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Terminating resuscitation for out-of-hospital cardiac arrest?

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Clinical question
Can a clinical prediction rule for the termination of basic life support resuscitation for out-of-hospital cardiac arrest (OHCA) identify those patients with little or no chance of survival?
Article chosen
Morrison LJ, Visentin LM, Kiss A, et al. Validation of a rule for termination of resuscitation in out-of-hospital cardiac arrest. N Engl J Med 2006;355:478–487.
Study objective
To validate a previously derived clinical prediction rule for terminating futile resuscitation for OHCA.

Background

Despite advances in prehospital care, survival rates from out-of-hospital cardiac arrest (OHCA) remain dismally low. In many large cities in the United States, the overall survival for OHCA is as low as 1%.[1–5] Yet, extensive resources are expended on resuscitation attempts and transport of patients who seem to have little or no chance of survival. This predicament has created the need to elucidate rational and evidence-based methods for providing prehospital resuscitation care.

Population studied

The study population consisted of consecutively enrolled adults (≥ 18 years of age) who were treated for an out-of-hospital arrest of presumed cardiac origin, as defined by Utstein criteria,[6] between Jan. 1, 2002, and Jan. 30, 2004. Patients who had a cardiac arrest were evaluated and given basic life support (BLS) exclusively by emergency medical technicians (EMTs) trained in the use of an automated external defibrillator (AED). Patients were excluded if they received advanced cardiac life support (e.g., intubation and administration of intravenous fluids and medication), had a written or oral do-not-resuscitate order or had an arrest attributable to an obvious noncardiac cause (e.g., trauma or asphyxia).

Study design

The authors employed a prospective cohort study design for validating a clinical prediction rule using methods described by Wasson and colleagues[7] and Laupacis and coauthors.[8]

All patients received BLS resuscitation consistent with the 2000 American Heart Association guidelines.[9] Following transfer of care, the EMTs completed a data collection form that described clinical characteristics of the arrest as well as elements of the prediction rule.

For the purpose of validation, the rule was considered positive (i.e., termination of resuscitation was recommended) when all of the following 3 events occurred:

1. There was no return of spontaneous circulation.

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2. No shock was administered (i.e., there was no shockable rhythm detected by the AED).
3. The arrest was not witnessed by emergency medical services (EMS) personnel.

If any of these criteria was lacking, the rule was considered negative and continued resuscitative efforts and transportation to hospital were recommended. For the purpose of this study, however, all patients were transported to hospital and the findings of the rule had no bearing on EMT actions.

Resuscitation algorithm

The treatment algorithm used by the EMTs conformed to the American Heart Association guidelines and included the use of AED. After either successful defibrillation or the completion of this algorithm, the patient was transported rapidly to hospital and cardiopulmonary resuscitation continued if necessary. For the purpose of the study, the cardiac rhythm was analyzed only 3 times and no more than 3 shocks were delivered at each analysis to consider terminating resuscitation.

Outcome measures

Primary outcome

The performance characteristics of the termination of resuscitation rule, that is, the specificity and positive predictive value of the rule.

Secondary outcome

To evaluate whether 2 additional variables further increase the predictive power of the rule. These variables were

1. a response interval of more than 8 minutes.
2. a cardiac arrest not witnessed by a bystander.

Information about the patients' outcomes was obtained by the study coordinators 6–8 months after the cardiac arrest. The outcomes were classified as follows.

Died:

- The patient was pronounced dead in the emergency department, or
- The patient died after admission to the hospital.

Survived:

- The patient was alive in the hospital at 6 months, or
- The patient was discharged home.

Cerebral performance was assessed using the Safar scale[10] either at discharge or at 6–8 months postenrolment if the patient was still in the hospital. The estimated sample size was calculated to be able to predict a survival rate of 1% or less when the prediction rule recommended the termination of resuscitation. The authors defined it as a medically futile act if it yielded a benefit less than 1% of the time.[11]

Results

The study analyzed results on 1240 patients for whom complete datasets were available, representing 76.5% of all cardiac arrests encountered during the recruitment period. EMT noncompletion of data-collection forms was the most common reason for exclusion, though demographic data and survival rates were similar for enrolled and nonenrolled patients. The prediction rule performed with a specificity (i.e., the percentage of survivors in whom the rule was negative compared with all survivors) of 90.2% (95% confidence interval [CI] 88.4–91.8), a sensitivity (i.e., the percentage of those deaths among patients in whom the rule was positive compared with all deaths) of 64.4% (95% CI 61.6–67.0), a positive predictive value (i.e., the percentage of nonsurvivors among all patients with a positive test) of 99.5% (95% CI 98.9–99.8) and a negative predictive value (i.e., the percentage of survivors among all patients who had a negative test) of 8% (95% CI 6.6–9.7). Among the 776 patients for whom the rule suggested termination, 4 survived (a false positive rate 0.5% [95% CI 0.1%–0.9%]) (Table 1). Of these 4 patients, 3 were discharged home or to a long-term care facility and were considered to have good cerebral performance (Cerebral Performance Category [CPC] 1) and 1 patient had severe cerebral disability (CPC 3).

The secondary outcomes of the study were as follows:

1. When the EMS response took more than 8 minutes, the prediction rule had a specificity of 97.6% (95% CI 96.5–98.3) and a positive predictive value of 99.7%

Table 1. Test characteristics of the clinical prediction rule

Action according to prediction rule	Outcome		
	Death	Survival	No. of cardiac arrests
Terminate BLS (test positive)	772	4	776
Transport to ED (test negative)	427	37	464
Total	1199	41	1240
Survival rate when termination recommended by TOR rule, % (95% CI)		0.5 (0.1–0.9)	
Sensitivity, % (95% CI)		64.4 (61.6–67.0)	
Specificity, % (95% CI)		90.2 (88.4–91.8)	
Positive predictive value, % (95% CI)		99.5 (98.9–99.8)	
Negative predictive value, % (95% CI)		8.0 (6.6–9.7)	

BLS = basic life support; CI = confidence interval; ED = emergency department; TOR = termination of resuscitation.

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(95% CI 99.2–99.9) (positive likelihood ratio [LR] 13.75 and negative LR 0.6). The survival rate based on this modification was 0.3% (95% CI 0.0–1.7).

2. When the cardiac arrest was not witnessed by bystanders, both the specificity and the positive predictive value were 100% (95% CI 99.6–100) (positive LR ∞). The survival rate among these patients was 0% (95% CI 0.0–1.0). (Note: both variables were analyzed separately in the post hoc analysis.)

Application of the original rule would have reduced the transport rate from 100% to 37.4% (this is derived from the inverse of the total rule positive rate of 62.6% [776/1240]). When one of the secondary outcomes was incorporated into the rule, this less sensitive but more specific version of the rule would have reduced the transport rate to 68.4% (> 8 min response time) and 61.1% (unwitnessed) depending on which variable was used. The outcomes of all patients involved in the study are shown in Table 2.

Study conclusion

The authors validated a clinical prediction rule for the termination of resuscitation for OHCA with BLS that was found to have good specificity but only moderate sensitivity. Although it failed to identify 4 out of 776 (95% CI < 1%) patients who survived, most of whom had good cerebral performance, this was within the level of "medical futility" as defined by the authors a priori, as well as by some bioethicists.[11] This rule may help EMS providers and directors implement protocols for the termination of BLS resuscitative efforts in patients experiencing OHCA.

Commentary

This study has validated a clinical prediction rule intended for use in OHCA by EMTs who are trained in BLS and the use of AEDs. Implementation of this rule would have resulted in a 62.6% reduction in the transport of patients at the expense of less than 1% of patients (4 in this study) who may have benefited from resuscitative efforts. This large reduction in transports may have a significant impact on resource consumption and reduced response times for other EMS calls. Moreover, it could also have a reduced risk for the community and EMS personnel in terms of transport safety. However, will any rule that carries in excess of a 0% miss rate be acceptable for implementation by EMS directors?

The question of whether this rule can be applied in its original form or with modification by additional variables may benefit from consideration of some Bayesian principles and an appreciation of the probability of survival from cardiac arrest in a given community. This can be achieved by using the rule's performance characteristics in the form of LRs and applying them with the use of a Fagan nomogram[12] against the pretest probability of death. The LR for any screening or diagnostic test expresses the relative likelihood that a given test result would be expected in a patient with a disorder of interest compared with the likelihood of the same result in a patient without the disorder.

Using the original rule's performance characteristics, we find a somewhat weak positive LR of 6.6 (positive test = rule recommended termination) and an equally unhelpful negative LR of 0.39 (negative test = rule recommended transportation). The average survival rates for OHCA, including this study, range from 1% to 6.1%.[4,13] Using the nomogram, we note that the termination of resuscitation rule performs quite differently at the extremes of these ranges (Fig. 1). In a setting with a low survival rate (1%), the application of the original termination of resuscitation rule makes it very unlikely for patients who would have benefited from resuscitation to have been missed. However, if we assume a survival rate in the range of 5%, the original rule carries just under a 1% risk of missing a patient who would have benefited from resuscitation.

Since a 1% miss rate may not be acceptable from a societal perspective, applying our modified version of the rule, which incorporates response times or a bystander witness, may be warranted in some settings. Applying the prediction rule in its original form led to a survival rate of 0.5% (95% CI 0.1%–0.9%) among patients in whom termination of resuscitation was recommended. However, when one of the secondary outcome variables is added, the survival rate is reduced to 0% or 0.3%, depending on the variable used, reflecting a postive LR of 13.75 or higher. Terminating resuscitative efforts for OHCA raises ethical concerns that

Table 2. Outcomes of 1240 reported cardiac arrests

Outcome	No. (and %) of patients
Death	1199 (97)
Pronounced in the ED	1140 (92)
After admission	59 (5)
Survival	41 (3)
In hospital 6 mo after cardiac arrest	2 (< 1)
Discharged from hospital	39 (3)
Category of cerebral performance*	
Good performance	29 (71)
Moderate disability	5 (12)
Severe disability	6 (15)
Coma, vegetative state	1 (2)

ED = emergency department.
* Values for categories of cerebral performance were calculated as percentages of the 41 survivors.

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must be taken into consideration. Some stakeholders may feel that defining medical futility as 1% in cardiac arrest is unacceptable and the modified version may be deemed more appropriate. Medical futility has always been a concern in this type of research and most studies have failed to address it in a quantitative manner.[5,14,15]

While other prediction rules for the termination of resuscitative efforts for OHCA have been validated, yielding similar results to this study,[4,13] no other trial has reported as robust a dataset.

Conclusion

Evidence-based rules for termination of resuscitation for OHCA are a priority in prehospital care. This study represents the most comprehensive validation of a rule for termination of resuscitation and offers even more specific variants (fewer false positives) to consider. Adoption of the termination of resuscitation should be done taking into consideration local OHCA survival rates and with an explicit understanding of the ethical implications of its use.

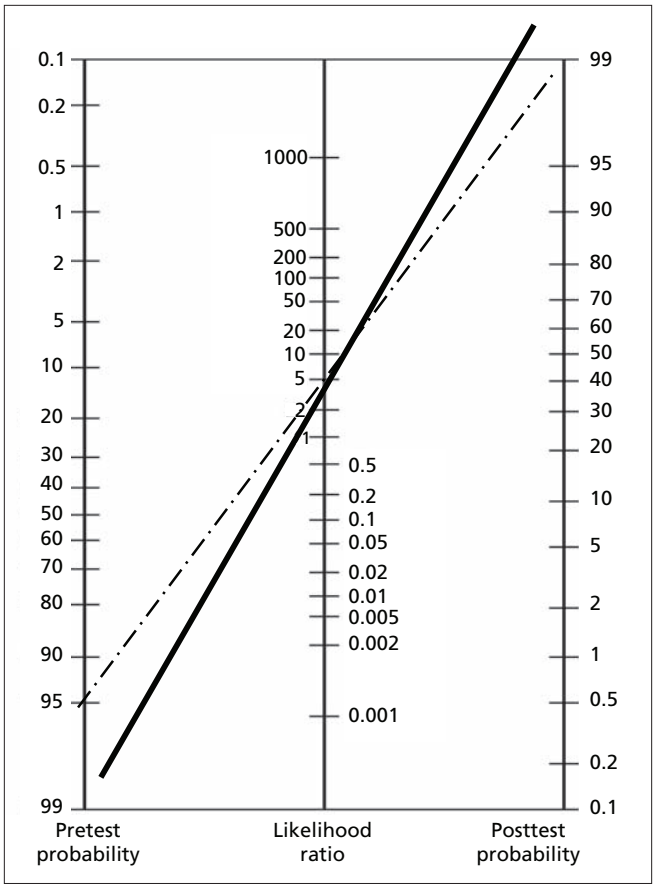

Fig. 1. Likelihood ratios for terminating out-of-hospital cardiac arrest. Survival rate = 5% (dashed line). Survival rate = 1% (solid line).

Competing interests: None declared.

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