Predictors Associated with Survival Among Elderly In-Patients Who Receive Cardiopulmonary Resuscitation in Japan: An Observational Cohort Study

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BACKGROUND: Little is known about the outcomes of in-hospital cardiopulmonary resuscitation (CPR) in Asian populations including elderly patients in Japan.
OBJECTIVE: To determine the survival outcome of in-hospital CPR among elderly patients in Japan, and to identify predictors associated with survival.
DESIGN: Retrospective cohort study in 81 Japanese hospitals from April 1, 2010 to March 31, 2016.
PATIENTS: We included elderly patients (age ≥ 65 years) who received CPR after 2 days of hospitalization.
MAIN MEASURES: The primary outcome was survival at hospital discharge and the secondary outcomes were the discharge disposition and consciousness level of patients who survived to hospital discharge. To determine predictors associated with survival after in-hospital CPR, we fit multivariable models for patient-level and institutional-level factors.
KEY RESULTS: Among the 5365 patients who received CPR, 595 (11%) survived to discharge. Of those who survived to discharge, 46% of patients were discharged home, and 10% of patients were comatose at discharge. Older age and higher burden of comorbidities were associated with reduced survival. The adjusted OR was 0.35 (95% CI, 0.22–0.55) for age ≥ 90 years compared to age 65–69 years, and 0.68 (95% CI, 0.48–0.97) for Charlson Comorbidity Index score of ≥ 4 compared with score of 0. Other predictors of reduced survival included receiving CPR on weekends compared to weekdays (AOR, 0.63; 95% CI, 0.51–0.77) and in small hospitals compared to large hospitals (AOR, 0.58; 95% CI, 0.40–0.83).
CONCLUSIONS: Among elderly patients in Japan, the survival rate of in-hospital CPR was approximately one in ten, and less than half of these patients were discharged home. In addition to older age and higher illness burden, receiving CPR on weekends and/or in small hospitals were significant predictors of reduced survival. These findings should be considered in advanced care planning discussions with elderly patients to avoid subjecting patients to CPR that are likely futile.

KEY WORDS: aging; end-of-life care; decision making; evidence base medicine.

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INTRODUCTION

Whether patients should receive cardiopulmonary resuscitation (CPR) is an important decision encountered by elderly patients and clinical teams; however, outcome data on inpatient CPR is unclear. Additionally, it has been reported that elderly patients and physicians overestimate the chance of survival after CPR when deciding whether a do-not-resuscitate (DNR) order might be appropriate.[1–5] Therefore, providing accurate outcomes on CPR may influence the decision-making on CPR for hospitalized elderly patients.[6]

A recent systematic review including 29 studies showed that the survival rate of CPR among elderly inpatients ranges from 11.6 to 18.7% and declines with increasing age. The vast majority of these patients were from the USA,[7] and survival rate after CPR has also been shown to vary by race.[8] A previous study using Medicare data reported that black and other non-white patients had a higher likelihood of receiving in-hospital CPR but had lower odds of survival.[9]

In contrast, only a few studies have examined the outcomes of in-hospital CPR in Asian populations including elderly patients in Japan, who have the longest life expectancy in the world.[10] In Japan, more than 70% of hospitalized patients are aged ≥ 65 years, approximately three in four die in the hospital, and two in ten do not have DNR orders.[11] In this context, we used a large population-based database from 81 Japanese hospitals to investigate the survival rate after CPR among hospitalized elderly patients and to identify predictors associated with survival.

METHODS

Date Source

Patients' data were extracted from the Diagnosis Procedure Combination (DPC) data[12] of the National Hospital Organization (NHO) Network in Japan. The DPC is nationally used for health care insurance claims for health service rendered in acute care hospitals in Japan, similar to medical claim codes used in the USA.[13, 14] The NHO is the largest hospital network in Japan, and stores DPC data from 81 acute care hospitals, typically teaching/tertiary hospitals in each district, affiliated with the NHO for administration and clinical information analysis. The DPC data includes hospital administrative data and discharge abstracts: unique identifiers of hospitals; characteristics of patients; admission and discharge status; diagnoses and comorbidities at admission, and complications after admission recorded in the International Classification of Diseases, Tenth Revision (ICD-10); surgical and non-surgical procedures; drugs and devices used; and length of stay.[13] To optimize the accuracy of medical information, attending physicians are responsible for registering the diagnoses. This retrospective study was approved by the Institutional Ethics Committees at the National Hospital Organization and Tokyo Medical Center.

Study Sample. This study included patients aged ≥ 65 years who were hospitalized and received CPR 2 days after admission from April 1, 2010 to March 31, 2016. We excluded patients who received CPR within 2 days of hospitalization due to the inability to distinguish patients who were in cardiac arrest on arrival to the hospitals. The procedure of CPR was identified as "Closed-chest cardiac massage (J046)" from the DPC database. For patients who went into more than one cardiac arrest event and received multiple CPR episodes during their hospitalization, we only included the first CPR in our analysis.

Outcome Variables. Our primary outcome was survival to hospital discharge among elderly in-patients who received CPR after the second day of their hospitalization. As secondary outcomes, we investigated the discharge disposition (home, nursing facilities, or other hospitals) of patients who survived to hospital discharge and the patient's level of consciousness at discharge (comatose or not). Consciousness level was categorized based on the Japan Coma Scale where comatose is defined by the three-digit code of 100, 200, or 300.[15]

Potential Predictors. We considered the following potential patient-level and institutional-level predictors: patient sex, age, body mass index (BMI), consciousness level on admission (based on the Japan Coma Scale),[15] admitting diagnosis, admitting comorbidities (based on the Charlson comorbidity index),[16] hospital size (defined by number of hospital beds: < 300, small; 300–499, medium; and ≥ 500, large), days from admission to CPR, and day of week of CPR (weekend vs. weekday). We also considered whether patients received the following interventions within 3 days prior to CPR in order to assess pre-resuscitation interventions: intensive care unit (ICU) admission, enteral nutrition, total parenteral nutrition, vasopressor use, and mechanical ventilation (defined by non-invasive positive pressure ventilation and/or invasive mechanical ventilation).

Statistical Methods. We compared baseline patient characteristics using chi-square test. To determine the predictors associated with survival after in-hospital CPR at the level of alpha = 0.05, we fit unadjusted and adjusted logistic regression models for each response using a forward selection approach. Non-significant variables were added sequentially; no potential confounders that altered estimates of significant factors by more than 10% were identified. Thus, candidate explanatory variables associated with survival were identified. Next, we analyzed the candidate variables using generalized estimating equations with a logit link function where the clustering effect associated with hospitals is accounted for by the robust sandwich standard error estimator. We tested the significance of BMI in a subset of patients with complete data as BMI was missing in 885 patients (16%), and found no significant importance. We also performed a sensitivity analysis excluding patients who underwent multiple CPR events. All analyses were performed with STATA 12 software (STATA Corp, College Station, TX). All P values were two-tailed and considered statistically significant with $P < 0.05$.

RESULTS

Patients. We identified 1,478,934 patients aged ≥ 65 years who were hospitalized for more than 2 days in 81 Japanese hospitals from April 1, 2010 to March 31, 2016. Among these, 78,360 patients experienced cardiac arrest after 2 days of admission, and 5365 patients received CPR.

Descriptive Statistics. Among the 5365 patients who received CPR, 595 patients (11%) survived to hospital discharge. Of the 4770 patients who died after CPR, 3768 patients (79%) died within the same day of receiving CPR. Overall, the median length of stay was 22 days, and the median length from hospital admission to event of cardiac arrest was 16 days. Table 1 shows the characteristics of the patients who

Table 1 Characteristics of Patients Who Received In-Hospital Cardiopulmonary Resuscitation (*N* = 5365)

Characteristics	Sample n	Sample (%)	Survival rate %	*P* value*
Overall	5365	(100.0)	11.1	
Sex				
Male	3375	(62.9)	10.8	0.35
Female	1990	(37.1)	11.6	
Age				
65–69	677	(12.6)	13.6	**0.006**
70–74	890	(16.6)	9.9	
75–79	1181	(22.0)	12.1	
80–84	1308	(24.4)	11.1	
85–89	888	(16.6)	11.3	
≥ 90	421	(7.9)	6.4	
Body Mass Index[a]				
< 18.5	1251	(23.3)	9.4	0.06
18.5–25	3487	(65.0)	11.4	
≥ 25	627	(11.7)	12.8	
Comatose on admission	296	(5.5)	15.2	**0.02**
Admitting diagnosis				
Cancer	984	(18.3)	6.5	**< 0.001**
Pneumonia	543	(10.1)	9.8	
Congestive heart failure	542	(10.1)	13.5	
Cerebrovascular diseases	377	(7.0)	13.0	
Other respiratory diseases	316	(5.9)	7.9	
Traumatic diseases	291	(5.4)	14.8	
Ischemic heart diseases	290	(5.4)	21.7	
Gastroenterological diseases	183	(3.4)	12.0	
Other infectious diseases[b]	168	(3.1)	4.8	
Aortic dissection	122	(2.3)	13.1	
Neurological diseases	101	(1.9)	13.9	
Renal failure	98	(1.8)	12.2	
Hematological diseases	92	(1.7)	1.1	
Arrhythmia	88	(1.6)	33.0	
Other	1170	(21.8)	10.5	
Charlson Comorbidity Index				
0	1669	(31.1)	12.2	**0.009**
1	1415	(26.4)	12.4	
2	1016	(18.9)	10.5	
3	714	(13.3)	8.8	
≥ 4	551	(10.3)	8.2	
Pre-resuscitation interventions				
Intensive care unit admission	532	(9.9)	17.9	**< 0.001**
Enteral nutrition	820	(15.3)	11.2	0.90
Total parental nutrition	758	(14.1)	8.8	**0.03**
Vasopressor use	1103	(20.6)	12.1	0.21
Mechanical ventilation	854	(15.9)	13.3	**0.02**
Days from admission to CPR				
3–7	1383	(25.8)	14.3	**< 0.001**
8–14	1064	(19.8)	12.3	
15–28	1174	(21.9)	9.5	
≥ 29	1744	(32.5)	8.8	
Day of CPR				
Weekday	3695	(68.9)	12.4	**< 0.001**
Weekend	1670	(31.1)	8.3	
Hospital size (number of hospital beds)				
< 300	845	(15.8)	6.2	**< 0.001**
300–499	3094	(57.7)	12.0	
≥ 500	1426	(26.6)	12.1	

Abbreviation: CPR cardiopulmonary resuscitation
**All the comparisons were made using chi-square tests*
[a] *16% missing*
[b] *Including sepsis*

received CPR and the survival rates. The median age was 79 years (IQR, 73–84 years) and 63% were male. Of 231 patients who underwent multiple CPR events during hospitalization, 32 (14%) patients survived to hospital discharge.

Status Among Patients Who Survived to Discharge After CPR. Among 595 patients who survived to discharge, the median length of hospitalization from receiving CPR to discharge was 46 days, and 59 (10%) patients were comatose at discharge (Table 2). Of 581 patients with data available on discharge dispositions, 279 (48%) patients were transferred to other hospitals, 266 (46%) patients were discharged home, and 18 (3%) patients were transferred to nursing facilities.

Multivariable Analysis. Table 3 presents significant predictors associated with survival to hospital discharge after adjustment. Age and higher burden of comorbidities were significant predictors of reduced survival. Admitting diagnoses of cancer, infectious disease, and hematological disease were also significant predictors of reduced survival, while admitting diagnoses of ischemic heart disease, arrhythmia on admission, and ICU admission prior to resuscitation were associated with greater survival. The patients who received CPR after 2 weeks from admission were less likely to survive. Receiving CPR on weekends and/or in small hospitals were also significant predictors of reduced survival. There was no effect modification between hospital size and receiving CPR on weekends or between hospital size and ICU admission. Other factors such as sex, BMI, consciousness level on admission, and pre-resuscitation interventions of enteral nutrition, total parental nutrition, vasopressor treatment, and mechanical ventilation were not significant predictors or confounders. In the sensitivity analysis excluding patients who underwent multiple CPR events, the significance and direction of the effect of the predictors were not different from the result in the main analysis.

DISCUSSION

In our study of over 5000 elderly patients who received in-hospital CPR in Japan, approximately one in ten survived, and less than half of these patients were discharged home. In

Table 2 Status Among Patients Who Survived to Discharge After Cardiopulmonary Resuscitation (*N* = 595)

	n	(%)
Discharge disposition[a]		
Other hospitals	279	(48.0)
Home	266	(45.8)
Nursing facilities	18	(3.1)
Other	18	(3.1)
Neurological status		
Comatose at discharge	59	(9.9)

[a] *581 patients' data (98%) were available on discharge dispositions*

Table 3 Multivariable Analyses for Predictors Associated with Survival to Hospital Discharge (adjusted for the year of admission)

Predictors	Odds ratio (95% CI)
Age	
65–69	Reference
70–74	**0.69 (0.50–0.95)**
75–79	0.84 (0.63–1.12)
80–84	**0.70 (0.52–0.94)**
85–89	**0.71 (0.52–0.97)**
≥90	**0.35 (0.22–0.55)**
Admitting diagnosis	
Pneumonia	Reference
Cancer	**0.61 (0.41–0.90)**
Congestive heart failure	1.32 (0.90–1.94)
Cerebrovascular diseases	1.16 (0.76–1.76)
Other respiratory diseases	0.73 (0.44–1.21)
Traumatic diseases	1.46 (0.94–2.26)
Ischemic heart diseases	**1.84 (1.21–2.80)**
Gastroenterological diseases	1.19 (0.69–2.03)
Other infectious diseases[a]	**0.40 (0.19–0.87)**
Aortic dissection	1.04 (0.56–1.92)
Neurological diseases	1.36 (0.72–2.59)
Renal failure	1.14 (0.58–2.25)
Hematological diseases	**0.08 (0.01–0.63)**
Arrhythmia	**3.96 (2.30–6.79)**
Other	1.02 (0.72–1.44)
Charlson Comorbidity Index	
0	Reference
1	0.99 (0.79–1.24)
2	0.83 (0.64–1.07)
3	0.75 (0.55–1.03)
≥4	**0.68 (0.48–0.97)**
Pre-resuscitation intervention	
Intensive care unit admission	**1.38 (1.06–1.80)**
Days from admission to CPR	
3–7	Reference
8–14	0.88 (0.69–1.12)
15–28	**0.68 (0.53–0.88)**
≥29	**0.67 (0.53–0.85)**
Day of CPR	
Weekday	Reference
Weekend	**0.63 (0.51–0.77)**
Number of hospital beds	
<300	**0.58 (0.40–0.83)**
300–499	1.05 (0.83–1.32)
≥500	Reference

The ORs of the predictors associated with survival or reduced survival after in-hospital CPR at the level of alpha = 0.05 are presented in bold
Abbreviation: CPR cardiopulmonary resuscitation
[a]Including sepsis

addition to older age and higher illness burden, receiving CPR on weekends and/or in small hospitals were significant predictors of reduced survival; in contrast, ischemic heart disease, arrhythmia on admission, and ICU admission before resuscitation were associated with greater survival.

To the best of our knowledge, this is the largest study outside of the USA examining the outcomes of in-hospital CPR among elderly patients, and the first study focusing on an Asian population. Further, this study considered pre-resuscitation interventions and institutional-level factors in addition to baseline characteristics on hospital admission.

Approximately half of the patients who survived to discharge after CPR were discharged home. In contrast, another half of those were transferred to other hospitals; one in ten were comatose at discharge. Many of the patients transferred to other hospitals were likely to move to rehabilitation hospitals or long-term care hospitals rather than other acute care hospitals though these data were not available in our study. Nonetheless, these findings suggest that these patients had physical complications after CPR and required longer-term medical treatment.

Our findings are consistent with prior data reporting the association between older age and reduced survival.[7, 9] A systematic review showed that the pooled survival rate after CPR was 18.7% for patients between 70 and 79 years old, 15.4% for those between 80 and 89 years old, and 11.6% for 90 years and older.[7] The survival rates of in-hospital CPR in the present study were even lower than that of prior studies. This difference may be partly explained by the different inclusion criteria of when CPR was performed; for example, we excluded patients who received CPR within 2 days of hospitalization due to our inability to distinguish patients who were in cardiac arrest on arrival to the hospitals.

Our finding that arrhythmia, ischemic heart disease, and ICU admission were associated with increased survival rates likely reflects increased use of cardiac monitoring and rapid response to event.[17] In addition, patients with arrhythmia or ischemic heart disease might be more likely to have initial rhythms of ventricular fibrillation or ventricular tachycardia, which are more responsive to CPR.[18, 19] Furthermore, there may be a selection bias in which patients are admitted to ICU based on physician's perception of patient's likelihood to benefit from ICU care. In contrast, cancer, infection, hematological disease, and higher burden of comorbidities were independently predictive of in-hospital mortality, and these findings are in line with previous studies.[9, 17] These predictors of poor prognosis can be applied to advanced care planning discussions and guide decision-making about do-not-resuscitate orders.

Our finding that receiving CPR on weekends compared to weekdays as an independent predictor of reduced survival is consistent with a previous study demonstrating that patients who received CPR during day on weekdays were more likely to survive, compared to those who received CPR during day on weekends.[20] Our findings also indicate that receiving CPR in smaller hospitals compared to larger hospitals were associated with reduced survival. The underlying mechanism of reduced survival after CPR on weekends and in small hospitals may be explained by different hospital staffing patterns in these settings. The difference in the availability of rapid response systems (RRS) between larger hospitals and smaller hospitals may be another explanation, since the shortage of medical staff is considered to be the main barrier of implementing RRS.[21] Addressing institutional systems, such as implementing RRS among small hospitals during weekends, may improve important outcomes associated with CPR.

While our study leverages a rich dataset, it is not without limitations. First, our definition of CPR was based on the DPC data in Japan, and the definition of CPR has not been validated in this data, although a previous validation study on the DPC data shows that the sensitivity and specificity of common procedures exceeds 90% and the sensitivity and specificity of primary diagnoses were 79% and 93%.[22] Second, our analyses were limited to patients who received CPR after 2 days of hospitalization, which may have underestimated the survival rate in our study. Third, the dataset had limited information on other potential predictors of survival such as initial arrest rhythm, presence of witness, use of telemetry, and the availability of rapid response systems. In addition, the dataset had also limited information on other outcomes such as physical function, quality of life, and details of hospitals to which patients were transferred.

In conclusion, among elderly patients in Japan, the survival rate of in-hospital CPR after 2 days of hospitalization was approximately one in ten, and less than half of these patients were discharged home. In addition to older patient age and higher illness burden, receiving CPR on weekends and in small hospitals were significant predictors of reduced survival. These findings suggest that patients' baseline status should be considered in advanced care planning discussions with elderly patients to avoid subjecting patients to CPR that are likely futile. Moreover, future studies should identify potential system factors that might underlie differences in outcomes after CPR between large and small hospitals.

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Compliance with Ethical Standards:

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