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Role of a rapid response system and code status discussion as determinants of prognosis for critical inpatients

An observational study in a Japanese urban hospital

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Abstract

Rapid response systems (RRS) have been introduced worldwide to reduce unpredicted in-hospital cardiac arrest (IHCA) and in-hospital mortality. The role of advance care planning (ACP) in the management of critical patients has not yet been fully determined in Japan.

We retrospectively assessed the characteristics of all inpatients with unpredicted IHCA in our hospital between 2016 and 2018. Yearly changes in the number of RRS activations and the incidence of unpredicted IHCA with or without code status discussion were evaluated from 2014 to 2018. Hospital standardized mortality ratios were assessed from the data reported in the annual reports by the National Hospital Organization.

A total of 81 patients (age: 70.9 ± 13.3 years) suffered an unpredicted IHCA and had multiple background diseases, including heart disease (75.3%), chronic kidney disease (25.9%), and postoperative status (cardiovascular surgery, 18.5%). Most of the patients manifested non-shockable rhythms (69.1%); survival to hospital discharge rate was markedly lower than that with shockable rhythms (26.8% vs 72.0%, $P < .001$). The hospital standardized mortality ratios was maintained nearly constant at approximately 50.0% for 3 consecutive years. The number of cases of RRS activation markedly increased from 75 in 2014 to 274 patients in 2018; conversely, the number of unpredicted IHCA cases was reduced from 40 in 2014 to 18 in 2018 ($P < .001$). Considering the data obtained in 2014 and 2015 as references, the RRS led to a reduction in the relative risk of unpredicted IHCA from 2016 to 2018 (ie, 0.618, 95% confidence interval 0.453–0.843). The reduction in unpredicted IHCA was attributed partly to the increased number of patients who had discussed the code status, and a significant correlation was observed between these parameters ($R^2 = 0.992$, $P < .001$). The reduction in the number of patients with end-stage disease, including congestive heart failure and chronic renal failure, paralleled the incidence of unpredicted IHCA.

Both RRS and ACP reduced the incidence of unpredicted IHCA; RRS prevents progression to unpredicted IHCA, whereas ACP decreases the number of patients with no code status discussion and thus potentially reducing the patient subgroup progressing to an unpredicted IHCA.

Abbreviations: ACP = advance care planning, CI = confidence interval, DNAR = do not attempt resuscitation, ECG = electrocardiography, GWTG = Get With The Guidelines, HSMR = hospital standardized mortality ratio, ICU = intensive care unit, IHCA = in-hospital cardiac arrest, RRS = rapid response system.

Keywords: advance care planning, rapid response system, unpredicted in-hospital cardiac arrest

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All data generated or analyzed during this study are included in this published article [and its supplementary information files]. The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the present study, and so are not publicly available. Data are available from the authors upon reasonable request and with the permission of the third party.

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1. Introduction

Cardiac arrest is one of the most serious events during hospitalization and is associated with a considerably high mortality rate and poor prognosis despite remarkable advances in clinical practice. Data from the Get With The Guidelines (GWTG)-Resuscitation registry have shown that the rate of survival to discharge after in-hospital cardiac arrest (IHCA) is 25.8%, and 45% of patients present with shockable rhythms, such as ventricular fibrillation and pulseless ventricular tachycardia.[1] To prevent these life-threatening events, multiple strategies have been developed, including the rapid response system (RRS),[2,3] and advance care planning (ACP), such as a do-not-resuscitate[4]/ do-not-attempt-resuscitate (DNAR) orders,[5,6] and have also been introduced into clinical practice. Indeed, several meta-analyses and reviews have demonstrated that RRS is associated with reductions in cardiopulmonary arrest and hospital mortality rates.[7–9] Moreover, we have recently shown that code status discussion upon hospital admission contributes to a decrease in cardiopulmonary resuscitation procedures in patients with advanced cancer and non-cancer disease.[10]

Despite the well-acknowledged function of the RRS in the prevention of in-hospital emergency events, there exists some controversy on the role of RRS in critically ill inpatients. The implementation of RRS during hospitalization is potentially justifiable because of possible benefits, such as the reduction in non-intensive care unit (ICU) cardiopulmonary arrest and hospital mortality.[6–8] However, a meta-analysis by Chan et al[11] revealed that the introduction of RRS was associated with a reduction in cardiac arrest rates, but failed to reduce in-hospital mortality. Lyons et al[12] showed that RRS potentially improves outcomes but elucidates inconclusive results, this is partly because of the heterogeneous nature of RRS, including the activation criteria. Alternatively, in patients who are in the terminal stages of various diseases (eg, advanced cancer, chronic kidney disease, and congestive heart failure), advance directives such as a DNAR order may determine code status and would be associated with the decreased application of RRS. Chan et al[11] surmised that the divergent status of DNAR orders may be responsible for the discordant reductions in the incidence of cardiopulmonary arrest and in-hospital mortality after RRS implementation. These findings therefore suggest the need for further investigations with identical levels of criteria for RRS intervention and code status orders to verify the effectiveness of RRS in reducing in-hospital mortality.

In 2013, we introduced the RRS and ACP into the emergency and critical care management protocols in our hospital and employed both strategies vigorously with increasing frequency since 2016. Along with the initiation of these systems, we developed criteria for RRS activation in our medical center and implemented code status discussions according to the guidelines of the Japanese Society of Intensive Care Medicine, which were created on the basis of the DNAR definition of the 2010 American Heart Association guidelines.[13] Nevertheless, it has not been determined whether our RRS plays a principal role in reducing unpredicted IHCA cases. Furthermore, it remains controversial whether the application of ACP to end-stage diseases influences the incidence of unpredicted IHCA. We therefore evaluated the beneficial role of the RRS and/or ACP in the development of unpredicted IHCA in patients admitted to our hospital between 2014 and 2018.

2. Methods

This retrospective study assessed the prognosis of patients who were admitted to the Tokyo Bay Urayasu-Ichikawa Medical Center and experienced unpredicted IHCA from 2016 to 2018 and evaluated the impact of an RRS and code status discussion on the incidence of unpredicted IHCA between January 2014 and December 2018. Our hospital has 344 beds and operates multiple high-care units and services, including a high dependency unit (12 beds), an ICU (14 beds), an emergency room (ER), and medical emergency teams. Approximately 8,700 patients were admitted to our hospital, and 10,000 patients were transported by ambulance in 2018. Almost all medical and ER/ICU physicians as well as other medical staff are required to regularly attend a series of lectures on ACP, code status, and the RRS.

2.1. Study population and parameters

All medical records of patients admitted to our hospital between January 2014 and December 2018 were reviewed. Code status was obtained upon admission to the hospital. Patients who expressed a DNAR order or discussed code status were deemed to have made a code status decision. The code status decision rate was determined by the number of patients who discussed code status upon admission. The AHA guidelines[13] were used to define DNAR.

The baseline characteristics, including age, sex, underlying disease, and Charlson Comorbidity Index, of patients with unpredicted IHCA were obtained from medical records. Electrocardiography (ECG) records were assessed to evaluate the occurrence of cardiac arrest, to determine whether the changes included shockable or non-shockable rhythms, and to evaluate the survival rate of these events. Furthermore, the annual hospital standardized mortality ratios (HSMRs) of this hospital from 2016 to 2018 were determined[14,15] as the ratio of the actual mortality rate in the hospital versus the expected mortality rate estimated from the National Hospital Organization Clinical Indicator ver. 4.[15]

In our hospital, the RRS is activated based on the derangements of circulatory and respiratory functions as well as neurological status (Table 1). Although the RRS was started in 2013 in an inpatient and outpatient setting,[16] it remained relatively less recognized among the facility staff until 2015, when the RRS specialty team was created. Therefore, the data obtained from 2014 to 2015 were considered as references.

The ACP was discussed upon admission with the Department of General Internal Medicine and was introduced in 2016. End-stage diseases were defined as follows: end-stage renal disease without dialysis, congestive heart failure (New York Heart Association, Class IV), cancer (Stage IV), chronic obstructive pulmonary disease (Stage IV), advanced dementia, and complex disease states where resuscitation was unlikely to be successful. Regarding the diagnosis of end-stage disease, 2 independent physicians and a certified registered nurse reviewed the medical records and made final decisions about the stage of underlying diseases. If a consensus was not reached among the 3 members, the opinion of 1 more intensivist was obtained.

This study was approved by the Institutional Review Board of Tokyo Bay Urayasu Ichikawa Medical Center, and the requirement for informed consent was waived because this was a retrospective study (institutional approval number: 581). This study was conducted in accordance with the principles of the

Table 1

Criteria for activation of the rapid response system in Tokyo Bay Urayasu-Ichikawa Medical Center.

Circulatory changes	Respiratory changes	Neurological changes	Others
Heart rate: >130/min or <40/min	Respiratory rate: >28/min or <8/min	Sudden change in consciousness	New-onset chest pain
Systolic blood pressure: <90 mmHg	New-onset hypoxemia: $SpO_2 < 90\%$ or escalating oxygen requirements	Delirium sustained >10 min	Cyanosis, mottling of the extremities, or pallor
Urine output: <50 mL/4 h			Suicidal attempt
			Severe bleeding or severe pain
			New-onset trauma
			Nausea or vomiting sustained >30 min
			Anaphylaxis
			Need response if the primary physician cannot attend
			Any concern indicative of deteriorating clinical condition

Declaration of Helsinki. Information from medical records was anonymized and de-identified prior to the final analyses. The study was registered at UMIN (UMIN R000049641).

2.2. Statistical analysis

The results are expressed as the mean ± SD or median (lower quartile-upper quartile), depending on the data distribution (eg, parametric vs non-parametric).[17] Continuous variables were analyzed using the Student *t* test or the Kruskal–Wallis test, as appropriate. The chi-square or Fisher exact test was used to evaluate categorical variables, including the incidence of RRS activation and unpredicted IHCA and the number of patients with or without the end-stage disease. Time-series multiple regression analysis with the stepwise regression model was applied to evaluate which parameters (total number of patients, age, or the number of RRS implementations) contributed more significantly to the number of unpredicted IHCA cases over the study period from 2014 to 2018. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25 (IBM Japan Ltd, Japan). Statistical significance was set at $P < .05$.

3. Results

3.1. Background data

Table 2 summarizes the demographic characteristics of the 81 patients who experienced unpredicted IHCA from 2016 to 2018. The mean age of the patients was 70.9 ± 13.3 years, and 67.9% of the patients were male. ECG wave patterns obtained upon the occurrence of the cardiac arrest showed that 30.9% were shockable rhythms, including ventricular fibrillation and pulseless ventricular tachycardia. Cardiovascular disease and chronic kidney disease (grade 5) were the 2 major background disorders that caused cardiac arrest during hospitalization (75.3% and 25.9%, respectively). Cardiac arrest ensued postoperatively in 25

Table 2

Demographic characteristics of inpatients who experienced unpredicted IHCA during 2016 to 2018.

Variables	Total	End-stage disease (+)	End-stage disease (−)	*P* value
n (male/female)	81 (55/26)	13 (12/1)	68 (43/25)	.052
Age (y/o, mean ± SD)	70.9 ± 13.3	69.0 ± 12.2	71.2 ± 13.5	>.5
ECG rhythms				.097
Shockable rhythm: n (%)	25 (30.9)	7 (53.4)	18 (26.5)	
Non-shockable rhythm: n (%)	56 (69.1)	6 (46.2)	50 (73.5)	
Background disease				
Cardiovascular disease: n (%)	62 (76.5)	10 (76.9)	52 (76.5)	>.5
CKD Grade5: n (%)	21 (25.9)	5 (38.5)	16 (23.5)	.306
Malignancies: n (%)	10 (12.3)	3 (23.1)	7 (10.3)	.197
COPD: n (%)	9 (11.1)	2 (15.4)	7 (10.3)	>.5
Post-operation: n (%)	25 (30.9)	3 (23.1)	22 (32.4)	>.5
Cardiovascular surgery: n (%)	15 (18.5)	2 (15.4)	13 (19.1)	
Neurosurgery: n (%)	2 (2.5)	0 (0)	2 (2.9)	
ICU patients: n (%)	16 (19.8)	4 (30.8)	12 (17.6)	.275
Charlson Comorbidity Index (median) [IQR25–IQR75]	1 [0–2]	1 [1–1]	1 [0–2]	
Departments				>.5
Internal medicine: n (%)	24 (29.6)	3 (23.1)	21 (30.9)	
Cardiology: n (%)	27 (33.3)	6 (46.2)	21 (30.9)	
Cardiovascular surgery: n (%)	18 (22.2)	3 (23.1)	15 (22.1)	
General surgery: n (%)	5 (6.2)	1 (7.7)	4 (5.9)	
Neurosurgery: n (%)	4 (4.9)	0 (0)	4 (5.9)	
Orthopedic surgery: n (%)	3 (3.7)	0 (0)	3 (4.4)	

CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, ECG = electrocardiogram, ICU = intensive care unit, IHCA = in-hospital cardiac arrest, IQR = interquartile range. Statistical analyses were conducted between end-stage disease (+) and (−), using Student *t* test or χ^2-test.

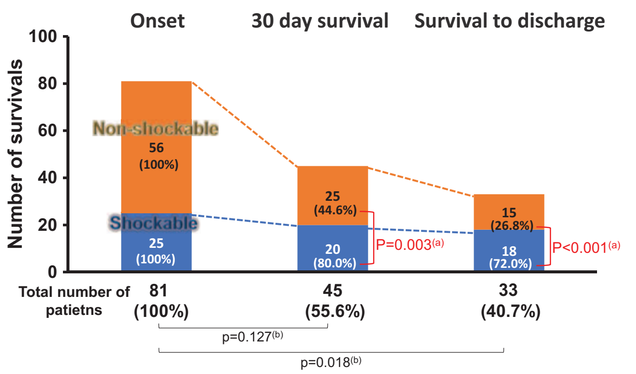

Figure 1. Serial changes in survival rates after cardiac arrest and the association with ECG rhythms. Data in parentheses in bar graphs indicate the percentage of the number at the onset of each rhythm. *P* values were estimated using the chi-square test, based on the number of survivors and non-survivors in shockable and non-shockable rhythms[(a)] or the number of patients with shockable/non-shockable rhythms at onset and at the time of discharge/30 days[(b)]. ECG = electrocardiogram.

patients, of whom 60% underwent cardiovascular surgery. Sixteen ICU patients suffered cardiac arrest, which corresponded to 19.8% of all events. End-stage disease accounted for 16.0% (ie, 13/81) of all unpredicted IHCA events in the patients.

3.2. ECG rhythms and survival rate

The ECG rhythms obtained upon cardiac arrest from 2016 to 2018 and their association with survival rates are shown in Fig. 1. Thirty-day survival rates and survival rates at hospital discharge were 55.6% and 40.7%, respectively. Evaluation of the ECGs indicated that 69.1% were non-shockable rhythms (56 vs 25 cases of non-shockable and shockable rhythms, respectively). The 30-day survival rate of the patients with non-shockable rhythms was reduced to 44.6%, whereas 80.0% of the patients with shockable rhythms survived ($P = .003$ by chi-square test). Only 26.8% of patients with non-shockable rhythms were alive at hospital discharge, whereas 72.0% of patients with shockable rhythms survived hospital discharge ($P < .001$). Neither sex nor age affected the differences in survival rates between these rhythms.

When the rate of survival to hospital discharge in this hospital was compared with that in the GWTG-Resuscitation registry,[1] more favorable results were obtained for our medical center (40.7% vs 25.8%, $P = .002$), where a higher rate of patients with shockable rhythms survived to discharge (22.2% vs 10.4%, for our hospital vs the GWTG-Resuscitation registry, respectively, $P = .007$; see Figure, Supplemental Digital Content, http://links.lww.com/MD/G346, which illustrates the comparison of survival rates between our hospital and that in the GWTG-Resuscitation registry).

3.3. Changes in various parameters

The total number of inpatients increased by 10% in the 3 years from 2016 to 2018, and the number of patients transported by ambulance markedly increased from 5692 in 2016 to 9998 in 2018 (Table 3). In contrast, only modest changes were observed in the incidence of unpredicted IHCA or death. The HSMR was 52.2 in 2016 and remained almost unaltered throughout the observation period.

Our medical center implemented the RRS in 2013, and the number of inpatients increased considerably. We therefore assessed the number of patients who received the RRS or were considered to have an unpredicted IHCA and evaluated the association between the RRS and the incidence of unpredicted IHCA from 2014 to 2018. Thus, there were 75 (10.2/1000 patients) and 62 (8.1/1000 patients) RRS activations in 2014 and 2015, respectively, and these increased gradually to 125 (15.6/1000 patients) in 2016 ($P = .003$) and 197 (23.1/1000 patients) in 2017 ($P < .001$); the number nearly quadrupled in 2018 (ie, 274 [31.3/1000 patients], $P < .001$, Fig. 2A). Alternatively, although the number of unpredicted IHCA cases remained at approximately 40 (40, 38, and 37 for 2014, 2015, and 2016, respectively), IHCAs decreased to 26 in 2017, and finally reached 18 in 2018 ($P < .001$). Thus, there was a tendency for a reciprocal relationship between these 2 parameters ($R^2 = 0.953$, slope coefficient $= -0.104$, $P = .004$). Multiple regression analysis demonstrated that the number of unpredicted IHCA cases correlated negatively correlated with that of the RRS implementation ($\beta = -0.621$, $P = .03$) and positively with age ($\beta = 0.965$, $P = .011$). Furthermore, when the data acquired in 2014 and 2015 were deemed as references, the activation of the RRS was associated with a reduction in the relative risk for unpredicted IHCA from 2016 to 2018 (RR 0.618, 95% CI 0.453–0.843; Fig. 2B).

Among all the patients with unpredicted IHCA, more than 90% decided the code status; in 2018, and this rate increased to 97.3% in 2018, a value that was significantly higher than that observed in 2014 (ie, 92.2%, $P = .004$; Fig. 3A). Among 40 patients with unpredicted IHCA observed in 2014, 28 (70.0%) did not decide code status (Fig. 3B). Although the incidence of unpredicted IHCA decreased over time (from 40 in 2014 to 18

Table 3

Serial changes in hospital standardized mortality ratios and other parameters during 2016 to 2018.

	Year			
	2016	**2017**	**2018**	***P* values**
Total number of inpatients (/year)	8035	8516	8745	–
Age (y/o, median) [IQR25–IQR75]	69.0 [42.0–82.0]	67.0* [39.0–80.0]	66.0 [39.0–79.0]	<.001
Number of patients carried in by ambulance (/year)	5692	8573	9998	–
Number of in-hospital cardiac arrest (/year)	340	301	333	.079
Number of in-hospital death (/year)	303	275	315	.173
Hospital standardized mortality ratio	52.2	45.2	48.8	>.5

IQR = interquartile range.
* $P < .001$.
# $P = .003$ vs 2016 (by Steel-Dwass multiple comparison post hoc test).

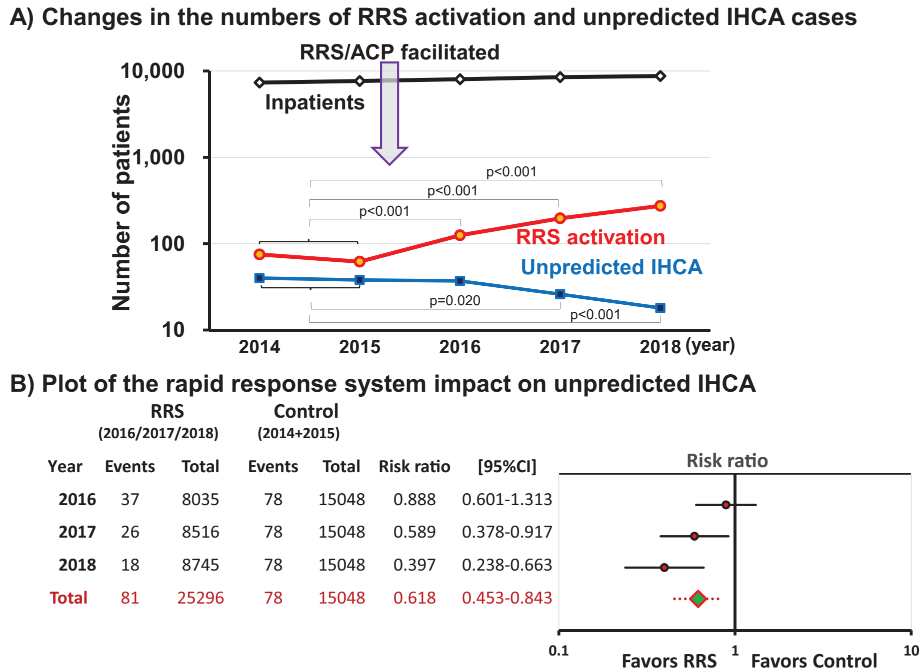

Figure 2. Association between the rapid response system and unpredicted IHCA from 2014 to 2018. (A) Changes in the numbers of RRS implementation and unpredicted IHCA. The number of patients with RRS or unpredicted IHCA in each year was estimated, using the data in 2014 and 2015 as references. (B) Impact of RRS on the development of unpredicted IHCA. Risk ratio in each year (ie, 2016–2018) was calculated using the data from 2014 to 2015 as control. IHCA = in-hospital cardiac arrest, RRS = rapid response system.

patients in 2018), the temporal changes were largely accounted for by the decrease in the subgroup without code status (from 28 in 2014 to 10 patients in 2018). Indeed, a strong correlation was noted between the incidence of unpredicted IHCA and the number of patients with no code status ($R^2 = 0.992$, slope coefficient = 1.151, $P < .001$). Conversely, the percentage of unpredicted IHCA cases with code status discussion remained almost unaltered throughout the observation period.

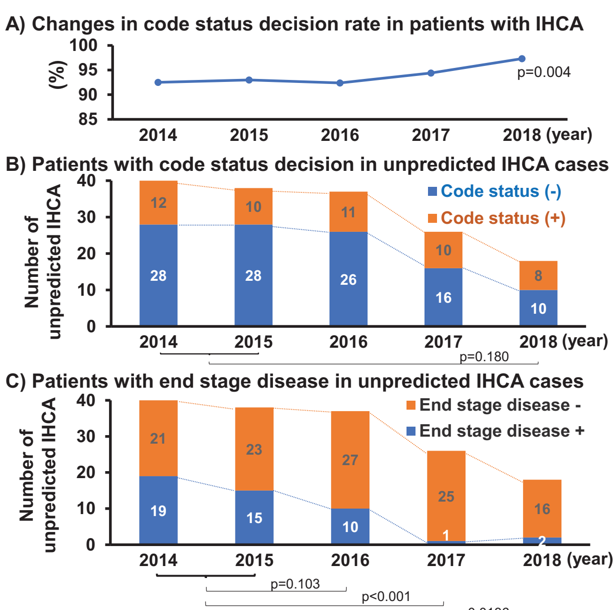

Figure 3. Serial changes in code status decision rate and the number of unpredicted IHCA from 2014 to 2018. (A) The code status decision rate was significantly elevated in 2018 compared with that observed in 2014 and 2015. The numbers in the bar graphs denote patients with or without code status (B) or end-stage disease (C). *P* values were calculated based on the number of patients with code status/end-stage disease in each year, using the chi-square or Fisher exact test. IHCA = in-hospital cardiac arrest.

Patients with end-stage disease (see Section 2 and Table, Supplemental Digital Content, http://links.lww.com/MD/G347, which show the characterization of the patients with end-stage disease), who should be a possible target for ACP, accounted for a considerable proportion of the group with unpredicted IHCA in 2014 (19 vs 40 cases) and 2015 (15 cases vs 38 cases; Fig. 3C). The number of this subset of patients decreased markedly in 2017 (1 patient) and 2018 (2 patients); a significant correlation was observed between the number of patients in this subgroup and the incidence of unpredicted IHCA over the observation period (correlation coefficient 0.984, $R^2 = 0.829$, $P = .032$).

4. Discussion

Unpredicted IHCA is a serious and unexpected event during hospitalization, but is relatively remediable and preventable with the early detection of ominous signs. A growing body of evidence indicates that the RRS is being introduced into critical care strategies in a substantial number of hospitals, and can actually reduce unpredicted IHCA cases and ameliorate in-hospital mortality rates.[7–9] Furthermore, in patients in terminal stages, advance directives, such as a DNAR order and ACP facilitate the decision-making among medical staff who managing these patients in the critical settings to determine which strategies should affect the code status decision rate, and possibly improve the rate of survival to discharge.[5,6] In contrast, there is controversy on the role of the RRS in hospital mortality; several reviews and meta-analyses revealed that the RRS failed to demonstrate a reduction in hospital mortality.[11,12,18] The clarification of this important issue, therefore, would confer substantial benefits in the context of in-hospital critical care medicine.

The findings of this study show that, among 81 unpredicted IHCA patients observed between 2016 and 2018, 33 (40.7%) survived to hospital discharge (Fig. 1). The survival rate to discharge was prominently higher in patients with shockable rhythms than in those with non-shockable rhythms (72.0% vs 26.8%, $P < .001$). The abovementioned findings are apparently more promising than those reported by the GWTG-Resuscitation registry.[1] Indeed, a more favorable survival rate was observed in our facility (ie, 40.7% vs 25.8%, $p = .002$; Figure, Supplemental Digital Content, http://links.lww.com/MD/G346, which illustrates the comparative survival rates for unpredicted IHCA patients at our hospital and those in the GWTG-Resuscitation registry). Additionally, 72% of participants with shockable rhythms survived to hospital discharge, whereas the survival to hospital discharge rate in the GWTG-Resuscitation registry was 45% ($P = .007$).[1] To the extent that shockable rhythms are reported to be preferable to non-shockable rhythms[19,20]; in this context, the background disease and the circumstances wherein the patients are situated may have differed between these study groups, and these factors may have contributed to the distinct responsiveness to the RRS. Thus, our hospital is characterized by managing a large number of patients with cardiovascular disease (75.3%, Table 2) in the wards of cardiology (33.3%), cardiovascular surgery (22.2%), and internal medicine (29.6%). More detailed analyses may clarify the reason for the higher survival rate following the incidence of cardiac arrest in this study.

There is a growing need for the standardization of medical care and the evaluation of its effectiveness in each hospital. The HSMR has been used as an international indicator for hospital quality of care and medical safety,[14] and now also represents a marker for not only comparing the quality of care between hospitals but also for evaluating serial changes in healthcare levels in an individual hospital. We, therefore, assessed HSMRs for the period extending from January 2016 to December 2018 and found values of 45.2 to 52.2 (Table 3). Since an HSMR of 100.0 indicates standard mortality, the abovementioned HSMR values imply that the mortality rate in our hospital is suppressed to a rate much lower than the expected number of deaths and suggest that our medical service is consistently well provided over these 3 consecutive years. Alternatively, the nearly constant HSMRs are apparently dissociated from reductions in the incidence of unpredicted IHCA (Fig. 2A) and may simply represent the stable medical care system in our facility.

There appears to be a growing recognition of the role of the RRS in the management of in-hospital critical care medicine. This study clearly demonstrates a substantial decrease in unpredicted IHCA cases, despite an increase in the number of inpatients over the years (Table 3, Fig. 2A). This result is attributed partly to the increased number of RRS implementations. Thus, the RSS was developed to reduce preventable in-hospital deaths[7–9] and has been widely introduced into many medical facilities, including our hospital. We therefore evaluated whether the RRS conferred substantial benefits to inpatients with various types of critical diseases. Thus, this study demonstrates that the number of RRS activations increased from 75 to 62 in 2014 to 2015 to 197 in 2017 ($P < .001$) and to 274 in 2018 ($P < .001$, Fig. 2A). Conversely, the incidence of unpredicted IHCA was reduced from 40 to 38 in 2014 to 2015 to 18 in 2018 ($P < .001$). The reciprocal relationship was further confirmed by the results of the multiple regression analysis, which showed a negative correlation between the incidence of unpredicted IHCA and the number of RRS implementations ($\beta = -0.621$, $P = .03$). Finally, the impact of the RRS on unpredicted IHCA indicated a favorable effect of the RRS, with a reduction in the RR (0.618; Fig. 2B). It is therefore reasonable to conclude that the active implementation of the RRS contributes substantially to a decrease in the unpredicted IHCA incidence.

Recently, greater attention has been focused on ACP and code status discussions in critical care medicine.[5,6] Code status discussion contributes to a reduction in unpredicted IHCA cases, possibly because of the exclusion of patients who express a DNAR order from the cases.[10] Our study demonstrated that the number of unpredicted IHCA cases at the end of the study reduced to approximately 50% of the initial value (Fig. 3B). Furthermore, the decrease was particularly noticeable in patients with no code status discussion. In this regard, end-stage disease (eg, advanced cancer, end-stage chronic kidney disease, and congestive heart failure; see Table, Supplemental Digital Content, http://links.lww.com/MD/G347) is generally regarded as a target for ACP.[10] Our results, which indicate a marked reduction in this subset of patients along with a decrease in the number of unpredicted IHCA cases (Fig. 3C), clearly suggest that the discussion of code status in these patients is absolutely essential for the establishment of a more sophisticated ACP. Collectively, these results suggest reducing the number of patients without code status is largely responsible, for the decrease in the number of unpredicted IHCA cases, and could contribute to an alleviated burden of healthcare costs. Of note, Damluji et al demonstrated that hospitalization after cardiac arrest was followed by a steady increase in the associated healthcare costs.[21] The application of the RRS and early implementation of ACP, including code status discussion, may therefore constitute a determinant of ameliorated in-hospital mortality and healthcare costs. These issues need to be evaluated comprehensively.

The critical roles of RRS and ACP in the development of unpredicted IHCA have been documented,[2–9] but it remains to be determined which of the 2 parameters contributes more significantly to the reduction in unpredicted IHCA. This study shows that the incidence of unpredicted IHCA is negatively associated with the number of RRS activation calls ($R^2 = 0.953$, $P = .004$), with a regression coefficient (ie, slope) of -0.104. In contrast, the unpredicted IHCA correlated positively correlated with the number of patients without code status ($R^2 = 0.992$, slope $= +1.151$, $P < .001$). Thus, the absolute values of the slope coefficients suggest a greater impact of the code status discussion on the incidence of unpredicted IHCA than of the RRS. However, we are unable to apply multiple regression analysis to our model because of discordant multicollinearity, which prevents the head-to-head comparison of the effects of the RRS and ACP. More extensive studies could facilitate a better understanding of the role of these management modalities in critical care medicine.

4.1. Limitations

In the present study, we adopted specific criteria for the activation of the RRS that were developed by the inclusion and modification of the criteria defined in other guidelines.[22] Accordingly, the criteria of this system have been distributed extensively among the hospital staff, which facilitates the activation of this system with strictly controlled application. Paradoxically, however, a single-center study design prevented the accumulation of cases. This drawback can be overcome by incorporating data from collaborative facilities.

4.2. Conclusions

Recent strategies for critical care medicine, including the implementation of the RRS and ACP, greatly modify the prognosis of critically ill patients. This study shows that the RRS plays an important role in reducing unpredicted IHCA cases and demonstrates that ACP constitutes a critical determinant in the reduction of this parameter. The application of ACP to patients with the end-stage disease could reduce the incidence of unpredicted IHCA. The experience in our hospital demonstrates that unpredicted IHCA cases have decreased considerably, and the survival to hospital discharge has improved since the comprehensive introduction of these systems. Intensified implementation of the RRS helps to decrease unpredicted IHCA and in-hospital death. Moreover, ACP, through code status discussion, not only decreases the number of end-stage disease patients who might be precipitated into unpredicted IHCA but also could prevent progression into unpredicted IHCA in patients with non-end-stage diseases. The RRS has not been widely introduced into medical institutions in Japan[23]; however, our findings suggest that the role of the RRS and ACP in critical care medicine should be expanded because of their beneficial impact on patients, without untoward effects. This is the first study to demonstrate a mutual relationship among RRS, code status discussion, and unpredicted IHCA in Japanese medical facilities.

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References

[1] Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. Circulation 2018;137:e67–492. doi: 10.1161/CIR.0000000000000558.
[2] Berwick DM, Calkins DR, McCannon CJ, Hackbarth AD. The 100,000 lives campaign: setting a goal and a deadline for improving health care quality. JAMA 2006;295:324–7. doi: 10.1001/jama.295.3.324.
[3] Jones DA, DeVita MA, Bellomo R. Rapid-response teams. N Engl J Med 2011;365:139–46.
[4] Zhang Z, Hong Y, Liu N, Chen Y. Association of do-not-resuscitate order and survival in patients with severe sepsis and/or septic shock. Intensive Care Med 2017;43:715–7. doi:10.1007/s00134-017-4690-7.
[5] Sittisombut S, Maxwell C, Love EJ, Sitthi-Amorn C. Effectiveness of advance directives for the care of terminally ill patients in Chiang Mai University Hospital, Thailand. Nurs Health Sci 2008;10:37–42. doi: 10.1111/j.1442-2018.2007.00371.x.
[6] Degenholtz HB, Rhee Y, Arnold RM. Brief communication: the relationship between having a living will and dying in place. Ann Intern Med 2004;141:113–7. doi: 10.7326/0003-4819-141-2-200407200-00009.
[7] Maharaj R, Raffaele I, Wendon J. Rapid response systems: a systematic review and meta-analysis. Crit Care 2015;19:254doi: 10.1186/s13054-015-0973-y.
[8] Solomon RS, Corwin GS, Barclay DC, Quddusi SF, Dannenberg MD. Effectiveness of rapid response teams on rates of in-hospital cardiopulmonary arrest and mortality: a systematic review and meta-analysis. J Hosp Med 2016;11:438–45. doi: 10.1002/jhm.2554.
[9] Winters BD, Weaver SJ, Pfoh ER, Yang T, Pham JC, Dy SM. Rapid-response systems as a patient safety strategy: a systematic review. Ann Intern Med 2013;158(5 Pt 2):417–25. doi: 10.7326/0003-4819-158-5-201303051-00009.
[10] Sasaki A, Hiraoka E, Homma Y, et al. Association of code status discussion with invasive procedures among advanced-stage cancer and noncancer patients. Int J Gen Med 2017;10:207–14.
[11] Chan PS, Jain R, Nallmothu BK, Berg RA, Sasson C. Rapid response teams: a systematic review and meta-analysis. Arch Intern Med 2010;170:18–26. doi: 10.1001/archinternmed.2009.424.
[12] Lyons PG, Edelson DP, Churpek MM. Rapid response systems. Resuscitation 2018;128:191–7. doi: 10.1016/j.resuscitation.2018.05.013.
[13] Morrison LJ, Kierzek G, Diekema DS, et al. Circulation-Part 3: Ethics: 2010 American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2010;122 (18 suppl 3):S665–75. doi: 10.1161/CIRCULATIONAHA.110.970905.
[14] Jarman B, Gault S, Alves B, et al. Explaining differences in English hospital death rates using routinely collected data. BMJ 1999;318:1515–20. doi: 10.1136/bmj.318.7197.1515.
[15] Shinjo D, Fushimi K. The degree of severity and trends in hospital standardized mortality ratios in Japan between 2008 and 2012: a retrospective observational study. Int J Qual Health Care 2017;29:705–12. doi: 10.1093/intqhc/mzx089.
[16] Ehara J, Hiraoka E, Hsu HC, Yamada T, Homma Y, Fujitani S. The effectiveness of a national early warning score as a triage tool for activating a rapid response system in an outpatient setting: a retrospective cohort study. Medicine 2019;98:e18475doi: 10.1097/MD.0000000000018475.
[17] Zhang Z. Univariate description and bivariate statistical inference: the first step delving into data. Ann Transl Med 2016;4:91doi: 10.21037/atm.2016.02.11.
[18] Sandroni C, D'Arrigo S, Antonelli M. Rapid response systems: are they really effective? Crit Care 2015;19:104doi: 10.1186/s13054-015-0807-y.
[19] Morrison LJ, Neumar RW, Zimmerman JL, et al. Strategies for improving survival after in-hospital cardiac arrest in the United States: 2013 consensus recommendations: a consensus statement from the American Heart Association. Circulation 2013;127:1538–63. doi: 10.1161/CIR.0b013e31828b2770.
[20] Andersen LW, Holmberg MJ, Berg KM, Donnino MW, Granfeldt A. In-hospital cardiac arrest: a review. JAMA 2019;321:1200–10. doi:10.1001/jama.2019.1696.
[21] Damluji AA, Al-Damluji MS, Pomenti S, et al. Health care costs after cardiac arrest in the United States. Circ Arrhythm Electrophysiol 2018;11:e005689.
[22] DeVita MA, Smith GB, Adam SK, et al. Identifying the hospitalised patient in crisis – a consensus conference on the afferent limb of rapid response systems. Resuscitation 2010;81:375–82. doi: 10.1016/j.resuscitation.2009.12.008.
[23] Naito T, Fujiwara S, Kawasaki T, et al. First report based on the online registry of a Japanese multicenter rapid response system: a descriptive study of 35 institutions in Japan. Acute Med Surg 2020;7:e454doi: 10.1002/ams2.454.