trial will need to assess EMS, EM physician/nurse, and family comfort in applying these decision aids real-time.
2	What was the impact on clinician behavior and patient-important outcomes?	There was no assessment of clinician behavior or patient outcomes because the rule was retrospectively applied and not used real-time.

Limitations

1) **Retrospective validation on a distinct population so at best still only a Level IV CDR. Prospective trials in various urban and rural settings to validate one or both CDR's will need to measure real-time:**
    a. **Accuracy reliability of interpreting individual variables and applying the rules;**
    b. **EMS comfort and psychological impact at using the rules to cease resuscitation efforts;**
    c. **Prognostic test characteristics of the CDR's;**
    d. **Cost-effectiveness of applying the rule in terms of pre-hospital pronouncements, EMS availability, and ED thoroughfare.**

Bottom Line

Retrospective application of BLS and ALS TOR indicate that both can safely increase pre-hospital pronouncements from 17% to 47% or 22%, respectively. The more conservative ALS TOR did not misclassify any patients. Future prospective trials are needed to validate this prognostic accuracy while assessing reliability and EMS community acceptance of these decision aids to decrease low-yield transports to the ED.