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The impact of COVID-19 pandemic on out-of-hospital cardiac arrest system-of-care: Which survival chain factor contributed the most?

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ABSTRACT

Objectives: In many communities, out-of-hospital cardiac arrest (OHCA) survival outcomes decreased after the coronavirus disease 2019 (COVID-19) pandemic. This study aimed to identify and compare the impacts of each survival chain factor on the change of survival outcomes after COVID-19.

Methods: Using a Korean out-of-hospital cardiac arrest registry, we analyzed OHCA patients whose arrest was not witnessed by emergency medical service (EMS) providers between 2017 and 2021. Because lack of hospital and survival information in 2021, the 2021 data were used only to identify the expected trend. We developed a prediction model for survival to discharge using patients from 2017 to 2019 (Pre-COVID-19 set) and validated it using patients from 2020 (post-COVID-19 set). Using Utstein elements, a stepwise logistic regression model was constructed, and discrimination and calibration were evaluated by c-statistics and scaled Brier score. Using the distribution change of predictors from one year before the pandemic (2019) to post-COVID-19, we calculated the magnitude of survival difference according to each predictor's distribution change using the marginal standardization method.

Results: Among 83,273 patients (mean age 67.2 years and 64.3% males), 61,180 and 22,092 patients belonged to pre-COVID-19 and post-COVID-19 sets. Survival to discharge was 5019 (8.2%) in pre-COVID-19 set and 1457 (6.6%) in post-COVID-19 set. The proportion of bystander cardiopulmonary resuscitation was 59.0% in the pre-COVID-19 set and 61.0% in the post-COVID-19 set. The median (interquartile range) response time was 7 (5–9) minutes in the pre-COVID-19 set and 8 (6–10) minutes in the post-COVID-19 set. The area under the receiver operating characteristic (AUROC) curve (95% confidence interval) was 0.907 (0.902–0.912) in the pre-COVID-19 set, and 0.924 (0.916–0.931) in the post-COVID-19 set, and scaled Brier score were 0.39 in pre-COVID-19 sets, and 0.40 in the post-COVID-19 set. Among various predictors, EMS factors showed the highest impact. Response time and on-scene management of EMS showed the highest impact on decreased survival. A similar trend was also expected in the 2021.

Conclusion: The effort to create a rapid response system for OHCA patients could have priority for the recovery of survival outcomes in OHCA patients in the post-COVID-19 period. Further studies to recover survival outcomes of OHCA are warranted.

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1. Introduction

After the coronavirus disease 2019 (COVID-19) pandemic, the incidence of OHCA increased by 120 to 140%, [1,2] and survival outcomes of OHCA decreased by 40–50% in several communities. [2,3] The

worsening survival outcomes of OHCA have been shown to not only occur in countries with a high number of infections but also in countries that have initially strongly suppressed the rate of COVID-19 infections. [4–6] The COVID-19 pandemic affects many aspects of the survival chain. During the COVID-19 pandemic, a decreased proportion of arrests in public locations, decreased bystander cardiopulmonary resuscitation (CPR) rates, delayed response to EMS, and delays to pre-hospital advanced life support have been reported in various studies. [2,3,5,7] To improve the survival outcomes of OHCA patients, it is necessary to make an effort to recover all of the changes in the survival chain, but it is also necessary to set priorities. Analyzing and comparing the effects

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of individual factors of the survival chain on the deterioration of survival outcomes would help prioritize efforts to recover survival outcomes during or after the COVID-19 pandemic.

This study aimed to identify and compare the impact of each factor of the survival chain on the change in survival outcomes after COVID-19. Using Utstein elements, [8] we developed a prediction model for survival to discharge of OHCA using the pre-COVID-19 data and validated it using the post-COVID-19 data. Because we assumed that the importance of Utstein elements for survival would be similar before and after COVID-19, the performance of the prediction model would also be similar between pre-COVID-19 data and post-COVID-19 data. After confirming the validity of the prediction model in the post-COVID-19 data, we investigated the impact of the distribution change of each Utstein element on the survival outcome. Using the prediction model and the information of the distribution change of each Utstein element, we compared the magnitude of the impact on the probability of survival according to each element and identified which Utstein elements contributed the most to the prediction of survival outcome change after COVID-19.

2. Materials and methods

2.1. Study setting

Korea operates the fire-based, basic to intermediate service level of the ambulance system. For patients with OHCA, EMS providers can provide CPR with automated defibrillator use, and advanced airway management or intravenous fluid infusion can also be provided under direct medical control. All EMS-treated OHCA patients should be transported to the hospital because EMS providers cannot declare the state of death in the field. Korean government has designated the following three levels of ED: Level 1 ($n = 36$) and Level 2 ($n = 119$) EDs, which provide the highest level of emergency care services with emergency physician on staff all times; and Level 3 EDs ($n = 261$), which may be staffed by general physicians. Level 4 EDs are operated by each center but not designated by government. All EDs generally perform acute cardiac care and post-resuscitation care in accordance with national guidelines.

The first confirmed COVID-19 patient in Korea was identified on January 20, 2020. The Korean government initially suppressed COVID-19 infection spread strictly with a 3 T strategy (testing-tracing-treatment), and the cumulative number of confirmed cases in 2020 was 60,740 (117 per 100,000 population). A total of 900 confirmed cases died in 2020; therefore, the case fatality rate was 1.5% in 2020. According to World Health Organization COVID-19 statistics, the cumulative confirmed case and a total death in 2020 were 19,581,844 (5943 per 100,000 population) and 352,099 (case fatality rate 1.8%) in the United States, and 2,564,375 (3814 per 100,000 population) and 75,202 (case fatality rate 2.9%) in the United Kingdom. In March 2020, a new EMS protocol for COVID-19 suspected patients began to be adopted and has been continuously revised. For OHCA patients, Level D personal protective equipment is required to respond to the protocol, regardless of the patients' symptoms or status.

2.2. Study design

This was a cross-sectional study based on data from the Korean Out-of-Hospital Cardiac Arrest Registry (KOHCAR) [9] and approved by the institutional review boards of Seoul National University Hospital. We adhered to the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement on reporting predictive models. [10]

2.3. Study population

EMS-treated OHCA patients whose cardiac arrest had not been witnessed by EMS providers from 2017 to 2020 were included in the

analysis. Because the number of confirmed COVID-19 patients was minimal and EMS protocols were not changed systemically until March 2020, patients were excluded if OHCA occurred between January and February in both pre-COVID-19 and post-COVID-19. Patients were also excluded if they had missing or invalid information regarding EMS response time (the time between EMS call and EMS arrival at the scene), EMS scene time (the time interval between EMS arrival on the scene and its departure), first recorded rhythm, or variables pertaining to the time of post-resuscitation care.

2.4. Variables and measurements

The KOHCAR captures all EMS-assessed OHCA incidents from the following four sources: ambulance runsheet for ambulance operational information, EMS cardiac arrest registry for Utstein factors, dispatcher CPR registry for dispatch information, and hospital medical record review for hospital care and outcomes. The Korean Disease Control and Prevention Agency (KCDA) conducts a review of hospital medical records. KOHCAR was constructed from 2006 onward based on the Utstein recommendation. [11]

We a priori selected predictors with known survival association (Utstein elements). We used age, sex, etiology of arrest (medical, trauma, asphyxia, drowning, and others), layperson witness status (yes or no), place of arrest (public or non-public), dispatcher arrest recognition status and time, bystander CPR (yes or no), EMS response time, EMS scene time, first recorded cardiac rhythm (shockable, PEA and asystole), pre-hospital defibrillation status and time, pre-hospital advanced airway management, pre-hospital epinephrine use, pre-hospital mechanical CPR device use, post-resuscitation care (coronary angiography [CAG], targeted temperature management [TTM], and extracorporeal membrane oxygenation [ECMO]) and its start time, and level of ED (1, 2, 3, or 4). We categorized the variables into deciles for continuous variables, including age and response time. In addition, we processed variables by merging the categories of Utstein elements to identify key interventions and their consequences. Details of variable processing are described in the Supplement methods. With the aforementioned predictors, stepwise model selection using the Akaike information criterion (AIC) was conducted to obtain a parsimonious model. Except for sex, all predictors were included in the final prediction model.

2.5. Outcome measures

The primary outcome was survival to discharge.

2.6. Statistical analysis

We developed a logistic regression model for survival to discharge. After deriving the final model, we tested for multicollinearity between predictors. The study population was split into a training set, which was used for the development of the prediction model, and a test set, in which the prediction model was tested. We planned to use the pre-COVID-19 data for training and post-COVID-19 data for testing. As the first confirmed COVID-19 cases occurred in January 2020 in Korea, the training set was derived from 2017 to 2019, and the test set comprised data from 2020.

The characteristics of the training and test sets were compared. Continuous variables were compared using Student's *t*-test or the Wilcoxon rank-sum test, and categorical variables were compared using the chi-squared test or the Fisher exact test, as appropriate. We assessed the discrimination performance of the prediction model by area under the receiver operating characteristic curve (AUROC) and the calibration power by scaled Brier score, which ranges between 0% for non-informative predictions and 100% for perfect predictions and calibration plot. [12,13] We also calculated the overall calibration as the ratio of the

observed outcomes and expected outcomes (O/E) with an optimal value of 1; O/E > 1 indicates underprediction and < 1 overprediction.

After verifying the validity of the prediction model for the post-COVID-19 period, we evaluated the change in the probability of outcome according to the distribution change of predictors from 2019 (one year before COVID-19) to 2020 (post-COVID-19). We used a marginal standardization method for this analysis. [14] Details of marginal standardization method are described in the Supplement methods. We plotted the difference in the probability of the outcome according to the change in the distribution of every predictor between 2019 and 2020. To evaluate the latest status, we also analyzed the change in the probability of outcome according to the distribution change of predictors from 2019 to 2021. Because information for post-resuscitation variables were not available in 2021, we assumed that the distribution of post-resuscitation remained as constant as in 2020.

We conducted sensitivity analyses to determine whether different categorizations of continuous variables changed the results of our study. Continuous variables were categorized into quintile and 20-quantiles. We also evaluated whether the difference in the probability of outcome according to the distribution change of predictors changed if the outcome was changed to good neurological recovery at discharge (cerebral performance category 1 or 2 at discharge). All statistical analyses were performed using R version 4.1.2.

2.7. Ethics statements

The study was approved by the Institutional Review Boards of Seoul National University Hospital (IRB No. H-1103-153-357) and the requirement for informed consent was waived.

3. Results

Among the 116,088 EMS-treated OHCA patients, 83,272 were included in the final analysis. The training set (pre-COVID-19 set), derived from 2017 to 2019, comprised 61,180 (73.5%) patients, and the test set (post-COVID-19 set), from 2020, comprised 22,092 (26.5%) patients (Fig. 1).

The mean (SD) age was 66.9 (18.8) years in the pre-COVID-19 set and 67.9 (18.5) in the post-COVID-19 set. The proportion of bystander CPR was 59.0% in the pre-COVID-19 set and 61.0% in the post-COVID-

19 set, respectively. The median (interquartile range) response time was 7 (5–9) minutes in the pre-COVID-19 set and 8 (6–10) minutes in the post-COVID-19 set. The proportion of shockable rhythm and defibrillation within 4 min decreased from 8.5% in the pre-COVID-19 set to 7.6% in the post-COVID-19 set. Among shockable rhythm, the proportion of patients with defibrillation within 4 min decreased from 64% (5217/8203) in the pre-COVID-19 set to 63% (1689/2679) in the post-COVID-19 set. The proportion of pre-hospital advanced life support with longer scene time intervals was higher in the post-COVID-19 set than in the pre-COVID-19 set. The proportion of advanced airway management with scene time over 14 min increased from 38.1% in the pre-COVID-19 set to 53.2% in the post-COVID-19 set. The proportion of epinephrine use or mechanical CPR device use with scene time over 14 min also increased from the pre-COVID-19 set to the post-COVID-19 set. Survival to discharge and good neurological recovery at discharge were 5019 (8.2%) and 3075 (5.0%) in the pre-COVID-19 set and 1457 (6.6%) and 991 (4.5%) in the post-COVID-19 set, respectively (Table 1).

The adjusted odds ratios of the predictors in the final model are presented in Table 2. No multicollinearity was observed among the final predictors.

Our prediction model showed an acceptable performance in the post-COVID-19 cohort. The AUROC (95% CI) was 0.907 (0.902–0.912) for the pre-COVID-19 set and 0.924 (0.916–0.931) for the post-COVID-19 set. The calibration power was similar between the pre-COVID-19 and post-COVID-19 sets (scaled Brier score: 0.39 in the training set and 0.40 in the test set). The observed to expected outcome ratio was 1.00 in the pre-COVID-19 set and 0.98 in the post-COVID-19 set. The calibration plot demonstrated acceptable calibration for both pre- and post-COVID-19 sets (Fig. 2).

Fig. 3 shows the differences in the probability of survival to discharge due to the change in distribution between 2019 and 2020. The characteristics of the study populations in 2019 and 2020 are listed in Supplementary Table 1. Among the various predictors, EMS had the highest negative impact. Response time and pre-hospital on-scene management had the highest impact on change. A longer response time and on-scene management with longer scene stay were associated with a lower likelihood of survival in the prediction model (Table 2). The changes in more patients who received bystander CPR, increased proportion of medical cause, and more cases visited higher levels of ED in

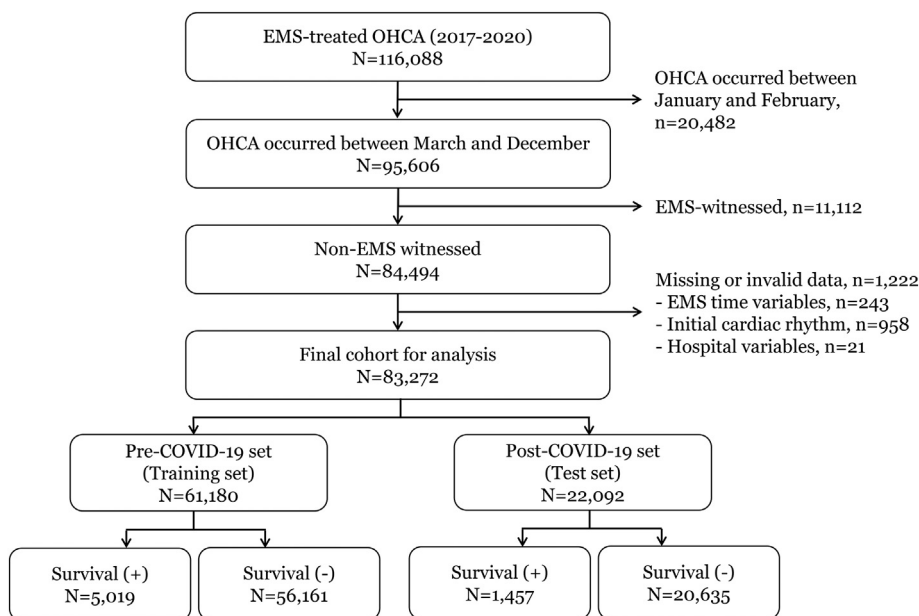


Fig. 1. Patient flow. OHCA, out-of-hospital cardiac arrest; EMS, emergency medical service.

Table 1
Patient characteristics of study cohort.

	Total	Pre-COVID-19 (Training set)	Post-COVID-19 (Test set)
Characteristics	N = 83,272	N = 61,180	N = 22,092
Age, mean (SD), y	67.2 (18.7)	66.9 (18.8)	67.9 (18.5)
Male sex	53,571 (64.3%)	39,438 (64.5%)	14,133 (64.0%)
Etiology of arrest			
Medical	63,992 (76.8%)	46,782 (76.5%)	17,210 (77.9%)
Trauma	10,392 (12.5%)	7918 (12.9%)	2474 (11.2%)
Asphyxia	4358 (5.2%)	3300 (5.4%)	1058 (4.8%)
Drowning	1209 (1.5%)	877 (1.4%)	332 (1.5%)
Others	3321 (4.0%)	2303 (3.8%)	1018 (4.6%)
Layperson witnessed	34,826 (41.8%)	25,788 (42.2%)	9038 (40.9%)
Public place	21,248 (25.5%)	16,027 (26.2%)	5221 (23.6%)
Bystander CPR			
No bystander CPR (dispatcher unrecognized)	20,884 (25.1%)	15,518 (25.4%)	5366 (24.3%)
No bystander CPR (dispatcher recognized)	12,802 (15.4%)	9559 (15.6%)	3243 (14.7%)
Bystander CPR (dispatcher unrecognized)	11,318 (13.6%)	8229 (13.5%)	3089 (14.0%)
Bystander CPR within 150 s of call (dispatcher recognized)	14,514 (17.4%)	9315 (15.2%)	5199 (23.5%)
Bystander CPR conducted after 150 s of call (dispatcher recognized)	20,225 (24.3%)	15,638 (25.6%)	4587 (20.8%)
Bystander CPR with unknown time (dispatcher recognized)	3529 (4.2%)	2921 (4.8%)	608 (2.8%)
EMS time interval, median (IQR)			
Response time, min	7.0 (5.0;9.0)	7.0 (5.0;9.0)	8.0 (6.0;10.0)
Scene time, min	14.0 (10.0;18.0)	14.0 (10.0;18.0)	15.0 (12.0;20.0)
Transport time, min	7.0 (4.0;11.0)	7.0 (4.0;11.0)	7.0 (5.0;12.0)
Initial cardiac rhythm / Defibrillation			
Shockable rhythm and defibrillation within 4 min	6906 (8.3%)	5217 (8.5%)	1689 (7.6%)
Shockable rhythm and defibrillation after 4 min	3839 (4.6%)	2888 (4.7%)	951 (4.3%)
Shockable rhythm but no defibrillation	137 (0.2%)	98 (0.2%)	39 (0.2%)
PEA but defibrillation	1312 (1.6%)	947 (1.5%)	365 (1.7%)
PEA and no defibrillation	14,545 (17.5%)	10,620 (17.4%)	3925 (17.8%)
Asystole but defibrillation	3939 (4.7%)	3065 (5.0%)	874 (4.0%)
Asystole and no defibrillation	52,594 (63.2%)	38,345 (62.7%)	14,249 (64.5%)
Prehospital AAM			
Non-conducted	15,557 (18.7%)	14,038 (22.9%)	1519 (6.9%)
Conducted and scene time within 14 min	32,643 (39.2%)	23,822 (38.9%)	8821 (39.9%)
Conducted and scene time over 14 min	35,072 (42.1%)	23,320 (38.1%)	11,752 (53.2%)
Prehospital epinephrine			
Non-conducted	69,095 (83.0%)	51,725 (84.5%)	17,370 (78.6%)
Conducted and scene time within 14 min	2232 (2.7%)	1529 (2.5%)	703 (3.2%)
Conducted and scene time over 14 min	11,945 (14.3%)	7926 (13.0%)	4019 (18.2%)
Prehospital mechanical CPR device use			
Non-conducted	66,833 (80.3%)	51,060 (83.5%)	15,773 (71.4%)
Conducted and scene time within 14 min	6351 (7.6%)	4418 (7.2%)	1933 (8.7%)
Conducted and scene time over 14 min	10,088 (12.1%)	5702 (9.3%)	4386 (19.9%)
ED level			
Level 1	19,305 (23.2%)	13,609 (22.2%)	5696 (25.8%)
Level 2	37,987 (45.6%)	27,997 (45.8%)	9990 (45.2%)
Level 3	23,202 (27.9%)	17,491 (28.6%)	5711 (25.9%)
Level 4	2778 (3.3%)	2083 (3.4%)	695 (3.1%)
CAG			
Non-conducted	81,349 (97.7%)	59,717 (97.6%)	21,632 (97.9%)
Conducted within 97 min after ED arrival	974 (1.2%)	754 (1.2%)	220 (1.0%)
Conducted after 97 min after ED arrival	949 (1.1%)	709 (1.2%)	240 (1.1%)
TTM			
Non-conducted	80,442 (96.6%)	59,100 (96.6%)	21,342 (96.6%)
Conducted within 182 min after ED arrival	1425 (1.7%)	1064 (1.7%)	361 (1.6%)
Conducted after 182 min after ED arrival	1405 (1.7%)	1016 (1.7%)	389 (1.8%)
ECMO			
Non-conducted	82,533 (99.1%)	60,656 (99.1%)	21,877 (99.0%)
Conducted within 77 min after ED arrival	373 (0.4%)	268 (0.4%)	105 (0.5%)
Conducted after 77 min after ED arrival	366 (0.4%)	256 (0.4%)	110 (0.5%)
Survival outcomes			
Any prehospital ROSC	8395 (10.1%)	6201 (10.1%)	2194 (9.9%)
ROSC at hospital handover	8916 (10.7%)	6613 (10.8%)	2303 (10.4%)
Survival to admission	15,765 (18.9%)	11,980 (19.6%)	3785 (17.1%)
Survival to discharge	6476 (7.8%)	5019 (8.2%)	1457 (6.6%)
Good neurological recovery at discharge	4066 (4.9%)	3075 (5.0%)	991 (4.5%)

SD, standard deviation; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; IQR, interquartile range; PEA, pulseless electrical activity; AAM, advanced airway management; ED, emergency department; ECMO, extracorporeal membrane oxygenation; ROSC, return-of-spontaneous circulation.

the post-COVID-19 period contributed to a positive impact on survival, but the magnitude was relatively small compared to other predictors negative results.

Fig. 4 shows the differences in the probability of survival to discharge due to distribution changes between 2019 (one year before COVID-19)

and 2021 (the second year of COVID-19). The characteristics of the study population in 2019 and 2021 are shown in Supplementary Table 1. EMS factors showed the highest negative impact in 2020, but the negative impact of delayed responses was more prominent in 2021.

Table 2
Adjusted odds ratio of predictors for good neurological recovery at discharge in prediction model

Variables	Adjusted odds ratio (95% CI)
Age	
1st quintile (0–42 years)	3.32 (2.77–3.97)
2nd quintile (43–53 years)	3.18 (2.66–3.78)
3rd quintile (54–59 years)	2.97 (2.49–3.53)
4th quintile (60–65 years)	2.50 (2.09–2.98)
5th quintile (66–71 years)	1.88 (1.56–2.25)
5th quintile (72–76 years)	1.24 (1.02–1.51)
5th quintile (77–79 years)	0.85 (0.68–1.07)
5th quintile (80–83 years)	Reference
5th quintile (84–87 years)	0.69 (0.54–0.88)
5th quintile (88– years)	0.53 (0.40–0.69)
Etiology of Arrest	
Medical	
Trauma	Reference
Asphyxia	0.19 (0.16–0.23)
Drowning	1.61 (1.37–1.90)
Others	0.82 (0.57–1.18)
Layperson witnessed	
Non-witnessed	Reference
Witnessed	2.07 (1.91–2.25)
Place of arrest	
Non-public	Reference
Public	1.33 (1.22–1.44)
Dispatcher recognition / Bystander CPR	
No bystander CPR (dispatcher unrecognized)	1.08 (0.97–1.20)
No bystander CPR (dispatcher recognized)	0.76 (0.66–0.87)
Bystander CPR (dispatcher unrecognized)	1.17 (1.05–1.31)
Bystander CPR within 150 s of call (dispatcher recognized)	0.99 (0.88–1.12)
Bystander CPR conducted after 150 s of call (dispatcher recognized)	Reference
Bystander CPR with unknown time (dispatcher recognized)	0.90 (0.75–1.07)
Response time	
1st quintile (1–4 min)	Reference
2nd and 3rd quintile (5 min)	0.88 (0.78–0.99)
4th quintile (6 min)	0.80 (0.71–0.90)
5th and 6th quintile (7 min)	0.72 (0.64–0.83)
7th quintile (8 min)	0.71 (0.62–0.82)
8th quintile (9–10 min)	0.58 (0.51–0.67)
9th quintile (11–13 min)	0.46 (0.39–0.55)
10th quintile (14– min)	0.32 (0.26–0.39)
Initial cardiac rhythm / Defibrillation	
Shockable rhythm and defibrillation within 4 min	16.22 (14.55–18.09)
Shockable rhythm and defibrillation after 4 min	13.43 (11.85–15.22)
Shockable rhythm but no defibrillation	4.86 (2.46–9.60)
PEA but defibrillation	1.24 (0.97–1.51)
PEA and no defibrillation	1.23 (1.12–1.34)
Asystole but defibrillation	0.23 (0.00–0.47)
Asystole and no defibrillation	Reference
Prehospital AAM	
Non-conducted	Reference
Conducted and scene time within 14 min	1.12 (1.01–1.23)
Conducted and scene time over 14 min	0.62 (0.56–0.68)
Prehospital epinephrine	
Non-conducted	Reference
Conducted and scene time within 14 min	0.78 (0.62–0.98)
Conducted and scene time over 14 min	0.67 (0.59–0.77)
Prehospital mechanical CPR device use	
Non-conducted	Reference
Conducted and scene time within 14 min	0.43 (0.36–0.52)
Conducted and scene time over 14 min	0.48 (0.40–0.56)
ED level	
Level 1	1.12 (1.03–1.22)
Level 2	Reference
Level 3	0.60 (0.54–0.66)
Level 4	0.34 (0.24–0.48)

Table 2 (continued)

Variables	Adjusted odds ratio (95% CI)
CAG	
Non-conducted	Reference
Conducted within 97 min after ED arrival	5.68 (4.64–6.94)
Conducted after 97 min after ED arrival	4.31 (3.50–5.30)
TTM	
Non-conducted	Reference
Conducted within 182 min after ED arrival	7.99 (6.77–9.42)
Conducted after 182 min after ED arrival	6.53 (5.51–7.75)
ECMO	
Non-conducted	Reference
Conducted within 77 min after ED arrival	0.20 (0.14–0.29)
Conducted after 77 min after ED arrival	0.31 (0.22–0.44)

CPR cardiopulmonary resuscitation; PEA, pulseless electrical activity; AAM, advanced airway management; ED, emergency department; CAG, coronary angiography; TTM, targeted temperature management; ECMO, extracorporeal membrane oxygenation.

The results of the analysis did not change according to the different methods of categorizing continuous variables (Supplementary Table 2). We also found a similar pattern of differences in the probability of outcome due to the distribution change between 2019 and 2020 or 2021 in the prediction model for good neurological recovery at discharge (Supplementary Fig. 1 and Supplementary Fig. 2).

4. Discussion

This study developed a survival-to-discharge prediction model using pre-COVID-19 data and validated it using post-COVID-19 data. We found that Utstein elements had sufficient explanatory power for survival outcomes in both pre- and post-COVID-19 periods. Using the distribution change of predictors from one year before the pandemic to the first year of the pandemic, we calculated the magnitude of the difference in survival according to each predictor's distribution change using marginal standardization methods. We found that most elements of the survival chain were affected by COVID-19; however, there was a large difference between them. EMS factors, including delayed response and on-scene management with longer scene stays, had the greatest impact on survival outcome change.

We used a prediction model to identify the most influential factor in decreased survival among various Utstein elements. Because the Utstein elements are closely interrelated, we thought it would be necessary to simplify the reality using a prediction model. Because our prediction model showed excellent performance in post-COVID-19 data, we were able to confirm that our method was plausible and that the Utstein element could also be a crucial factor in explaining survival outcomes in the pandemic period. [8,15] We used the marginal standardization method to estimate and compare the impact of distribution change on survival outcomes. Common methods to estimate predicted probability for logistic regression models include prediction at the mode (calculating predicted probabilities by setting each predictor to the most frequent value), prediction at the means (calculating predicted probabilities by each predictor to its mean value), and marginal standardization (calculating predicted probabilities by summing to a weighted average reflecting the predictor distribution in the overall population). [14] The predicted probabilities of each method are different because each method corresponds to a different target population. Marginal standardization is recommended when making inferences about the overall population is needed. [14] Because we wanted to evaluate the overall impact of distribution change between pre- and post-COVID-19, we adapted the marginal standardization methods in our analysis. The difference in the actual survival to discharge was 1.2% between the first year of COVID-19 (2019) and post-COVID 19

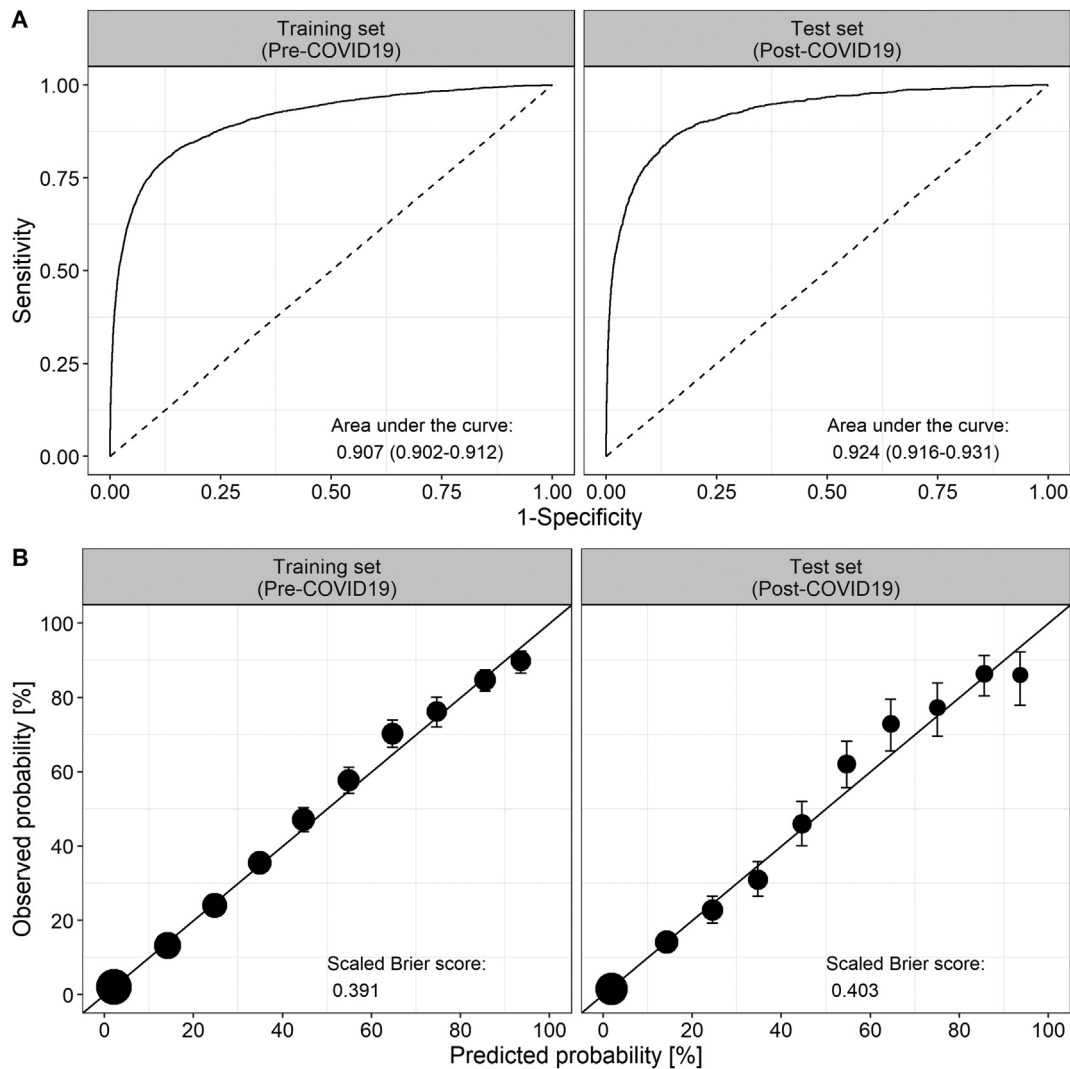


Fig. 2. Area-under the curve plot and calibration plot of prediction model in training and test set.

(2020) (Supplementary Table 1). The sum of the differences in the probability of survival to discharge in our analysis was 1.1%, which is similar to the actual difference and also showed good calibration power of our prediction model (Supplementary Table 2).

As we wanted to evaluate the distribution change among predictors with respect to time, we incorporated time factors in categorizing each predictor. Using this method, we found that delayed pre-hospital defibrillation, on-scene management with longer scene stays, and delays in post-resuscitation care were prominent in the post-COVID-19 period. Those findings may be related to delays in management due to the limited number of providers, use of personal protective equipment, or frequently changing protocols. However, on-scene management with longer stays or delayed management cannot be directly interpreted as the cause of decreased survival among these patients. On-scene management with longer scene stays could be more frequent if patients did not achieve ROSC than if they achieved ROSC in the early period of on-scene management. Delayed post-resuscitation care could also occur more frequently in patients with longer CPR times. Because our analysis was retrospective, we could estimate which stage of the survival chain was associated with lower survival rates; however, we could not evaluate causal relationships in this analysis.

EMS factors were the most influential factors for decreased survival in our analysis. Although this might seem obvious, our results could vary depending on the change in other survival chains. One of the

essential reasons for our results could be that there was no decrease in bystander CPR in the pandemic period (Supplementary Table 2). Because early factors of the survival chain could contribute more to survival outcomes of OHCA patients, [16] bystander CPR might be the main cause of decreased survival if the bystander CPR rate decreases significantly. The importance of bystander CPR and dispatcher-assisted CPR during the pandemic period should not be underestimated even in pandemic period because traditional CPR education programs could not be conducted after COVID-19. [17,18] Moreover, because the proportion of delayed EMS response increased, the importance of bystander CPR or first responder system is even greater. Our study also showed that EMS factors could be more affected by the pandemic than community factors, and those finding are also difficult to be certain until the analysis was completed.

In Korea, overall EMS transport volume was decreased from 2019 to 2020 (1.86 million in 2019 and 1.62 million in 2020). However, the NFA participated in additional work, including a response system for vaccine centers and interhospital transfers for COVID-19 confirmed cases. In addition, the prevalent delay in access, handover, and protocols related to infection also increased the burden of EMS providers during the pandemic. This resulted in a delayed response of OHCA patients with OHCA. For example, a median 1 min delay in response time in 2020 resulted in >0.4% decrease survival from 2019. The negative impact of delayed response time on survival would be expected to be more severe

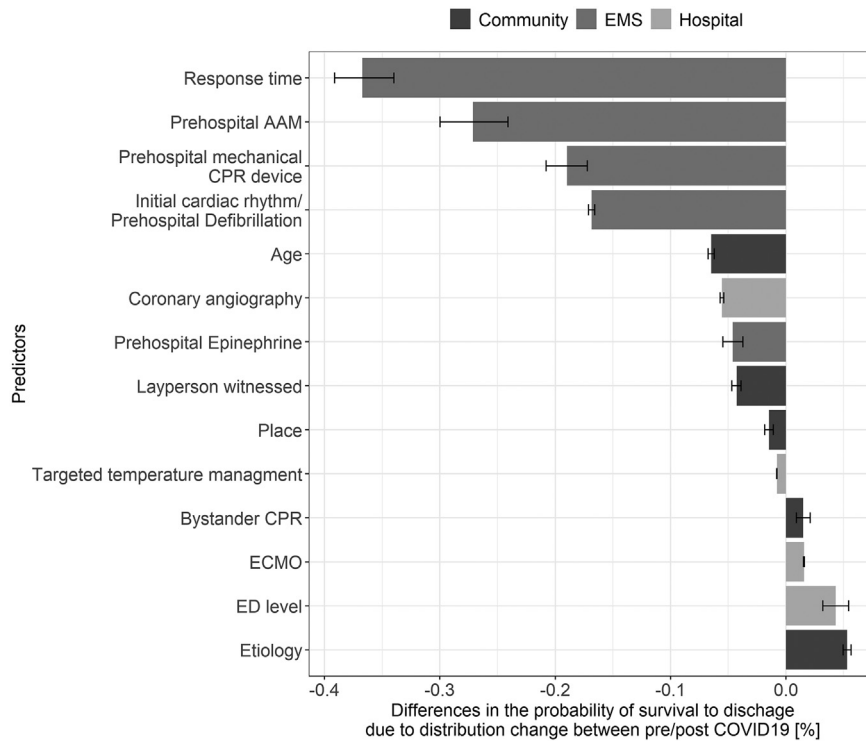


Fig. 3. Differences in the probability of survival to discharge due to distribution change between one year before COVID-19 pandemic (2019) and first year of the COVID-19 pandemic (2020). We identified the change in the marginal probability of survival to discharge when the distribution of predictors in 2019 changes to the distribution in 2020.

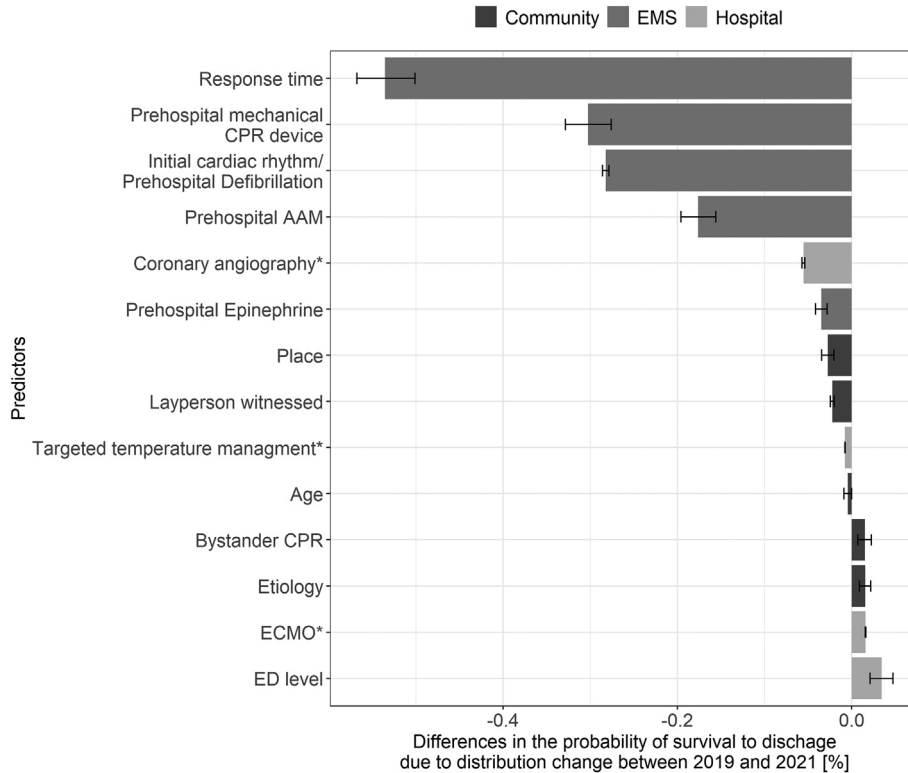


Fig. 4. Differences in the probability of survival to discharge due to distribution change between one year before pandemic (2019) and second year of the post-COVID-19 period (2021). We identified the change in the marginal probability of survival to discharge when the distribution of predictors in 2019 changes to the distribution in 2021. *Variables pertaining to post-resuscitation care were not collected in 2021. Therefore, their distribution was assumed to be the same in the first year after post-COVID-19 (2020).

in 2021, when we estimated that almost 0.5% survival decreased from 2019. In addition to a 1-min delay in an ambulance, there might also be an additional delay for CPR by EMS providers due to PPE and further cautions for infection. Reducing the response time and recovering the quality of immediate CPR should be considered top priorities in the recovery of survival rates of OHCA patients in our setting. In addition, overall high-quality advanced life support in the field should also be considered as one of the main factors for survival recovery. Although mechanical CPR device use, advanced airway management, and pre-hospital epinephrine itself were not associated with decrease in survival compared to conventional management in OHCA patients, [19–21] we found a negative effect of delay in such on-scene management in our analysis (Table 2). Education and training programs for team CPR protocols for EMS providers should be underlined to maintain the quality of CPR while providing accurate advanced life support.

5. Limitations

This study had several limitations. First, because this study was performed in an EMS system without paramedic or physician field response, where the number of COVID-19 cases was initially strongly restricted, the generalization of the findings should be made with caution according to different EMS settings and pandemic situations. Second, the impact of survival chain factors may differ according to predefined predictors. However, we included most Utstein elements in our analysis and conducted variable selection to achieve the parsimonious model. In addition, we also evaluated the collinearity of our predictors, and found no multicollinearity among these parameters in the model. Third, 1.4% of data with missingness of predictors were excluded. If unknown predictors were included, the analysis results might change. Fourth, we did not collect information on post-resuscitation care and survival outcomes in 2020. If we could use hospital information in 2021, we would be able to evaluate the model's validity with more data. We compared the survival chain, assuming that the post-resuscitation care in 2021 would be similar to those in 2020, but this could be changed. The proportion of CAG, TTM, and ECMO were relatively stable since 2017 (2.5%, 3.2% and 0.9% in 2017, 2.7%, 3.8%, and 0.9% in 2018, 2.9%, 3.5%, and 0.9% in 2019, and 2.4%, 3.5% and 1.0% in 2020). Fifth, there could be unmeasured confounding. Although the performance of our prediction model was acceptable, unmeasured confounding could affect our results. Last, we developed a prediction model; however, external validation was not conducted.

6. Conclusion

We found that the Utstein element is still important for explaining the survival decrease of OHCA during the pandemic period. We also found that bystander CPR rate was well maintained in the pandemic, and EMS factors were more affected from the pandemic's beginning. EMS factors including delayed response and on-scene management with longer scene stay were the most important factors in decreased survival in our setting. The effort to recover a rapid EMS response system with high-quality on-scene EMS CPR could prioritize the recovery of survival outcomes in OHCA patients in the post-COVID-19 period. Further research is required to determine what components of the chain of survival must be improved in order to OHCA survival rates comparable to pre-pandemic levels.

CRedit authorship contribution statement

Jeong Ho Park: Writing – original draft, Methodology, Data curation. **Kyoung Jun Song:** Writing – review & editing, Conceptualization. **Sang Do Shin:** Supervision, Conceptualization. **Ki Jeong Hong:** Writing – review & editing, Investigation, Data curation.

Declaration of Competing Interest

All authors have no other relationships/conditions/circumstances that present potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajem.2022.10.023>.

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