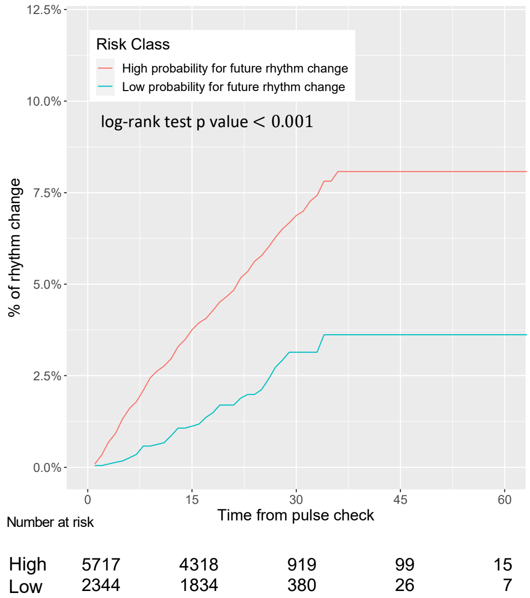
News Release

Development and validation of
a score to predict pre-hospital change
of the cardiac rhythm
from non-shockable to shockable
in cardiac arrest patients:

Using 25,804 patients from the data
from an OHCA registry of the Japanese
Association for Acute Medicine
(JAAM-OHCA)



Title

Prediction of pre-hospital change of the cardiac rhythm from non-shockable to shockable in out-of-hospital cardiac arrest patients: a post hoc analysis of a nationwide, multicenter prospective registry

Key Points

- Our study from a nationwide database of out-of-hospital cardiac arrest patients identified seven factors as predictors of a spontaneous rhythm change from non-shockable to shockable prior to hospital arrival.
- Shock with automated external defibrillator (AED) substantially increased the hazard ratio for spontaneous rhythm change, while asphyxiation and trauma as causes of CA decreased the hazard ratio for spontaneous rhythm change.
- The rhythm Change before Hospital Arrival for Non-Shockable score (CHANS) score was developed to can help predict a potential rhythm change from non- shockable to shockable prior to hospital arrival.
- The CHANS score is expected to help emergency medical service that are simultaneously performing complex and urgent tasks.
- The CHANS score may lead to the development of new management strategies in pre-hospital settings such as pulse checks at different times depending on the patient, instead of the uniform two-minute pulse checks that have been used. This could enable rapid identification of spontaneous rhythm change, which is expected to lead to improved prognosis.
- The Harrell's C-index values of the CHANS score were nearly 0.70, which means that although the score has great predictive potential, other characteristics may need to be applied to further improve the score for optimal performance.

Summary

Assistant Professor Ryo Emoto (first author), Professor Shigeyuki Matsui at the Department of Biostatistics, Nagoya University Graduate School of Medicine, Assistant Professor Kazuki Nishida at Center for Advanced Medicine, Nagoya University Graduate School of Medicine, Assistant Professor Mitsuaki Nishikimi (corresponding author) at the Department of Emergency and Critical Care Medicine, Graduate School of Biomedical and Health Sciences, Hiroshima University / Department of Emergency and Critical Care Medicine, Nagoya University Graduate School of Medicine, and their collaborators have identified predictors of a spontaneous rhythm change from non-shockable to shockable prior to hospital arrival and have developed a predictive scoring system.

The survival rate of out-of-hospital cardiac arrest (OHCA) patients with an initial non-shockable rhythm remains unacceptably low, and better management strategies in pre-hospital settings are required to further improve patient outcomes. Immediate defibrillation upon cardiac rhythm change from non-shockable to shockable prior to hospital arrival, hereinafter, spontaneous rhythm change, is particularly important with the timing of this rhythm change being urgent. A previous study showed that subsequent spontaneous conversion of the initial rhythm from non-shockable to shockable during emergency medical resuscitation efforts was associated with a high likelihood of favorable neurological outcomes if defibrillation was performed within 20 minutes, which implies that prompt identification of a spontaneous rhythm change is critical. However, few studies have been conducted to identify predictors of a spontaneous rhythm change in OHCA patients, and there is no tool/methodology presently available to predict rhythm change prior to hospital arrival.

The research group identified seven factors (age, sex, the presence of witness, initial rhythm, chest compression by bystander, shock with AED by bystander, and cause of cardiac arrest) using the data from an OHCA registry of the Japanese Association for Acute Medicine (JAAM-OHCA). In addition, a predictive score was developed and validated to predict rhythm change prior to hospital arrival. The developed score helps emergency medical service immediately defibrillate when the opportunity arises, as well as triage CA patients who may have a better outcome based upon predicted rhythm change possibility. These results are expected to lead to new options of management strategies in pre-hospital, such as changing the interval of pulse checks according to predicted rhythm change possibility.

Research Background

Despite the notable progress in the field of resuscitation science, the survival rate of out-of-hospital cardiac arrest (OHCA) patients with an initial non-shockable rhythm remains unacceptably low and better management strategies in pre-hospital settings are required to further improve patient outcomes. Emergency medical services (EMS) in the ambulance require immediate and intensive care as their outcomes are time-sensitive. On the other hand, EMS must engage in multitasking while performing cardiopulmonary resuscitation (CPR), such as obtaining and recording medical information, securing vascular access to allow for timely pharmacological interventions, securing the airway by performing intubation when needed, and ensuring prompt transfer to the hospital. These could result in some important tasks, such as recognition of a conversion to a shockable rhythm, failing to be prioritized. Among the duties of EMS, immediate defibrillation upon cardiac rhythm change from non-shockable to shockable prior to hospital arrival, hereinafter, spontaneous rhythm change, is particularly important with the timing of this rhythm change being urgent.

A previous study showed that subsequent spontaneous conversion of the initial rhythm from non-shockable to shockable during emergency medical resuscitation efforts was associated with a high likelihood of favorable neurological outcomes if defibrillation was performed within 20 minutes, which implies that prompt identification of a spontaneous rhythm change is critical. If EMS can predict such spontaneous rhythm change, they could be better prepared to prioritize immediate defibrillation when the opportunity arises as well as triage CA patients who may have a better outcome based upon a change in rhythm from non-shockable to shockable. However, few studies have been conducted to identify predictors of a spontaneous rhythm change in OHCA patients, and there is no tool/methodology presently available to predict rhythm change prior to hospital arrival. We conducted this study to identify predictors and develop a predictive score that would allow EMS to predict spontaneous rhythm change in OHCA patients and help them prepare for immediate defibrillation in the event of a spontaneous rhythm change.

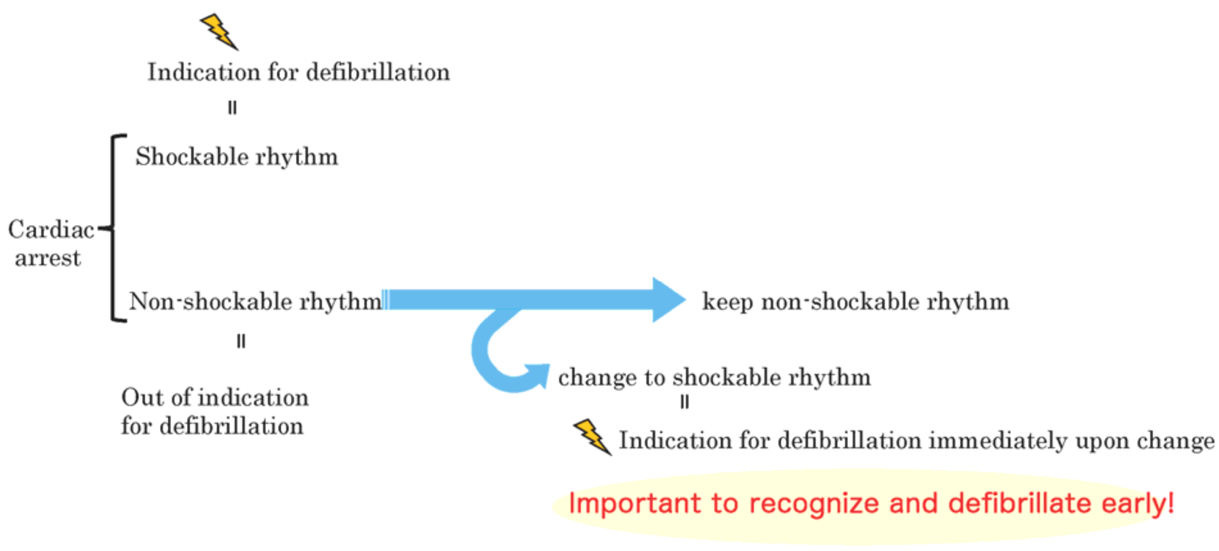


Figure 1: Flow chart of indications for defibrillation to cardiac arrest patients

Research Results

Data from an OHCA registry of the Japanese Association for Acute Medicine (JAAM-OHCA), which is a nationwide, prospective, multicenter registry of OHCA patients who are transported to critical care medical centers or hospitals with an emergency care department across Japan (total of 125 institutions) was used in this study. The registry included data from OHCA patients enrolled from June 2014 through December 2017. Adult OHCA patients who were judged by the attending EMS as having a non- shockable rhythm at the time of the first pulse check were included in the analysis.

Identification of predictors of a spontaneous rhythm change from non-shockable rhythm to a shockable rhythm was performed by multivariate analysis using Cox regression models. The primary outcome was the time to shockable rhythm change from the initial pulse check. Patients who arrived at the hospital prior to the rhythm change were treated as censored. The covariates included in the analysis were those that could be assessed by the time EMS arrived at the site. The analysis identified the following variables as being associated with a significantly increased hazard for spontaneous rhythm change: presence of witness, pulseless electrical activity (PEA) as the initial rhythm, shock with an AED by a bystander, and a non-exogenous cause of CA. Conversely, age >65 years, female, chest compression by bystander, and trauma and asphyxiation as the cause of the CA were associated with a significantly decreased hazard for spontaneous rhythm change. Initiation of mouth-to-mouth resuscitation by a bystander had no statistically significant influence on the likelihood of spontaneous rhythm change. As a sensitivity analysis, we performed a Cox proportional hazards regression analysis by adding the variables of advanced airway management and epinephrine injection as time dependent adjustment factors, neither of which were included in our predictive score. We confirmed that the addition of these parameters did not appreciably alter the results from our original analysis.

We developed a predictive score using the derivation cohort (patients seen from June 2014 to December 2016), and confirmed the predictive accuracy of the scores using the validation cohort (patients seen from January 2017 to December 2017). After confirming the validity of the predictive model and its predictive performance for unknown data through nested cross-validation using data from the derivation cohort, the Rhythm Change before Hospital Arrival for Non-Shockable (CHANS) score was derived by Ridge penalized Cox regression. The coefficients for each variable in the CHANS score are summarized in Figure 2. Based on CHANS score, we created a risk classification that could differentiate between patients with a high probability and low probability for spontaneous rhythm change. The Harrell's C-index of the CHANS score in the validation cohort was 0.67 [0.64-0.70]. The KM curves were significantly different between the two groups divided according to the proposed risk classification in the validation cohort (log-rank test; $p < 0.001$) (Fig. 2).

Variable	Coefficients*
Age, > 65 yrs ($\cdot_{1}$)	-0.368 ($\cdot_{1}$)
Gender, female ($\cdot_{2}$)	-0.436 ($\cdot_{2}$)
Witnessed ($\cdot_{3}$)	0.382 ($\cdot_{3}$)
PEA ($\cdot_{4}$)	0.678 ($\cdot_{4}$)
CPR by bystander ($\cdot_{5}$)	-0.208 ($\cdot_{5}$)
AED by bystander ($\cdot_{6}$)	1.376 ($\cdot_{6}$)
Mouth to mouth resuscitation by bystander ($\cdot_{7}$)	0.081 ($\cdot_{7}$)
Reason for CA	
Trauma ($\cdot_{8}$)	-0.904 ($\cdot_{8}$)
Hanging ($\cdot_{9}$)	-0.428 ($\cdot_{9}$)
Drowning ($\cdot_{10}$)	0.174 ($\cdot_{10}$)
Choke ($\cdot_{11}$)	-0.760 ($\cdot_{11}$)
Addiction ($\cdot_{12}$)	-0.183 ($\cdot_{12}$)
Unknown exogenous ($\cdot_{13}$)	-0.339 ($\cdot_{13}$)
Non-exogenous ($\cdot_{14}$)	0.380 ($\cdot_{14}$)

Calculation formula

$$\mathrm{Score}(\cdot) = \cdot_{1}\cdot_{1} + \cdot_{2}\cdot_{2} \cdots + \cdot_{14}\cdot_{14}$$

$\cdot_i$: coefficient of ·th variable ($\cdot = 1, \cdots, 14$)
$\cdot_i$: value of ·th variable ($\cdot = 1, \cdots, 14$)
$\cdot_i = 1$ if the subject is in the category,
$\cdot_i = 0$ otherwise.

$$\mathrm{Risk\ Class}(\cdot) = \begin{cases} \mathrm{High}\ (\cdot \geq -1.523) \\ \mathrm{Low}\ (\cdot < -1.523) \end{cases}$$

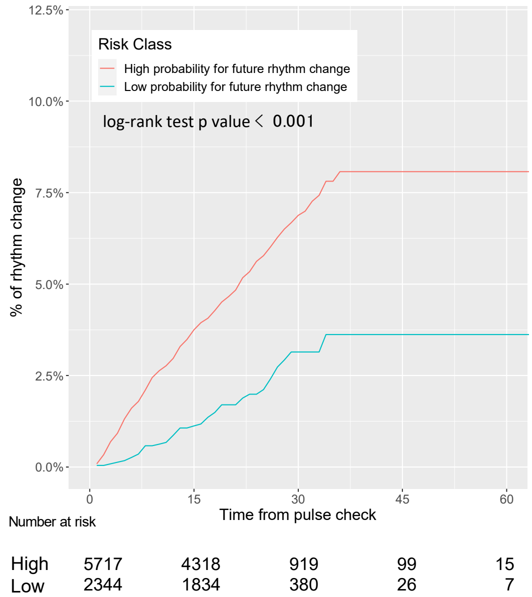


Figure 2. Calculation formula of the developed CHANS score and results of the validation of the risk classification using the CHANS score.

Research Summary and Future Perspective

Among the variables associated with spontaneous rhythm change, the hazard ratio of shock with AED was especially high (3.97 [2.67-5.89]) as compared with other variables. This result is very consistent with reports from clinical practice because defibrillating a patient with an AED before the arrival of paramedics is suggestive of a cardiogenic component to the CA, in which case, the patient has a higher probability of a spontaneous rhythm change. On the other hand, asphyxiation and trauma as the causes of CA were associated with a lower probability of spontaneous rhythm change. Although future studies are needed, at present, the data suggest that patients with CA most likely caused by the above mechanisms may still be able to achieve ROSC, irrespective of a spontaneous rhythm change. In fact, a direct treatment option for these etiologies may more easily alleviate the CA, such as mitigating the causal agent in asphyxiation, or hydration and blood transfusion after an accident.

The Harrell's C-index of CHANS score is approximately 0.70 and it is regarded as acceptable but may need to be improved for optimal performance. To improve the predictive performance of the prediction model, we considered that it may be effective to add other clinical variables to the model. Most of the variables included in our registry were those that are known to be strongly related to the outcome of CA patients, such as the presence of a witness, the initial rhythm, etc., and there were few variables directly associated with the electrophysiology of the heart, such as the electrical frequency of PEA. Variables associated with the quality of bystander CPR before the initial pulse check, such as the depth of chest compression, can also improve the performance of our score, but are more challenging to accurately ascertain. In future studies, addition of such data may be considered to further improve the predictive accuracy of the CHANS score.

Guidelines on cardiopulmonary resuscitation recommend a rhythm check every 2 minutes, based on the results of a few randomized clinical trials performed about two decades ago. Today, with the development if new resuscitation technologies such as mechanical CPR devices that enable continuous CPR without user fatigue19 and devices that can detect shockable rhythm during CPR, it remains unclear if the appropriate interval for pulse check should still be every 2 minutes. Our results suggest the potential for varying the interval for pulse checks according to the risk of change of the rhythm. For example, if the risk of change of the rhythm is low, the pulse could be checked less frequently, like every 3 minutes, which could reduce the total time of no flow due to pulse check. On the other hand, if the risk of change of the rhythm is high, the pulse may need to be checked more frequently than every 2 minutes. Evidence from our current study alone is not sufficient, and further prospective studies are required to validate our findings. However, we believe that our current study may pave the way for individualization of the interval for pulse checks according to the risk of change of the rhythm in individual patients.

Publication

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