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Termination of Resuscitation Rules for In-Hospital Cardiac Arrest

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IMPORTANCE There are no validated decision rules for terminating resuscitation during in-hospital cardiac arrest. Decision rules may guide termination and prevent inappropriate early termination of resuscitation.

OBJECTIVE To develop and validate termination of resuscitation rules for in-hospital cardiac arrest.

DESIGN, SETTING, AND PARTICIPANTS In this prognostic study, potential decision rules were developed using a national in-hospital cardiac arrest registry from Denmark (data from 2017 to 2022) and validated using registries from Sweden (data from 2007 to 2021) and Norway (data from 2021 to 2022). Six variables (age, initial rhythm, witnessed status, monitored status, intensive care unit location, and resuscitation duration) were considered based on their bedside availability. Prognostic metrics were computed for all possible variable combinations. CIs were obtained using bootstrapping. Rules with a false-positive rate below 1% (predicting death in patients who might otherwise survive) and a positive rate of more than 10% (proportion of all cases for whom termination is proposed) were considered appropriate.

MAIN OUTCOMES AND MEASURES The primary outcome was 30-day mortality.

RESULTS The cohorts included 9863 Danish, 12 781 Swedish, and 1308 Norwegian patients. The overall median (IQR) age was 74 (66-81) years, 63% were male, and the median (IQR) resuscitation duration was 13 (5-23) minutes. Of 53 864 possible termination rules, 5 were identified as relevant for clinical use. The best performing rule included 4 variables (unwitnessed, unmonitored, initial rhythm of asystole, and resuscitation duration more than or equal to 10 minutes). The rule proposed termination in 110 per 1000 cardiac arrests (positive rate, 11%; 95% CI, 10%-11%) and predicted 30-day mortality incorrectly in 6 per 1000 cases (false-positive rate, 0.6%; 95% CI, 0.3%-0.9%). All 5 rules performed similarly across all 3 cohorts.

CONCLUSIONS AND RELEVANCE In this prognostic study, 5 termination of resuscitation rules were developed and validated for in-hospital cardiac arrest. The best performing rule had a low false-positive rate and a reasonable positive rate in all national cohorts. These termination of resuscitation rules may aid decision-making during resuscitation.

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Editor's Note page 398

Supplemental content

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Current resuscitation guidelines provide little guidance on terminating resuscitation for in-hospital cardiac arrest.[1,2] A recent systematic review identified only 3 studies describing the derivation and validation of a single termination of resuscitation rule for in-hospital cardiac arrest.[3]

The most recent and largest study used data from the Get With The Guidelines-Resuscitation (GWTG-R) registry, an in-hospital cardiac arrest registry from the US, to validate a previous termination of resuscitation rule, known as the *UN10 rule*.[4] This rule was found to have insufficient discrimination for use in clinical practice, with a false-positive rate of 6%. Consequently, there is currently no reliable rule for terminating resuscitation in patients with in-hospital cardiac arrest.

Appropriate termination of resuscitation rules can prevent futile resuscitation attempts and, more importantly, may reduce inappropriate early termination of resuscitation. The International Liaison Committee on Resuscitation recently highlighted the need to avoid early termination of resuscitation as a strategy to improve in-hospital cardiac arrest outcomes.[5]

The objective of this study was to develop and validate a termination of resuscitation rule for in-hospital cardiac arrest. Specifically, the aim was to develop a rule with a very low false-positive rate (predicting death in patients who might otherwise survive), a reasonable positive rate (overall proportion of cases for whom termination is proposed), and as few

variables as possible to ensure that the rule would be relevant in a clinical setting.

Key Points

Question Can a clinical decision rule guide termination of resuscitation efforts during in-hospital cardiac arrest?

Findings In this prognostic study, 5 termination of resuscitation rules were developed and validated in 23 952 patients from Denmark, Sweden, and Norway. The best-performing rule included 4 variables (unmonitored, unwitnessed, initial rhythm of asystole, and resuscitation duration ≥10 minutes) and predicted 30-day mortality with a false-positive rate of 0.6% (predicting death in patients who might otherwise survive) and a positive rate of 11% (proportion of proposed terminations to avoid prolonged resuscitation).

Meaning These termination of resuscitation rules may aid decision-making during resuscitation.

Methods

Study Design and Data Sources

This was an observational study based on prospectively collected data from national registries in Denmark, Sweden, and Norway, each providing data on in-hospital cardiac arrests with a clinical indication for cardiopulmonary resuscitation.[6-8] The termination of resuscitation rule was derived using Danish data from 2017 to 2022, then validated using Swedish data from 2007 to 2021 and Norwegian data from 2021 to 2022. Details on data sources and resuscitation practices are provided in Supplement 1.

The study was approved by the Swedish Ethical Review Authority in April 2022 (approval number 2022-00805-01). Ethical approval for observational registry-based studies is not required in Denmark and Norway.

Patient Population

We included adult patients (≥18 years) with an index in-hospital cardiac arrest and no pulse-generating rhythm at the first rhythm analysis. For the primary analysis, we excluded patients with incomplete data on the primary outcome and those with incomplete data on covariates used to develop the termination of resuscitation rule.

Outcomes

The primary outcome was mortality at 30 days, identified as a core outcome by the International Liaison Committee on Resuscitation.[9] Secondary outcomes included no return of spontaneous circulation, poor neurological status at hospital discharge, and mortality at 1 year. Outcome definitions are provided in Supplement 1.

Variables

The following variables were a priori considered for the termination of resuscitation rule based on their association with mortality,[10] their immediate availability at the bedside during a cardiac arrest, and their availability in each registry: age, location of cardiac arrest (intensive care unit or not intensive care unit), monitored status (continuous electrocardiographic [ECG] monitoring), witnessed status, initial rhythm, and duration of resuscitation. All variables were converted into a binary format to facilitate clinical decision-making. Age and duration of resuscitation were dichotomized at specific thresholds. Initial rhythm was dichotomized into groups of categories (presence or absence of specific rhythms). Each dichotomization was treated as a separate variable in the analysis. Additional details are provided in Supplement 1.

Statistical Analysis

This study aimed to develop and validate a decision rule with a very low false-positive rate to avoid termination of resuscitation in patients who might otherwise survive to 30 days. A false-positive rate of less than 1% was considered acceptable, as suggested by the European Resuscitation Council (ERC),[11] the American Heart Association (AHA),[12] and others.[13] The decision rule also had to be straightforward, ie, incorporating few variables that are readily available for the clinician, and have a reasonable positive rate (overall proportion of cases for whom termination is proposed) to ensure clinical relevance. A positive rate greater than 10% was considered reasonable based on discussion among all authors.

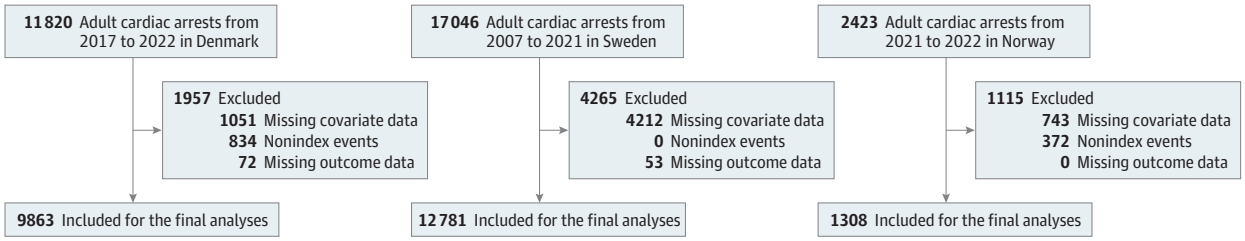
The decision rule was developed using data from the Danish registry. The positive rate, sensitivity, specificity, negative predictive value, positive predictive value, false positive rate, and false-negative rate (see eTable 1 in Supplement 1 for definitions) for predicting 30-day mortality were calculated for all possible combinations of the included variables, assuming each individual combination represented a termination of resuscitation rule.

Combinations of variables (or termination of resuscitation rules) with a false-positive rate less than 1% and a positive rate greater than 10% were inspected manually. The final rules deemed most appropriate for use in clinical practice were selected based on author discussion, considering the false-positive rate, positive rate, and number of variables. Preference was given to rules with fewer variables when the performance was comparable.

To assess the precision of the final rules, 95% CIs were estimated by bootstrapping 100 000 samples using unrestricted random sampling with replacements, with each bootstrap sample having the same sample size as the original dataset.[14] The CIs were constructed using the 2.5th and 97.5th percentiles of the bootstrap. External validation was performed using data from the Swedish and Norwegian registries, separately. The final rules were applied to these datasets and prognostic metrics with 95% CIs were calculated using the method described.

Additional analyses were performed in a combined dataset including data from all 3 registries. First, calculations were repeated for each final rule to predict the primary and secondary outcomes. Second, sensitivity analyses were performed for the primary outcome to address the potential limitation of a self-fulfilling prophecy, where early termination based on the included variables might reinforce negative prognoses. These analyses included subsets of patients younger than 65 years, as a proxy

Figure 1. Flow Diagram for the Derivation and Validation Cohorts



Flow diagram illustrating the number of in-hospital cardiac arrest patients meeting the inclusion and exclusion criteria in the datasets from the 3 national registries. Missing outcome data refers to incomplete data on the primary outcome.

for patients where early termination of resuscitation was unlikely, and patients with a resuscitation duration of 20 minutes or longer. Lastly, an additional analysis was performed for the primary outcome to assess the performance of the UN10 rule.[4]

Multiple imputation was performed as a post hoc analysis using the fully conditional specification method to account for missing data in the combined dataset, including data from all 3 registries. A total of 100 imputed datasets were created. Details of the analysis are provided in Supplement 1.

No formal power calculation was performed given that the sample size was restricted to the obtained datasets. However, for a 1-sample test of a proportion assuming an α of 5%, a positive rate of 10% (or approximately 800 patients in the Danish cohort), and a false-positive rate of 1%, we would have 98% probability of obtaining an upper CI less than or equal to 2% for the false-positive rate, which was considered acceptable.

All analyses were prespecified unless explicitly stated. The statistical analyses were performed using SAS statistical software (version 9.4; SAS Institute).

Results

Overview

Of 23 952 registered in-hospital patients with cardiac arrest in the Danish, Swedish, and Norwegian datasets, 9863, 12 781, and 1308 were included in the main analyses, respectively (**Figure 1**).

Patient demographics were consistent across the cohorts, with an overall median (IQR) age of 74 (66-81) years, a 15 114 (63%) male population, and median (IQR) resuscitation duration of 13 (5-23) minutes (**Table 1**). Cardiac arrest characteristics varied across cohorts in the proportion of intensive care unit events (Denmark: 13%, Sweden: 29%, Norway: 22%), initial shockable rhythms (Denmark: 18%, Sweden: 26%, Norway: 25%), and cases presenting with asystole (Denmark: 37%, Sweden: 43%, Norway: 31%).

Derivation Cohort

The cohort from Denmark was used to develop the termination of resuscitation rule for predicting 30-day mortality. Of the 9863 included patients, 7642 (77%) died within 30 days.

Of 53 864 generated rules, 109 (0.2%) met the criteria of a false-positive rate less than 1% and a positive rate greater than 10%. Five rules were identified as potentially relevant for clinical practice, including combinations of 3 to 4 variables: unwitnessed, unmonitored, initial rhythm of asystole, and resuscitation duration of 5 or more or 10 or more minutes. All rules included unwitnessed and an initial rhythm of asystole. The specific combination of variables for each rule is presented in **Table 2**.

The 5 rules had low false-positive rates, ranging from 0.5% (95% CI, 0.2%-1.0%) to 0.9% (95% CI, 0.5%-1.5%). Positive rates were relatively consistent across rules, ranging from 12% (95% CI, 11%-12%) to 14% (95% CI, 14%-15%). The best-performing rule (rule 1) had a false-positive rate of 0.5% with an upper confidence limit lower than 1% and incorporated 4 variables: unwitnessed, unmonitored, initial rhythm of asystole, and resuscitation duration of 10 minutes or longer.

Additional details are provided in Supplement 1, including a comprehensive list of metrics for the 5 rules (eTables 2-6 in Supplement 1), an illustration of how rule 1 could be applied in a clinical setting (**Figure 2**), and a list of all 109 rules considered by the investigators (eTable in Supplement 2).

Validation Cohorts

The Swedish and Norwegian cohorts were used to validate the 5 rules for predicting 30-day mortality. Of the included patients, 8810 (69%) in Sweden and 972 (74%) in Norway died within 30 days.

In the Swedish cohort, false-positive rates varied from 0.7% (95% CI, 0.3%-1.2%) to 1.5% (95% CI, 0.9%-2.1%), and positive rates ranged from 10% (95% CI, 9.6%-11%) to 13% (95% CI, 12%-13%). In the Norwegian cohort, false-positive rates varied from 0.0% (95% CI, incalculable) to 0.7% (95% CI, 0.0%-2.2%), and positive rates ranged from 9.9% (95% CI, 8.3%-12%) to 12% (95% CI, 10%-14%). Some rules had zero false-positive cases in the Norwegian cohort, resulting in incalculable CIs (Table 2; eTables 2-6 in Supplement 1).

The best-performing rule (rule 1) maintained a low false-positive rate in both cohorts, with a false-positive rate of 0.7% (95% CI, 0.3%-1.2%) in Sweden and no false-positive cases in Norway.

Secondary Outcomes

The 5 rules were applied to the combined cohort to predict the secondary outcomes. Incomplete data for these outcomes were minimal, ranging from 1% to 6% (Table 1). For patients with

Table 1. Patient Characteristics

Characteristic	No (%) Combined (N = 23 952)	Denmark (n = 9863)	Sweden (n = 12 781)	Norway (n = 1308)
Demographics				
Age, median (IQR), y	74 (66-81)	74 (66-81)	74 (66-82)	74 (65-81)
Mean (SD)	72 (13)	72 (13)	72 (13)	72 (13)
Sex[a]				
Male	15 114 (63)	6266 (64)	8010 (63)	838 (64)
Female	8834 (37)	3597 (36)	4767 (37)	470 (36)
Event characteristics				
Location				
Intensive care unit	5285 (22)	1331 (13)	3660 (29)	294 (22)
Not intensive care unit	18 667 (78)	8532 (87)	9121 (71)	1014 (78)
Witnessed				
Yes	18 967 (79)	7674 (78)	10 249 (80)	1044 (80)
No	4985 (21)	2189 (22)	2532 (20)	264 (20)
Monitored				
Yes	13 118 (55)	4913 (50)	7529 (59)	676 (52)
No	10 834 (45)	4950 (50)	5252 (41)	632 (48)
Initial rhythm				
Shockable rhythm	5400 (23)	1813 (18)	3263 (26)	324 (25)
Pulseless electrical activity	9046 (38)	4415 (45)	4051 (32)	580 (44)
Asystole	9506 (40)	3635 (37)	5467 (43)	303 (31)
Resuscitation duration, median (IQR), min	13 (5-23)	14 (7-23)	12 (4-22)	14 (7-27)
Mean (SD)	16 (14)	17 (15)	15 (13)	19 (18)
Outcomes				
No ROSC[b]				
Yes	11 792 (50)	5024 (52)	6095 (48)	673 (51)
No	11 867 (50)	4674 (48)	6558 (52)	635 (49)
Mortality at 30 d				
Yes	17 424 (73)	7642 (77)	8810 (69)	972 (74)
No	6528 (27)	2221 (23)	3971 (31)	336 (26)
Poor neurological status[c,d]				
Yes	8888 (74)	NA	8888 (74)	NA
No	3061 (26)	NA	3061 (26)	NA
Mortality at 1 y[e]				
Yes	18 331 (79)	7980 (84)	9365 (75)	986 (75)
No	4976 (21)	1499 (16)	3155 (25)	322 (25)

Abbreviations: ROSC, return of spontaneous circulation; NA, not applicable.

[a] Incomplete data on 4 patients (<1%) in Sweden.

[b] Incomplete data on 293 patients (1%) (Denmark, 165 [2%]; Sweden, 128 [1%]).

[c] Incomplete data on 832 patients (6%) in Sweden.

[d] Cerebral Performance Category score of 3 to 5 at hospital discharge.

[e] Incomplete data on 645 patients (3%) (Denmark, 384 [4%]; Sweden, 261 [2%]).

complete data, 11 792 (50%) did not achieve return of spontaneous circulation, 8888 (74%) had poor neurological status, and 18 331 (79%) died within 1 year (Table 1).

For the outcome of no return of spontaneous circulation, false-positive rates were substantially higher than the primary outcome, ranging from 12% (95% CI, 11%-13%) to 13% (95% CI, 12%-14%), suggesting that the rules were unreliable for predicting immediate outcomes. The results for poor neurological status and 1-year mortality were similar to the primary outcome (**Table 3**; eTables 7-11 in Supplement 1).

Additional Analyses

In the combined cohort, the best-performing rule (rule 1) maintained a low false-positive rate of 0.6% (95% CI, 0.3%-0.9%) and a positive rate of 11% (95% CI, 10%-11%) for predicting 30-day mortality (Table 3; eTables 2-6 in Supplement 1).

The performance of the 5 rules was evaluated in patients less likely to be biased by self-fulfilling prophecies related to terminating resuscitation (Table 3; eTables 12-16 in Supplement 1). In patients younger than 65 years, results were similar to the main analyses. In patients with a resuscitation du-

Table 2. Final Termination of Resuscitation Rules

Variable	Rule 1[a]	2	3	4	5
Variables					
No. of variables	4	3	4	3	3
Monitored status	No		No	No	
Witnessed status	No	No	No	No	No
Initial rhythm	Asystole	Asystole	Asystole	Asystole	Asystole
Resuscitation duration, min	≥10	≥10	≥5	NA[b]	≥5
Key metrics, % (95% CI)					
Denmark					
Positive rate	12 (11-12)	12 (11-13)	14 (13-14)	14 (13-15)	14 (14-15)
False-positive rate	0.5 (0.2-1.0)	0.7 (0.3-1.2)	0.7 (0.3-1.2)	0.9 (0.4-1.4)	0.9 (0.5-1.5)
Sweden					
Positive rate	10 (10-11)	11 (10-11)	12 (11-12)	12 (12-13)	13 (12-13)
False positive rate	0.7 (0.3-1.2)	1.0 (0.5-1.6)	1.0 (0.5-1.5)	1.4 (0.8-2.0)	1.5 (0.9-2.1)
Norway					
Positive rate	9.9 (8.3-12)	10 (8.5-12)	12 (9.8-13)	12 (10-14)	12 (10-14)
False positive rate	0 (NA)	0 (NA)	0.7 (0.0-2.2)	0.6 (0.0-2.1)	0.7 (0.0-2.1)

Abbreviation: NA, not applicable.

[a] Best-performing rule.

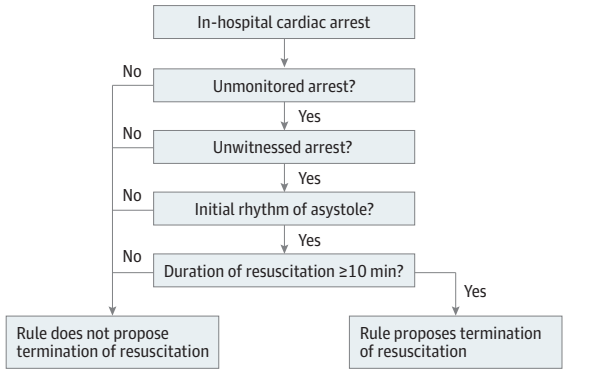
[b] This variable was not included in the model.

ration of 20 minutes or longer, false-positive rates were lower, ranging from 0.2% (95% CI, 0.0%-0.4%) to 0.5% (95% CI, 0.2%-0.9%), and positive rates were higher, ranging from 15% (95% CI, 14%-15%) to 15% (95% CI, 15%-16%).

In the original 3 cohorts, 6131 patients (20%) had missing data on at least 1 variable considered for the decision rules (mean [SD] missing variables per patient, 0.2 [0.4]), most often initial rhythm and resuscitation duration (eTable 17 in Supplement 1). The results of the multiple imputation analysis were similar to the primary analysis, albeit with systematically lower positive rates by 2 to 3 percentage points (Table 3; eTable 18 in Supplement 1).

When applying the UN10 rule to the combined cohort, the false-positive rate was 1.6% (95% CI, 1.2%-2.0%) and the positive rate was 15% (95% CI, 15%-16%).

Figure 2. Sample Decision Tree for Best-Performing Rule



An illustration of how the best-performing rule (rule 1) could be applied in clinical practice.

Discussion

We developed and validated 5 termination of resuscitation rules for in-hospital cardiac arrest using data from national registries in Denmark, Sweden, and Norway. The best-performing rule included 4 variables: unwitnessed, unmonitored, initial rhythm of asystole, and resuscitation duration of 10 minutes or longer. The performance of the rules was similar across all cohorts and for most secondary outcomes, although the rules did not reliably predict no return of spontaneous circulation.

The 5 rules developed in this study had consistently low false-positive rates and clinically relevant positive rates across the Danish, Swedish, and Norwegian cohorts. In the combined cohort, the best-performing rule (rule 1) had a false-positive rate of 0.6% (95% CI, 0.3%-0.9%), meaning that for every 1000 patients where the rule proposes termination, approximately between 3 to 9 patients might otherwise survive to 30 days. The positive rate of 11% (95% CI, 10%-11%) indicates that the rule would propose termination in a meaningful proportion of cases, potentially reducing futile resuscitation attempts.

An example of how the best-performing rule could be applied in clinical practice is provided in Supplement 1 (Figure 2). According to the rule, in a hospitalized patient with a nonmonitored and nonwitnessed cardiac arrest, for which the initial rhythm is asystole, and resuscitation has been attempted for 7 minutes, resuscitation should not be terminated. If resuscitation was still ongoing at 10 minutes, the decision rule would be revisited, now proposing that resuscitation can be terminated. In contrast, the rule would never propose termination of resuscitation in cardiac arrests that are monitored, witnessed, or where the initial rhythm is not asystole.

Table 3. Additional Analyses in the Combined Cohort

Variable	Rule, % (95% CIs)				
	1[a]	2	3	4	5
Primary outcome					
Mortality at 30 d					
Positive rate	11 (10-11)	11 (11-12)	13 (12-13)	13 (12-13)	13 (13-14)
False-positive rate	0.6 (0.3-0.9)	0.8 (0.5-1.2)	0.9 (0.6-1.2)	1.1 (0.8-1.5)	1.2 (0.8-1.6)
Secondary outcomes					
No ROSC					
Positive rate	11 (10-11)	11 (11-12)	13 (12-13)	13 (13-13)	13 (13-14)
False-positive rate	12 (11-13)	12 (11-14)	12 (11-14)	13 (11-14)	13 (12-14)
Poor neurological status[b]					
Positive rate	11 (10-11)	11 (11-12)	13 (12-13)	13 (12-14)	13 (13-14)
False-positive rate	0.5 (0.2-0.9)	0.6 (0.2-1)	0.6 (0.3-1)	0.9 (0.5-1.4)	0.9 (0.4-1.4)
Mortality at 1 y					
Positive rate	11 (11-11)	12 (11-12)	13 (13-13)	13 (13-14)	14 (13-14)
False-positive rate	0.4 (0.2-0.7)	0.6 (0.3-0.9)	0.5 (0.3-0.8)	0.7 (0.4-1)	0.8 (0.5-1.1)
Sensitivity analyses[c]					
Age <65 y					
Positive rate	9.8 (9.0-11)	10 (9.3-11)	11 (9.7-11)	11 (9.9-12)	11 (10-12)
False-positive rate	0.6 (0.0-1.3)	0.7 (0.2-1.5)	1.1 (0.3-2.0)	1.2 (0.4-2.2)	1.2 (0.4-2.2)
Duration ≥20 min					
Positive rate	15 (14-15)	15 (15-16)	15 (14-15)	15 (14-15)	15 (15-16)
False-positive rate	0.2 (0.0-0.4)	0.5 (0.2-0.9)	0.2 (0.0-0.4)	0.2 (0.0-0.4)	0.5 (0.2-0.9)
Multiple imputation					
Positive rate, median (IQR)	8.6 (8.6-8.6)	9.1 (9.1-9.1)	10 (10-10)	11 (11-11)	11 (11-11)
False-positive rate, median (IQR)	0.6 (0.6-0.6)	0.8 (0.8-0.8)	0.9 (0.9-0.9)	1.2 (1.2-1.2)	1.2 (1.2-1.2)

Abbreviations: ROSC, return of spontaneous circulation; NA, not applicable.

[a] Best-performing rule.

[b] Cerebral Performance Category score of 3 to 5.

[c] For the primary outcome of 30-day mortality.

The performance of the rules in the Swedish and Norwegian cohorts was largely consistent with the results of the Danish cohort, supporting their generalizability within Scandinavian health care systems. The estimates also need to be considered in relation to the prevalence of 30-day mortality. When considering the rules in settings with higher or lower mortality rates, such as 90% and 60%, the false-positive rate of the best-performing rule (rule 1) would decrease to 0.2% or increase to 1.2%, respectively, assuming a constant specificity. The identified termination of resuscitation rules should ideally be validated in local, regional, or national cohorts prior to implementation and revisited as survival rates changes.

The absence of a validated termination of resuscitation rule for in-hospital cardiac arrests has been a knowledge gap in the cardiac arrest literature.[3] This knowledge gap may trigger clinicians to use unvalidated rules or homemade heuristics during resuscitation, leading to inappropriately early termination of resuscitation, and potential lives lost.[15] A US study[16] of 64 339 in-hospital cardiac arrests found that hospitals with longer resuscitation durations (25 vs 16 minutes) had higher rates of both return of spontaneous circulation and survival to discharge, suggesting that early termination of resuscitation at a hospital level might decrease survival. Using validated termination of resuscitation rules might avoid inappropriate termination of resuscitation and hence increase overall survival.

A systematic review identified only 3 studies aimed at developing and validating the UN10 rule for in-hospital cardiac arrest.[3] The rule included 3 variables: unwitnessed, initial nonshockable rhythm, and resuscitation duration of more than 10 minutes.[17] Although the rule had a false-positive rate of 0% in the derivation cohort, later validation revealed a false-positive rate of 1.1% in a single-center cohort and 6.3% in the GWTG-R registry, making the rule unreliable for clinical use.[4,18] In the Scandinavian cohort, the UN10 rule had a false-positive rate of 1.6% and positive rate of 15%, suggesting that the rule was able to identify a large proportion of potential cases for termination, but with the trade-off of exceeding the acceptable false positive threshold of 1% for clinical use.[11] The performance differences of the UN10 rule in our Scandinavian data and the GWTG-R registry suggest that the rules identified in our study may not be generalizable to the US.

Bias from self-fulfilling prophecies is a major concern in studies of termination rules. This bias may occur if clinicians terminate resuscitation early based on expected poor outcomes, derived from the variables included in the rule, thereby inflating the performance of the rules. Our sensitivity analyses provided some evidence against such bias. In patients with an actual prolonged resuscitation of 20 minutes or more, where resuscitation efforts were not terminated early, the false-positive rates were lower (0.2% to 0.5% across rules) than in

the full cohort (0.6% to 1.2% across rules; Table 3). This observation supports the validity of our main results. The results in patients younger than 65 years, as a proxy for not terminating resuscitation early, were similar to the main analyses, further supporting the robustness of our findings.

Limitations

The results should be interpreted in the context of some limitations. First, the study leveraged data from Denmark, Sweden, and Norway, and the rules may not be generalizable to other settings (comparisons with US and UK characteristics are reported in eTable 19 in Supplement 1). Second, we were limited by the availability of variables across the 3 cohorts. Other factors, such as rhythm transitions during the cardiac arrest, may have increased the performance of the rules. Third, missing data varied across the cohorts: 10% in the Danish cohort, 25% in the Swedish cohort, and 36% in the Norwegian cohort (eTable 17 in Supplement 1). Multiple imputation analyses yielded similar results as the primary analyses, providing some reassurance in the performance of the rules. Fourth, data from the 3 registries were collected between 2007 and 2022, including periods of the COVID-19 pandemic. However, annual reports from these registries showed no decrease in survival rates for in-hospital cardiac arrests during the COVID-19 period, suggesting the pandemic likely did not affect our results (eFigure in Supplement 1).[6-8] Lastly, the 5 termination rules were selected based on author discussion. Other teams may have favored alternative rules based on their specific preferences and risk profiles.

Conclusions

We developed and validated 5 termination of resuscitation rules for in-hospital cardiac arrest. The rules had low false-positive rates and reasonable positive rates for predicting mortality and poor neurological status in cohorts from Denmark, Sweden, and Norway, indicating potential clinical utility in these settings. These rules may aid decision-making during resuscitation.

ARTICLE INFORMATION

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