Predicting Cardiac Arrest on the Wards

A Nested Case-Control Study

Matthew M. Churpek, MD, MPH; Trevor C. Yuen, BA; Michael T. Huber, BA;
Seo Young Park, PhD; Jesse B. Hall, MD, FCCP; and Dana P. Edelson, MD

Background: Current rapid response team activation criteria were not statistically derived using ward vital signs, and the best vital sign predictors of cardiac arrest (CA) have not been determined. In addition, it is unknown when vital signs begin to accurately detect this event prior to CA.

Methods: We conducted a nested case-control study of 88 patients experiencing CA on the wards of a university hospital between November 2008 and January 2011, matched 1:4 to 352 control subjects residing on the same ward at the same time as the case CA. Vital signs and Modified Early Warning Scores (MEWS) were compared on admission and during the 48 h preceding CA.

Results: Case patients were older (64 ± 16 years vs 58 ± 18 years; $P = .002$) and more likely to have had a prior ICU admission than control subjects (41% vs 24%; $P = .001$), but had similar admission MEWS (2.2 ± 1.3 vs 2.0 ± 1.3 ; $P = .28$). In the 48 h preceding CA, maximum MEWS was the best predictor (area under the receiver operating characteristic curve [AUC] 0.77; 95% CI, 0.71-0.82), followed by maximum respiratory rate (AUC 0.72; 95% CI, 0.65-0.78), maximum heart rate (AUC 0.68; 95% CI, 0.61-0.74), maximum pulse pressure index (AUC 0.61; 95% CI, 0.54-0.68), and minimum diastolic BP (AUC 0.60; 95% CI, 0.53-0.67). By 48 h prior to CA, the MEWS was higher in cases ($P = .005$), with increasing disparity leading up to the event.

Conclusions: The MEWS was significantly different between patients experiencing CA and control patients by 48 h prior to the event, but includes poor predictors of CA such as temperature and omits significant predictors such as diastolic BP and pulse pressure index. *CHEST* 2012; 141(5):1170-1176

Abbreviations: AUC = area under the receiver operating characteristic curve; AVPU = alert, responsive to voice, responsive to pain, and unresponsive; CA = cardiac arrest; MEWS = Modified Early Warning Score; ROC = receiver operating characteristic; RRT = rapid response team; T_0 = time of case patient cardiac arrest

More than 150,000 adult in-hospital cardiac arrests (CAs) occur in the United States each year, with up to half occurring outside of intensive care settings.^{1,2} Mortality for these patients is > 80%, but there is evidence to suggest that some of these deaths may be preventable.^{1,3} Rapid response teams (RRTs) were created to decrease adverse outcomes by bringing crit-

ical care resources to deteriorating patients on the hospital wards. However, results have been mixed, with some studies demonstrating benefit but others showing no improvement in mortality and hospital-wide CA rates.⁴⁻⁶

A major cited weakness of the RRT is the failure to identify patients in sufficient time to intervene prior to CA.⁷⁻⁹ For example, in the Medical Emergency Response Intervention Trial (MERIT), the only multicenter randomized trial of RRTs, most patients were identified < 15 min before CA, death, or ICU transfer.^{6,7} Furthermore, the criteria used to activate the intervention had a sensitivity < 50%.^{6,7} Currently, there are > 50 different published criteria designed

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Affiliations: From the Section of Pulmonary and Critical Care (Drs Churpek and Hall), Section of Hospital Medicine (Mr Yuen and Dr Edelson), Pritzker School of Medicine (Mr Huber), and Department of Health Studies (Dr Park), University of Chicago, Chicago, IL.

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Correspondence to: Dana Edelson, MD, Section of Hospital Medicine, University of Chicago, 5841 S Maryland Ave, MC 5000, Chicago, IL 60637; e-mail: dperes@uchicago.edu

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to detect physiologic decline and activate the RRT, and each use varying vital sign combinations.^{10,11} However, these criteria, including the frequently described Modified Early Warning Score (MEWS) (Fig 1),¹²⁻¹⁴ are based on expert opinion rather than being derived using ward vital signs, and most have not been scientifically validated.

It is unknown whether further optimization of vital sign selection and thresholds would improve rapid response systems or whether vital sign changes occur too late in the course of physiologic deterioration to alter outcomes. To address these gaps in knowledge, we investigated the accuracy of the MEWS and of vital signs routinely collected on the wards, including systolic and diastolic BP, pulse pressure, heart rate, respiratory rate, oxygen saturation, mental status, and temperature, for predicting CA on the wards. We also evaluated the MEWS at different time points prior to CA to determine when the vital signs of these patients begin to differ significantly from other patients on the ward.

MATERIALS AND METHODS

Study Setting and Population

We conducted a retrospective nested case-control study at an academic, tertiary care hospital with approximately 500 inpatient beds grouped by clinical service. Our hospital has had an RRT in place since 2008 that is led by a critical care nurse and respiratory therapist with consultation from a hospitalist physician and/or pharmacist upon request. The RRT activation criteria include “tachypnea,” “tachycardia,” “hypotension,” and “staff worry,” but specific vital sign thresholds are not stated. This team is separate from the team that responds to a CA.

Cases were consecutive adult patients who experienced a CA, defined as the loss of a palpable pulse with attempted resuscitation, on the ward between November 1, 2008, and January 31, 2011. All patients residing on the same ward at the time (T_0) of the case patient's CA were eligible to be control subjects. Four control subjects were then selected for each case patient using a random number generator.

Case patients were identified using a prospectively collected and verified CA quality improvement database. Our process of data collection on patients who had a CA has been previously described.¹⁵⁻¹⁷ Briefly, trained data abstractors are paged concurrently with the CA response team, and follow-up within 48 h of the event to download the transcripts for every resuscitation on our hospital wards and ICUs. Each transcript is then reviewed and cross-referenced with the medical record to verify that those classified as having a true CA did indeed have a loss of pulse with attempted resuscitation. Patients were excluded if they had no ward vital signs in the 48 h prior to T_0 . If a case patient had more than one CA on the ward during the hospitalization, only the first event was included.

The study protocol, consent, and data collection mechanisms were approved by the University of Chicago Institutional Review Board (no. 16995A). A waiver of consent was granted on the basis of minimal harm and general impracticability. Collection of patient information was designed to comply with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) regulations.

Data Collection

Patient demographic data were obtained from administrative databases. Time and location stamped vital signs, including temperature, heart rate, BP, oxygen saturation, respiratory rate, and mental status, were obtained from the electronic medical record (EPIC) on admission and from 48 h prior to until 30 min before T_0 . Vital signs within 30 min of T_0 were excluded because the goal was to predict CA early enough to potentially intervene. Pulse pressure (systolic BP – diastolic BP) and pulse pressure index (pulse pressure divided by systolic BP) were also calculated. For each vital sign, change from baseline was calculated by subtracting each patient's closest value prior to 30 min before T_0 by the admission value.

Mental status was collapsed from four drop-down menu fields in the electronic medical record (orientation, level of consciousness, motor response, and responsiveness) into one score (alert, responsive to voice, responsive to pain, and unresponsive [AVPU]).¹⁸ Because AVPU was not specifically available in our medical record, we recoded mental status as “alert” if “alert” was documented in either the level of consciousness or the orientation field. “Responsive to voice” was coded if “to voice” was documented in the responsiveness field or if “easy to arouse” was documented in the level of consciousness field. We recoded mental status as “responsive to pain” if “localizes” or “withdraws” was documented in the motor response field or if “to pain” was documented in the responsiveness field. Finally, “unresponsive” was coded if “comatose” or “does not arouse” was found in the level of consciousness field or if “unresponsive” was documented in the responsiveness field. For each time point, the patient's best mental status was used for AVPU recoding.

A MEWS was calculated for each patient on admission using the first respiratory rate, heart rate, systolic BP, temperature, and mental status documented in the hospital regardless of location, and then every 8 h during the 48-h time period prior to T_0 using the closest vital signs measured prior to that time point. The MEWS was used in this study because it is the most commonly cited multiparameter RRT activation criteria.¹⁹⁻²¹ A normal value for mental status (ie, “alert”) was imputed for patients without any mental status documentation, similar to previous studies evaluating clinical scoring systems.^{22,23}

Statistical Analysis

Baseline characteristics as well as admission and change from baseline vitals signs and MEWS were compared between case and control patients using χ^2 tests for categorical data and t tests or Wilcoxon rank-sum tests for continuous data, as appropriate. The maximum and minimum recorded values of each vital sign and MEWS in the 48 h preceding T_0 were compared by creating receiver operating characteristic (ROC) curves and then calculating the area under the ROC curve (AUC) using the trapezoidal rule. The sensitivities and specificities of different cutoff thresholds were investigated for predictors with an AUC of at least 0.6. CIs for the AUC, sensitivity, and specificity of vital signs and MEWS were calculated using bootstrapping, a nonparametric method that involved taking 1,000 samples of the data with replacement to obtain an empirical sampling distribution.²⁴ All tests of significance used a 2-sided $P < .05$. Statistical analyses were completed using R (R Foundation for Statistical Computing) and Stata, version 11.1 (StataCorp).

RESULTS

Patient Characteristics

During the study period there were 55,121 hospital admissions, 436 index CAs (7.9 arrests per

Score	3	2	1	0	1	2	3
Respiratory rate		≤8		9-14	15-20	21-29	>29
Heart rate		≤40	41-50	51-100	101-110	111-129	>129
Systolic BP	≤70	71-80	81-100	101-199		≥200	
Temperature		≤35	35.1-36	36.1-38	38.1-38.5	≥38.6	
Neurological				Alert	Voice	Pain	Unresp

FIGURE 1. Modified Early Warning Score (MEWS). Unresp = Unresponsive.

1,000 admissions), and 462 RRT calls (8.4 calls per 1,000 admissions).

Eighty-nine patients experienced a CA on the ward during the study period. One patient had no ward vital signs prior to CA and was excluded. Eighty-eight case patients were matched to 352 control subjects. Patient demographic data are shown in Table 1. Seventy-three percent of admissions were medical, and 27% were surgical. Case patients were older (mean age 64 ± 16 years vs 58 ± 18 years; $P = .002$), had been hospitalized longer prior to T_0 , and were more likely to have had a prior RRT call (15% vs 2%; $P < .001$) or ICU admission (41% vs 24%; $P = .001$). For cases, RRT calls occurred a median of 3.9 h (interquartile range [IQR], 0.6-211.9) prior to CA, with seven (53.8%) occurring within 24 h of the arrest. Forty-three percent of case patients and 40% of control subjects were transferred to the ICU following their RRT call ($P = .78$). Survival to dis-

charge was lower in case patients (31% vs 99%; $P < .001$).

Vital Sign Comparisons

Vital signs were similar on admission except case patients had lower diastolic BP (Table 1). The AUCs for different maximum and minimum vital signs and MEWS are shown in Table 2. Maximum MEWS had the highest AUC (0.77; 95% CI, 0.71-0.82), followed by maximum respiratory rate (0.72; 95% CI, 0.65-0.78), maximum heart rate (0.68; 95% CI, 0.61-0.74), maximum pulse pressure index (0.61; 95% CI, 0.54-0.68), and minimum diastolic BP (0.60; 95% CI, 0.53-0.67). Maximum pulse pressure performed similarly to pulse pressure index (data not shown). The AUCs for systolic BP, temperature, and oxygen saturation were not statistically significant. The sensitivities and specificities of different vital sign cutoff values are shown in Table 3.

Vital Sign Change Over Time

From admission to 30 min prior to T_0 , heart rate and respiratory rate increased in case patients by $9.6\% \pm 27\%$ ($P = .002$) and $9.3\% \pm 28\%$ ($P < .0001$), respectively, without significant change in control subjects (Figure 2). Systolic BP fell in both groups, while diastolic BP decreased and pulse pressure index increased in control patients. However, these changes were not significantly different between the two groups. The mean MEWS was similar between case patients and control subjects on admission (2.2 ± 1.3 vs 2.0 ± 1.3 ; $P = .28$), but was significantly higher in case patients than control subjects at 48 h (2.1 ± 1.0 vs 1.6 ± 1.0 ; $P = .005$) and 24 h (2.3 ± 1.3 vs 1.5 ± 0.9 ; $P < .001$) prior to T_0 (Figure 3).

DISCUSSION

In this longitudinal nested case-control study, we demonstrated that patients who experience a CA on the ward have vital signs that are similar to other

Table 1—Patient Characteristics

Characteristic	Case Patients (n = 88)	Control Subjects (n = 352)	P Value
Mean age, y (SD)	64 (16)	58 (18)	.002
Female sex	50 (57)	179 (51)	.32
Admitting service			.95
Cardiac medical	18 (20)	75 (21)	
Cardiac surgical	8 (9)	27 (8)	
Noncardiac medical	47 (53)	184 (52)	
Noncardiac surgical	15 (17)	66 (19)	
Mean admission vital signs (SD)			
Systolic BP, mm Hg	129 (29)	129 (24)	.86
Diastolic BP, mm Hg	71 (18)	75 (17)	.04
Heart rate, min	91 (19)	90 (21)	.81
Respiratory rate, min	20 (3)	20 (3)	.17
Temperature, °C	36.2 (0.7)	36.3 (0.7)	.07
Oxygen saturation, %	96 (8)	97 (3)	.26
Median days since admission (IQR)	7 (1-15)	3 (1-7)	.006
Prior RRT call	13 (15)	8 (2)	< .001
Prior ICU admission	36 (41)	83 (24)	.001
Survived to discharge	27 (31)	347 (99)	< .001

Data are shown as No. (%) unless otherwise specified. IQR = interquartile range; RRT = rapid response team.

Table 2—AUC of Different Vital Signs and MEWS

Vital Sign	Maximum	Minimum
Respiratory rate	0.72 (0.65-0.78)	0.56 (0.49-0.62)
Heart rate	0.68 (0.61-0.74)	0.56 (0.49-0.63)
Diastolic BP	0.53 (0.45-0.60)	0.60 (0.53-0.67)
Systolic BP	0.55 (0.48-0.62)	0.58 (0.50-0.65)
Pulse pressure index	0.61 (0.54-0.68)	0.58 (0.50-0.65)
Temperature	0.48 (0.42-0.56)	0.55 (0.48-0.63)
Oxygen saturation	...	0.54 (0.47-0.61)
MEWS	0.77 (0.71-0.82)	...

Data shown are AUC (95% CI). AUC = area under the receiver operating characteristic curve; MEWS = Modified Early Warning Score.

patients on admission but significantly different in the 48 h prior to the event. The most accurate individual predictors of CA were maximum respiratory rate, heart rate, pulse pressure index, and minimum diastolic BP. Our results have significant implications for the detection arm of the RRT because most activation criteria use poor predictors of ward CA such as systolic BP, temperature, hypoxia, and bradycardia.^{10,11,13} By identifying the best predictors of CA, our study provides direction regarding which predictors should be included in future derivation studies of RRT activation criteria. In addition, our findings suggest that for many patients there is ample time prior to CA to provide potentially life-saving interventions.

Importantly, we found that minimum diastolic BP and maximum pulse pressure index were significant predictors of CA. To our knowledge, no study has evaluated the accuracy of these variables for predicting CA on the ward. Although sepsis can cause an increasing pulse pressure and decreasing diastolic BP, the fact that these variables changed similarly between the two patient groups over time suggests other explanations are also possible. Interestingly, low diastolic BP has also been associated with increased levels of atherosclerosis and cardiovascular disease.²⁵ Similarly, a high pulse pressure has been associated with adverse cardiovascular outcomes such as myocardial infarction, stroke, and increased cardiovascular mortality.²⁶⁻²⁹ Some authors have suggested that pulse pressure index may be superior to pulse pressure, as the latter has no relationship to the absolute BP.²⁸ Therefore, although systolic BP is commonly used in RRT activation criteria,^{10,11} incorporation of pulse pressure, pulse pressure index, or diastolic BP in place of systolic BP into the predictive model may be superior. Future studies should validate the utility and predictive ability of these variables for predicting CA and other serious adverse events. In addition, as pulse pressure is less intuitive than other vital signs and requires a calculation, automated derivation in the electronic medical record may be necessary for this predictor to be most effective.

Other investigators have also demonstrated that systolic BP is a poor predictor of clinical deterioration. In a prior case-control study in surgical patients, Cuthbertson et al³⁰ found that there was no significant difference in mean systolic BP between groups in the 24 h prior to ICU transfer. Similarly, Fieselmann et al³¹ found that systolic BP was a poor predictor of CA in medical patients. In contrast, Cretikos and colleagues³² reported that a systolic BP reading ≤ 90 mm Hg had a sensitivity of 34% and specificity of 93% for a combined end point of ICU transfer, death, or CA.

Similar to our study, all three of the previous case-control studies found that respiratory rate was the best vital sign predictor of adverse outcomes on the ward.³⁰⁻³² This may be because many causes of CA on the ward, including pulmonary embolism, sepsis, myocardial infarction, and respiratory failure, are associated with tachypnea.^{2,3,33,34} Importantly, the RRT activation criteria in the MERIT study used a respiratory rate cutoff of > 36 breaths/min.⁶ This threshold in our study had a sensitivity of $< 20\%$ for detecting CA, similar to the 18% sensitivity for the combined end point reported by Cretikos and colleagues.³² One difficulty in choosing an ideal cutpoint is that respiratory rate is often inaccurately measured and poorly documented in hospitalized patients.^{8,35,36} Automated methods, such as transthoracic impedance, have

Table 3—Sensitivity and Specificity of Different Vital Sign and MEWS Cutoff Values

Vital Sign	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Maximum respiratory rate, min		
> 20	67 (56-77)	70 (51-80)
> 22	49 (38-60)	86 (78-92)
> 24	32 (20-43)	94 (89-97)
> 26	25 (13-37)	96 (92-99)
Maximum heart rate, min		
> 110	44 (29-57)	80 (70-88)
> 120	28 (18-40)	92 (81-98)
> 130	19 (9-29)	97 (92-99)
Maximum pulse pressure index		
> 0.55	49 (38-61)	67 (56-80)
> 0.6	29 (18-40)	85 (77-92)
> 0.65	14 (7-24)	94 (88-98)
Minimum diastolic BP, mm Hg		
< 50	45 (33-55)	77 (57-84)
< 45	29 (17-38)	90 (79-96)
< 40	16 (7-28)	96 (92-99)
Maximum MEWS		
> 2	69 (61-83)	69 (59-83)
> 3	51 (33-58)	87 (76-90)
> 4	24 (13-39)	95 (92-99)
> 5	8 (2-21)	98 (96-100)

See Table 2 legend for expansion of abbreviations.

FIGURE 2. Change in individual vital signs from admission. For each vital sign, change from admission was calculated by subtracting each patient's closest value prior to time of case patient cardiac arrest (T_0) by the admission value. P values refer to case patient vs control subject change from baseline comparisons. An asterisk signifies that the change from baseline for the individual vital sign is statistically significant.

been created to overcome human error, but questions remain regarding their accuracy.³⁶ It is unknown how more accurate documentation of respiratory rate would alter its ability to accurately identify patients at risk for adverse outcomes.

Although reports of its implementation are widespread, the MEWS was not derived using ward vital signs.^{13,14,37,38} As illustrated in our study and suggested by other groups,^{7,13,39,40} it contains variables that are poor predictors of CA such as temperature, systolic BP, and bradycardia. One study derived and validated a risk prediction model using admission vital signs,³⁹ but similar studies using ward vital signs are lacking. Given that we found the most predictive changes to occur after admission, a scoring system derived using ward vital signs would likely have improved accuracy for detecting clinical deterioration.

Our finding that the MEWS of case patients were similar to control subjects on admission but then differed significantly at 48 h prior to the event demonstrates that while some studies have suggested that vital signs measured in the ED can determine the need for higher level care,¹³ they may not reliably predict which patients will go on to have a ward CA. Also, our findings confirm those of previous case series demonstrating that patients begin to show abnormal physiology several hours prior to the event.^{3,33,34} This suggests that many patients can be identified prior to CA, enabling potentially life-saving interventions.

One of the strengths of our study is how control patients were identified. By selecting control subjects on the same ward at the same time as the matched case patient, we controlled for factors other than vital signs that may contribute to CA risk such as day of week and nurse staffing ratios. Previous studies

selected control subjects admitted during a specified period of time that may not have coincided with their matched case patient admission.^{30-32,41} In addition, other studies matched on characteristics other than the admission type or ward, such as age and sex, which makes control subjects less representative of the hospitalized population and therefore the results less useful in clinical practice.^{31,32}

This study has several limitations. First, because this was a single-center study at a tertiary care hospital, the results may not be generalizable to some hospitals. Our survival-to-discharge rate of 31% for our CA patients is higher than the average reported by previous large studies.^{2,42} However, our hospital is actively involved in several cardiopulmonary resuscitation quality improvement projects that have previously been described,^{15,16} and this survival rate is within the range reported in the literature.⁴³⁻⁴⁵ In addition, our goal was to investigate vital sign changes before CA, and postarrest survival was not a focus of the study. Second, our case-control design did not allow us to calculate positive and negative predictive values. Finally, when calculating the MEWS every 8 h, not all vital signs were simultaneously collected and therefore imputation was sometimes necessary. However, by imputing the previously collected value if a vital sign was missing, we simulated what clinicians often do in practice.

In conclusion, we have shown that vital signs correlate with CA on the ward. Although similar on admission, the MEWS differs between case and control patients at least 48 h prior to the event. Because many

FIGURE 3. Change in MEWS over time. Vital signs on admission and in the 48 h prior to T_0 were used to calculate MEWS scores, and comparisons were made between case and control mean scores at 8-h time points in the 48 h prior to T_0 . See Figure 1 and 2 legends for expansion of abbreviations.

published RRT activation criteria use poor predictors of CA such as temperature, minimum heart rate, and minimum respiratory rate, further work into deriving and validating a CA prediction tool is essential. Although individual vital signs are modest predictors of CA, deriving a scoring system using combinations of vital signs would likely result in a more accurate system. The next step will involve deriving a CA risk prediction model that uses the predictors we identified in this study. This would allow maximum sensitivity while minimizing false positives, decreasing the unnecessary burden on the RRT and giving it the best chance to improve outcomes.

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Dr Churpek: contributed to the design of the study, data analysis, and manuscript preparation.

Mr Yuen: contributed to data collection and revisions to the manuscript.

Mr Huber: contributed to design of the study, data collection, and revisions to the manuscript.

Dr Park: contributed to data analysis and revisions to the manuscript.

Dr Hall: contributed to the design of the study and revisions to the manuscript.

Dr Edelson: contributed to the design of the study, data analysis, and manuscript preparation.

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