Association between the number of prehospital defibrillation attempts and a sustained return of spontaneous circulation: a retrospective, multicentre, registry-based study

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ABSTRACT

Background Currently, there is no consensus on the number of defibrillation attempts that should be made before transfer to a hospital in patients with out-of-hospital cardiac arrest (OHCA). This study aimed to evaluate the association between the number of defibrillations and a sustained prehospital return of spontaneous circulation (ROSC).

Methods A retrospective analysis of a multicentre, prospectively collected, registry-based study in Republic of Korea was conducted for OHCA patients with prehospital defibrillation. The primary outcome was sustained prehospital ROSC, and the secondary outcome was a good neurological outcome at hospital discharge, defined as Cerebral Performance Category score 1 or 2. Cumulative incidence of sustained prehospital ROSC and good neurological outcome according to number of defibrillations were examined. Multivariable logistic regression analysis was used to examine whether the number of defibrillations was independently associated with the outcomes.

Results Excluding 172 patients with missing data, a total of 1983 OHCA patients who received prehospital defibrillation were included. The median time from arrest to first defibrillation was 10 (IQR 7–15) min. The numbers of patients with sustained prehospital ROSC and good neurological outcome were 738 (37%) and 549 (28%), respectively. Sustained ROSC rates decreased as the number of defibrillation attempts increased from the first to the sixth (16%, 9%, 5%, 3%, 2% and 1%, respectively). The cumulative sustained ROSC rate, and good neurological outcome rate from initial defibrillation to sixth defibrillation were 16%, 25%, 30%, 34%, 36%, 36% and 11%, 18%, 22%, 25%, 26%, 27%, respectively. With adjustment for clinical characteristics and time to defibrillation, a higher number of defibrillations was independently associated with a lower chance of a sustained ROSC (OR 0.81, 95% CI 0.76 to 0.86) and a lower chance of good neurological outcome (OR 0.86, 95% CI 0.80 to 0.92).

Conclusions We observed no significant increase in ROSC after five defibrillations, and no absolute increase in ROSC after seven defibrillations. These data provide a starting point for determination of the optimal defibrillation strategy prior to consideration for prehospital extracorporeal cardiopulmonary resuscitation (ECPR) or conveyance to a hospital with an ECPR capability.

Trial registration number NCT03222999

WHAT IS ALREADY KNOWN ON THIS SUBJECT

⇒ In out-of-hospital cardiac arrest (OHCA), a longer interval from cardiac arrest to sustained return of spontaneous circulation (ROSC) is associated with worse outcomes.
⇒ Two or more prehospital defibrillation attempts are typically required in OHCA owing to the high likelihood of recurrence of a shockable rhythm.

WHAT THIS STUDY ADDS

⇒ Sustained ROSC rates decreased as the number of defibrillation attempts increased from the first to the sixth (16%, 9%, 5%, 3%, 2% and 1%, respectively).
⇒ No significant and absolute increase in the chance of ROSC was observed after five and seven defibrillation attempts, respectively.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These data provide a starting point for the optimal defibrillation strategy prior to consideration of extracorporeal cardiopulmonary resuscitation.

INTRODUCTION

With advances in cardiac arrest resuscitation, the rate of survival to hospital discharge in patients with out-of-hospital cardiac arrest (OHCA) ranges from 7.5% to 10.8%.[1–3] The first monitored rhythm is ventricular fibrillation (VF) and pulseless ventricular tachycardia (pVT) in approximately 20% of cardiac arrests, but the incidence of VF/pVT can vary according to bystander cardiopulmonary resuscitation (CPR) rates.[4–7] These shockable rhythms occur at some stage during resuscitation in about 25% of cardiac arrests with an initial documented rhythm of asystole or pulseless electrical activity.[8]

Early defibrillation is one step in the chain of cardiac arrest survival, and plays an important role in improving patient survival after shockable rhythm.[9] During treatment of VF/pVT, with every minute that passes between collapse and defibrillation, the likelihood of survival decreases by 7%–10% if no CPR is provided and by 3%–4% if bystander CPR is provided.[10,11] Guidelines for CPR recommend a strategy of immediate single-shock per application without escalating shock energy. If return of spontaneous circulation (ROSC) is not achieved by the third shock, guidelines recommend the use of antiarrhythmic drugs to increase the likelihood of successful defibrillation. However, the optimal number of defibrillation attempts in OHCA patients with VF/pVT is unknown.

Refractory VF is defined as fibrillation that persists after three or more shocks and occurs in approximately 20% of patients who present in VF.[12] Duration of VF correlates negatively with good outcome, suggesting that knowledge of the effective number of defibrillation attempts is important.[13] Furthermore, implementation of extracorporeal CPR (ECPR) functions as a bridge to recovery of effective cardiac output. ECPR cannulation of OHCA patients has been demonstrated to be feasible internationally with encouraging survival outcomes.[14,15] Patients with refractory VF can be candidates for ECPR if they arrive at the hospital within a reasonable time since arrest. The analysis of ROSC rate according to the increase in the number of defibrillation in OHCA patients with shockable rhythm could encourage prompt transfer to a hospital for further advanced treatment.

This study aimed to investigate defibrillation success rates based on the number of defibrillation attempts in OHCA patients that received prehospital defibrillation.

METHODS

Study design and population

This retrospective review of a multicentre, prospective, observational registry was conducted between October 2015 and June 2017, using data from the Korean Cardiac Arrest Research Consortium (KoCARC). The KoCARC is a multi-institutional, nationwide collaborative research network of 62 institutions developed to investigate the various studies conducted in the field of OHCA and to enhance collaborative study efforts.[16] A detailed description of the registry has been presented elsewhere.[16,17] The KoCARC registry was designed to include OHCA patients that had been transported to participating EDs by emergency medical services (EMS) with resuscitation efforts and patients who had a medical aetiology identified by an emergency physician.

The registry excludes OHCA patients with terminal illness documented by medical records, hospice care, pregnancy or predocumented 'No Resuscitation' cards. Also excluded are those with clear non-medical aetiology including trauma, drowning, poisoning, burns, asphyxiation or hanging. The quality assurance plan includes integrity checks for required fields and built-in validation rule cross-checks for data fields. The quality control committee provides feedback to research coordinators and investigators regarding quality control processes through quarterly meetings.

This particular study only included OHCA patients in the registry who underwent prehospital defibrillation. Patients without defibrillation or outcome data were excluded.

Study design and data variables

Patient characteristics (age, sex), prehospital characteristics (initial rhythm, bystander CPR, witnessed by a bystander, automated external defibrillator use and defibrillation), drug administration by EMS personnel, prehospital advanced airway, sustained prehospital ROSC (defined as restoration of a palpable pulse ≥20 min), time intervals (arrest time to first defibrillation, response time from EMS call to scene arrival, scene time defined as the time interval from scene arrival to scene departure and transport time defined as the time interval from scene departure to hospital arrival) and hospital outcomes were abstracted from the KoCARC registry.

The defibrillation strategies for VF/pVT in Republic of Korea follow the 2015 American Heart Association guideline and Korean Guidelines for Cardiopulmonary Resuscitation for basic life support and advanced cardiovascular life support, including single shock per application and fixed energy dose for all shocks.[18–20] However, the duration of field resuscitation and defibrillation attempts vary by institution.[21] EMS personnel are unable to abandon on-site resuscitation attempts unless OHCA patients showed obvious signs of death, defined as presence of decapitation, incineration, decomposition, rigour mortis or livor mortis. Therefore, all EMS-treated OHCA patients should have been transferred to the ED.

Success of prehospital defibrillation was defined as achievement of sustained ROSC. The primary outcome of this study was sustained prehospital ROSC. The secondary outcome was a good neurological outcome at hospital discharge and was defined as a Cerebral Performance Category (CPC) score of 1 (good cerebral performance) or 2 (moderate cerebral disability).[22]

Statistical analysis

Continuous variables were reported as mean±SD, or median and IQR, and categorical variables were analysed as absolute or relative frequency. Student's t-test or a Mann-Whitney U test was used to compare continuous variables, and categorical variables were analysed with a χ^2 or Fisher's exact test, as appropriate.

The baseline characteristics of the whole study population were analysed. Multivariable logistic regression analysis was used to determine the predictors for sustained prehospital ROSC and good neurological outcome. The variable of interest was whether number of defibrillations was independently associated with the outcomes after adjusting for clinical characteristics and time to initial defibrillation. Univariate and multivariable logistic regression analysis includes all cases where the primary variable of interest, number of defibrillations, was investigated. If the number of defibrillations and prehospital ROSC were investigated, they were not excluded from the analysis, even if there were other missing values. The adjustment variables included in the multivariable logistic regression analysis included previously set variables regardless of the results of the univariate analysis. Potential confounding factors that were adjusted for in the multivariable analyses were: sex, age, prehospital initial rhythm, bystander CPR, witnessed by a bystander, drug administration by EMS personnel, prehospital advanced airway and time intervals (time to first defibrillation, arrest time, response time, scene time and transport time). Associations were presented as ORs with 95% CIs in multivariable logistic regression analysis.

Cumulative incidence of sustained prehospital ROSC and good neurological outcome according to number of defibrillations were examined. Subgroup analysis of patients who underwent defibrillation within the median time in the whole cohort from arrest to first defibrillation was performed to minimise the effect of delayed defibrillation on outcome. The time from arrest to first defibrillation was reported as median (IQR).

All statistical analyses were performed using PASW Statistics V.24 (SPSS, Chicago, Illinois, USA). All tests were two-tailed, and p alues <0.05 were considered statistically significant.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Patients included for analysis

During the study period, data on 2155 patients with OHCA who received prehospital defibrillation were abstracted. Among them, 165 patients were excluded due to lack of defibrillation information and 13 patients due to lack of outcome (of these, 6 patients were missing both outcome and defibrillation information). Finally, a total of 1983 patients was included in the study and used for analysis. Comparisons between the 1983 included patients and 172 excluded patients are presented in online supplemental table 1. The patient group included in the analysis had a statistically significantly higher proportion of early shock rhythm than the excluded patient group (77.4% vs 63.7%, p<0.001). The median transfer time of the patient group included in the analysis was significantly shorter than that of the excluded patient group (9 min vs 13 min, p<0.001).

Characteristics of study subjects

The median age of the total population was 61 years, and the majority were male (1553, 78.3%) (table 1). In the prehospital stage, 738 (37.2%) patients responded with sustained ROSC. The median age was significantly lower in the group of patients with sustained prehospital ROSC compared with those without. The proportion of males was significantly higher in the group with sustained ROSC. The proportions of initial shockable rhythm, witnessed cardiac arrest, and bystander CPR were significantly higher in the group with sustained ROSC compared with those without sustained ROSC. The median number of prehospital defibrillations was 2 (IQR 1–4). The median time from arrest to initial defibrillation was 10 min (IQR 7–15). The survival to hospital discharge rate was 33.2%, and the proportion with a good neurological outcome was 27.7%. Other characteristics are summarised in table 1.

Sustained prehospital ROSC rate and number of defibrillations

There were 738 (37%) patients who responded with sustained prehospital ROSC and 549 (28%) with good neurological outcome. The sustained ROSC rate decreased as the number of prehospital defibrillation attempts increased from the first to the sixth (16%, 9%, 5%, 3%, 2% and 1%, respectively) (online supplemental figure 1). The cumulative sustained prehospital ROSC rate from the first to sixth defibrillation were 15.9%, 25.3%, 30.3%, 33.6%, 35.5%, 36.4% and good neurological outcome rate increased from the first to sixth defibrillation attempt as 11%, 18%, 22%, 25%, 26%, 27% (figure 1 and online supplemental figure 2). Sustained ROSC rate did not increase when the number of defibrillations was greater than five (35.5%). The cumulative proportion of patients with good neurological prognosis did not increase when the number of defibrillations exceeded five.

Subgroup analysis

As the time from arrest to first defibrillation affects patient outcome, subgroup analysis was performed on patients who received a first defibrillation within 10 min (the sample median). This group comprised 888 patients (44.7%). Similar to the main analysis, no increase in the cumulative sustained ROSC rate was observed when the number of defibrillations exceeded five (figure 2). A subgroup analysis also was performed on patients whose first defibrillation was >10 min after the onset of OHCA. Similar to the other analyses, an increase in the cumulative sustained ROSC rate was not evident when the number of defibrillations exceeded five (figure 2). We analysed the interaction between the time from collapse to first defibrillation attempt and the number of defibrillation attempts, which demonstrated no interaction (interaction term p=0.309) (online supplemental figure 3). However, there was an interaction between the time interval from the initial call to the emergency services (911 call) and the first defibrillation attempt, and the number of defibrillation attempts (interaction term p=0.011) (online supplemental

Table 1 Demographic and prehospital characteristics of the study population

Characteristics	Total (n=1983)	Sustained prehospital ROSC (+) (n=738, 37.2%)	Sustained prehospital ROSC (–) (n=1245, 62.8%)	P value
Demographics				
Age, years, median (IQR), years	61(61–72)	57 (48–57)	65 (53–75)	<0.001
Male, n (%)	1553 (78.3%)	598 (81%)	955 (76.7%)	0.024
History, n (%)				
Hypertension	725 (36.6%)	264 (35.7%)	461 (37.0%)	0.015
Diabetes mellitus	400 (20.2%)	132 (17.9%)	268 (21.5%)	0.003
Dyslipidaemia	102 (6.5%)	52 (7.1%)	50 (4.0%)	0.021
Cardiac arrest-related factors				
Initial shockable rhythm, n (%)	1535 (77.4%)	654 (88.6%)	881 (70.8)	<0.001
Witnessed by bystander, n (%)	1459 (73.6%)	596 (80.8%)	863 (69.3%)	<0.001
Bystander CPR, n (%)	1210 (61%)	486 (65.9%)	724 (58.2%)	<0.001
Defibrillation number, median (IQR)	2 (1–4)	2 (1–3)	2 (1–4)	<0.001
Drug administration by EMS personnel, n (%)	351 (17.7%)	84 (11.4%)	267 (21.5%)	<0.001
Prehospital advanced airway, n (%)	141 (7.1%)	47 (6.4%)	94 (7.6%)	0.366
Number of attempt				
1	804	315	489	
2	399	187	212	
3	253	99	154	
4	193	66	127	
5	136	37	99	
>5	198	34	164	
Time variables				
Arrest time to first defibrillation, median (IQR), min	10 (7–15)	9 (7–13)	11 (8–17)	<0.001
Response time, median (IQR), min	7 (5–9)	7 (5–9)	7 (5–10)	<0.001
Scene time, median (IQR), min	12 (9–18)	11 (8–15)	14 (9–20)	<0.001
Transport time, median (IQR), min	9 (6–14)	11 (7–16)	9 (6–12)	<0.001
Outcomes				
Survival to hospital discharge, n (%)	659 (33.2%)	528 (71.6%)	131 (10.5%)	<0.001
Good neurological outcome at hospital discharge, n (%)	549 (27.7%)	478 (64.8%)	71 (5.7%)	<0.001

CPR, cardiopulmonary resuscitation; EMS, emergency medical services; ROSC, return of spontaneous circulation.

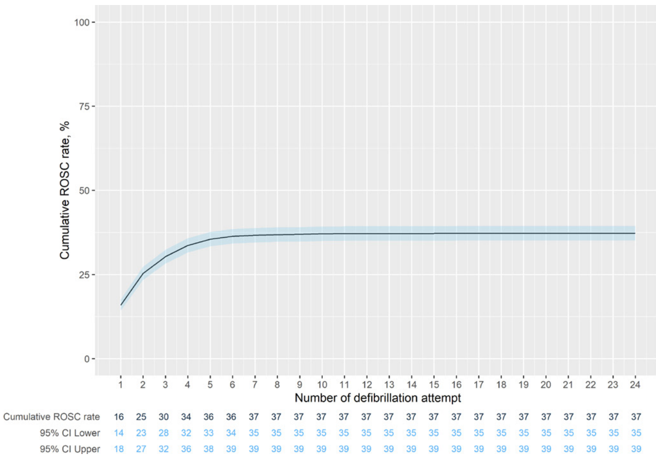

Figure 1 The cumulative sustained ROSC rate according to the number of defibrillation attempts. ROSC, return of spontaneous circulation.

figure 4). Depending on the time interval between the first emergency call and the first defibrillation attempt, there appears to be a difference in the relationship between the number of defibrillation attempts and ROSC rate.

Univariate logistic regression analyses

Univariate logistic regression analyses were conducted to identify predictors of sustained prehospital ROSC. Age was significantly associated with reduced sustained prehospital ROSC on univariate analysis (OR 0.97, 95% CI 0.97 to 0.98) (table 2). An initial shockable rhythm, witnessed arrest and bystander CPR were significantly associated with a greater chance of sustained prehospital ROSC (OR 4.04, 2.06 and 1.5, respectively). An increasing number of defibrillation attempts was significantly associated with a lower chance of a sustained prehospital ROSC (OR 0.86, 95% CI 0.82 to 0.90, p<0.001).

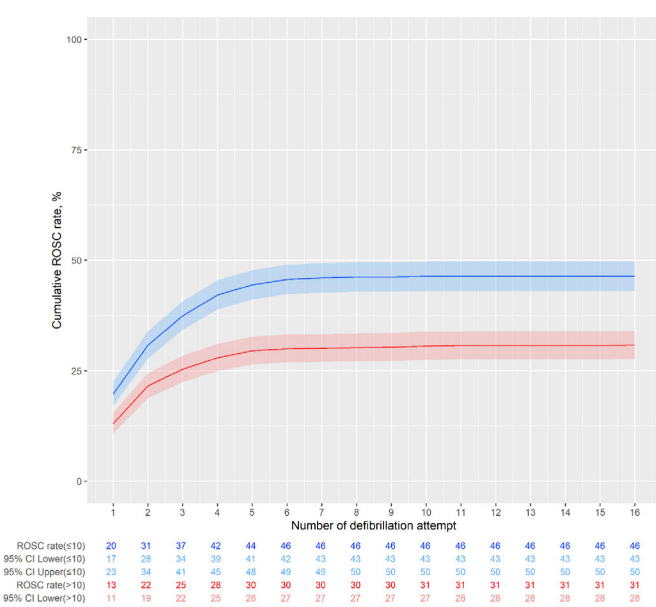

Figure 2 The cumulative sustained ROSC rate according to the number of defibrillation attempts in patients who received initial defibrillation ≤10 min, and initial defibrillation >10 min of cardiac arrest. ROSC, return of spontaneous circulation.

Multivariable logistic regression analysis

Multivariable logistic regression analysis was performed to identify variables associated with a sustained prehospital ROSC. The OR of older age for predicting sustained prehospital ROSC was 0.96 (95% CI 0.96 to 0.97, p<0.001) (table 3). Bystander CPR, shockable rhythm and witnessed arrest were significantly associated with a greater chance of a sustained prehospital ROSC (OR 1.41, 6.13 and 1.59, respectively). A higher number of defibrillations was significantly associated with a lower chance of sustained prehospital ROSC (OR 0.81, 95% CI 0.76 to 0.86, p<0.001). Multivariable logistic regression analysis predicting good neurological outcome at hospital discharge showed similar results to sustained prehospital ROSC; a higher number of defibrillations was significantly associated with a worse neurological outcome (OR 0.86, 95% CI 0.8 to 0.92, p<0.001). Shockable rhythm was associated with good neurological outcome, while age and drug administration by EMS was significantly associated with a poor neurological outcome (table 3).

DISCUSSION

We observed that the number of patients with sustained prehospital ROSC and good neurological outcome increased with successive shock attempts up to a maximum of six shocks. Further shocks did not increase these positive outcomes. On the other hand, the likelihood of sustained ROSC or good neurological outcome decreased as the number of prehospital defibrillation attempts increased from the first to the sixth. Results in a subgroup of patients that received initial defibrillation in <10 min (the median time from cardiac arrest to first defibrillation in this dataset), were similar to the main results.

There is no consensus for number of prehospital defibrillation attempts prior to hospital transfer for patients in a shockable rhythm. Our study suggests that the proportion of patients with sustained prehospital ROSC will not increase after six or more defibrillation attempts, providing a basis for standardisation of number of defibrillation attempts that should be made before transfer to hospital. If sustained prehospital ROSC is not achieved, even after four or five defibrillation attempts, it is suggested that specialised treatment at the hospital, such as ECPR, should be considered.

Early defibrillation is vital for survival of OHCA cases.[23 24] Effectiveness of defibrillation and chest compressions decreases rapidly, and survival rates decrease when collapse time is >10 min.[25] Several studies have shown that an increased number of defibrillations in OHCA patients is associated with poor prognosis.[25 26] One study conducted in Japan reported a cut-off point in the number of defibrillations of patients with OHCA most closely related to 1 month survival was between 2 and 3.[26] In that study, the primary end point was 1 month survival, and the cumulative outcome rate according to number of defibrillations was not analysed. Signal detection analysis (determining the largest χ^2 value at a certain cut-off point) was used to estimate the ideal number of prehospital defibrillations. Since only patients with witnessed cardiac arrests were included, the number of patients used in the final analysis was limited to 4.2% of the total cohort. In addition, our study differs from that study in defining the ideal number of defibrillations as associated with >95% of sustained ROSC achievement. Our study has demonstrated that even after the first shock, an increasing number of defibrillations was significantly associated with a lower chance of a sustained prehospital ROSC and a lower chance of favourable neurological outcome, even in patients who received defibrillation within 10 min.

Table 2 Univariate and multivariable logistic regression analysis for predicting prehospital sustained ROSC

	Univariate regression analysis		Multivariable regression analysis*	
Characteristics	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Age, median, years	0.97 (0.97 to 0.98)	<0.001	0.97 (0.95 to 0.98)	<0.001
Male	1.3 (1.04 to 1.63)	0.024		
History				
Hypertension	0.78 (0.64 to 0.95)	0.015		
Diabetes mellitus	0.69 (0.55 to 0.88)	0.002		
Dyslipidaemia	1.63 (1.09 to 2.43)	0.018		
Initial shockable rhythm	4.04 (3.03 to 5.39)	<0.001	4.06 (2.8 to 5.88)	<0.001
Witnessed by bystander	2.06 (1.64 to 2.59)	<0.001	1.71 (1.28 to 2.28)	<0.001
Bystander CPR	1.5 (1.22 to 1.83)	<0.001	1.39 (1.09 to 1.77)	0.009
Defibrillation number	0.86 (0.82 to 0.90)	<0.001	0.81 (0.76 to 0.86)	<0.001
Drug administration by EMS personnel	0.48 (0.37 to 0.63)	<0.001	0.57 (0.41 to 0.79)	<0.001
Prehospital advanced airway	0.83 (0.58 to 1.2)	0.323		
Time variables				
Arrest time to first defibrillation, min	0.99 (0.99 to 1.0)	0.164		
Response time, min	0.96 (0.93 to 0.98)	<0.001	0.95 (0.92 to 0.97)	<0.001
Scene time, min	0.95 (0.93 to 0.96)	<0.001		
Transport time, min	1.01 (1.01 to 1.02)	<0.001		

*Covariates were adjusted for in the multivariable analyses included sex, age, prehospital initial shockable rhythm, bystander CPR, witnessed by a bystander, number of defibrillation attempts, drug administration by EMS personnel, prehospital advanced airway and time interval (arrest time to first defibrillation, response time, scene time and transport time).
CPR, cardiopulmonary resuscitation; EMS, emergency medical services; ROSC, return of spontaneous circulation.

An evolving alternative to conventional CPR is ECPR, which has been reported to be effective for patients who do not fit the criteria for conventional CPR.[27–29] Patients in cardiac arrest that is refractory to prehospital defibrillation should be considered for immediate transfer to a specialised centre. This study provides a basis for further research regarding the optimal number of prehospital defibrillation attempts.

There is a fundamental debate concerning the intra-arrest management of OHCA, whether to continue on-scene treatment until either ROSC or termination of resuscitation (TOR), or to immediately transport during resuscitation efforts to hospital for definitive care. A recent study, data from the Resuscitation Outcomes Consortium in the USA and Canada, reported survival to hospital discharge occurred in 4.0% of who underwent intra-arrest transport vs 8.5% of who were resuscitated on-scene.[30] These findings may suggest a strong clinical benefit associated with continuing the resuscitation on scene until a definitive outcome has been achieved. This is contrasted by our results, where survival with good outcome did not increased after six or more defibrillation attempts. The possible reasons for this are from the heterogeneity of study inclusion, region difference of EMS system and TOR rule. Our study only included OHCA patients with prehospital defibrillation who most likely received definitive care at the hospital. Thus, it was difficult to directly compare their result with our results.

Table 3 Multivariable logistic regression analysis for predicting good neurological outcome at hospital discharge

Characteristics	OR	95% CI	P value
Age, median, years	0.96	0.96 to 0.97	<0.001
Male	1.23	0.88 to 1.71	0.224
Bystander CPR	1.41	1.08 to 1.85	0.013
Shockable rhythm	6.13	3.74 to 10.06	<0.001
Witnessed by bystander	1.59	1.16 to 2.2	0.004
Response time, min	0.94	0.91 to 0.97	0.049
Drug administration by EMS personnel	0.2	0.13 to 0.32	<0.001
Arrest time to first defibrillation, min	1.0	0.99 to 1.0	0.878
Defibrillation number	0.86	0.8 to 0.92	<0.001

CPR, cardiopulmonary resuscitation; EMS, emergency medical services.

Determining the optimal range of defibrillation attempts before hospital transport is unanswered question. In general, hospital transport should be considered for OHCA patients with refractory shockable rhythm, usually defined as no response to the three consecutive defibrillation. We believe that our results of this study may be beneficial to EMS directors and providers who must make decisions every day between more defibrillation attempts in the field and hospital transport for OHCA patients with refractory shockable rhythms without on-scene ROSC. However, the diversity and heterogeneity across different patient populations and EMS systems should be considered.

Thus, translation of the optimal number of defibrillation attempts in different prehospital settings may be an important topic for future investigation.

This study has some limitations. Our report used prospectively collected registry data that were not gathered for the specific purpose of our study; 165 cases (7%) were excluded from the analysis due to missing defibrillation-related information. This study did not differentiate between defibrillation conducted by a bystander versus EMS, which also can affect sustained prehospital ROSC. However, as only 40 of all cases of defibrillation were performed by a bystander, the main result was unlikely to be meaningfully affected. Another limitation is the type of defibrillator (automated external defibrillator, monophasic or biphasic and the energy level), which may have affected the results. However, that information could not be obtained from this registry. In Korea, biphasic defibrillators are more commonly used than monophasic and are superior to monophasic in terms of short-term and long-term prognoses of patients with OHCA.[25] We did not address target temperature management or coronary angiography in-hospital, which can also affect long-term patient outcomes. However, since our primary end point was sustained prehospital ROSC, we do not believe that this information would have affected the main results. In addition, our study reflects the inability of EMS personnel to discontinue on-scene resuscitation without prominent signs of death. It is not necessarily the case that all EMS-treated OHCA patients should be transferred to hospital, depending on a range of factors within the health system. Finally, although we included OHCA patients who had received at least one prehospital defibrillation, we cannot be sure that we did not include cases with shockable rhythm due to non-cardiac causes.

In conclusion, we observed no significant increase in ROSC after five defibrillations, and no absolute increase in ROSC after seven defibrillations. These data provide a starting point for determination of the optimal defibrillation strategy prior to consideration for prehospital ECPR or conveyance to a hospital with an ECPR capability.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The Korean Cardiac Arrest Research Consortium data collection protocol was reviewed and approved by the institutional review board of each participating hospital.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The data that support the findings of this study are available from the corresponding author, (WYK), on reasonable request.

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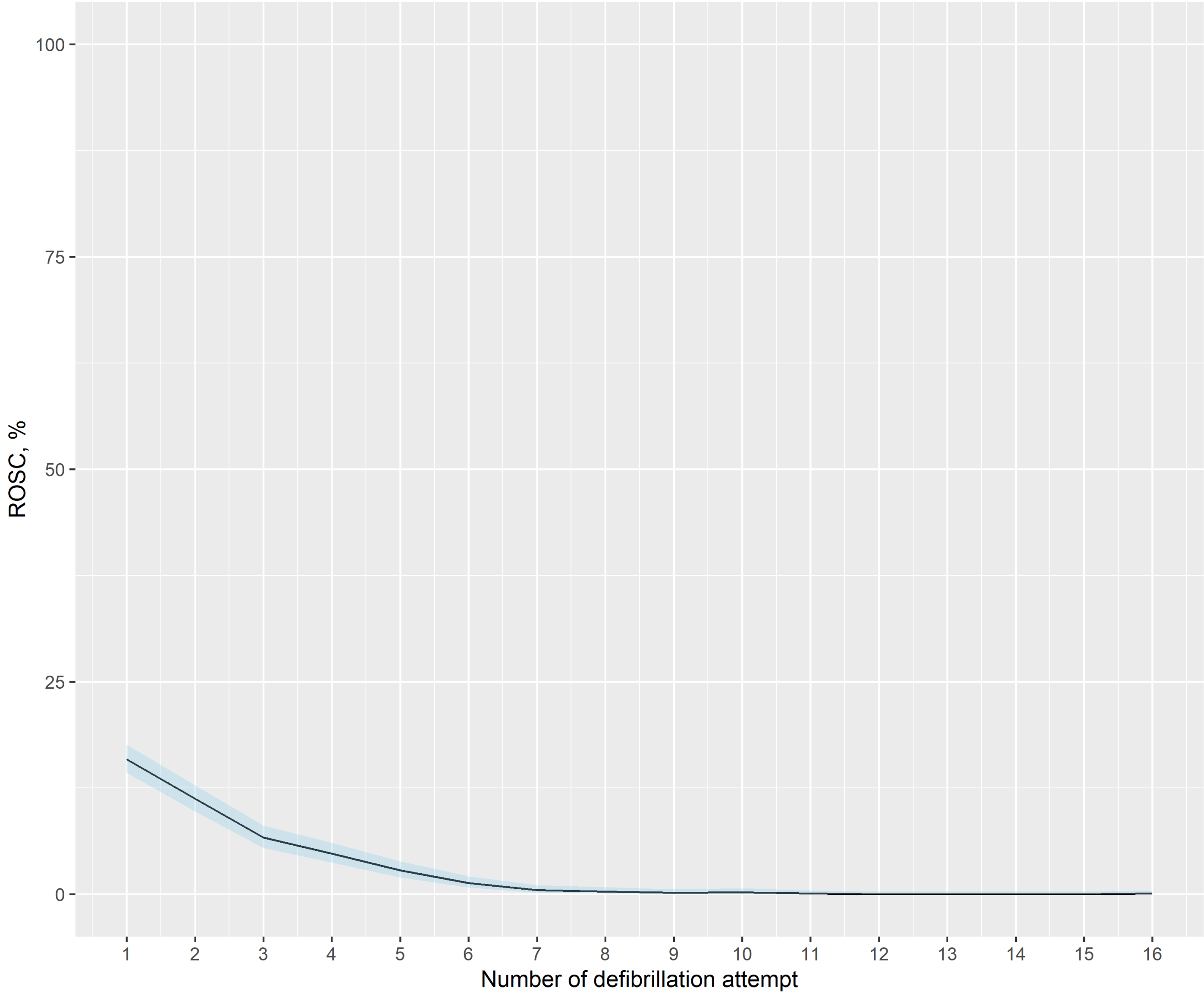
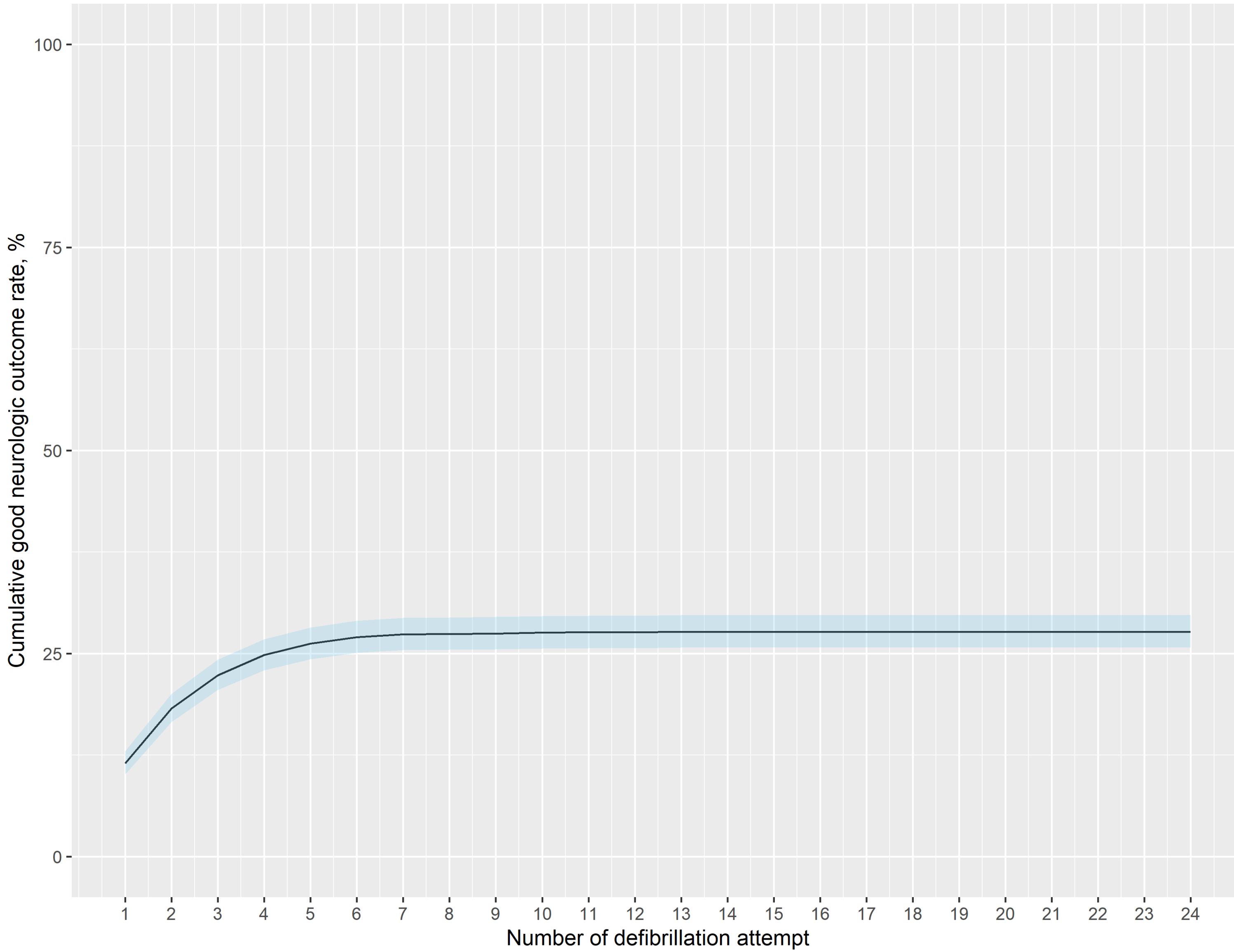
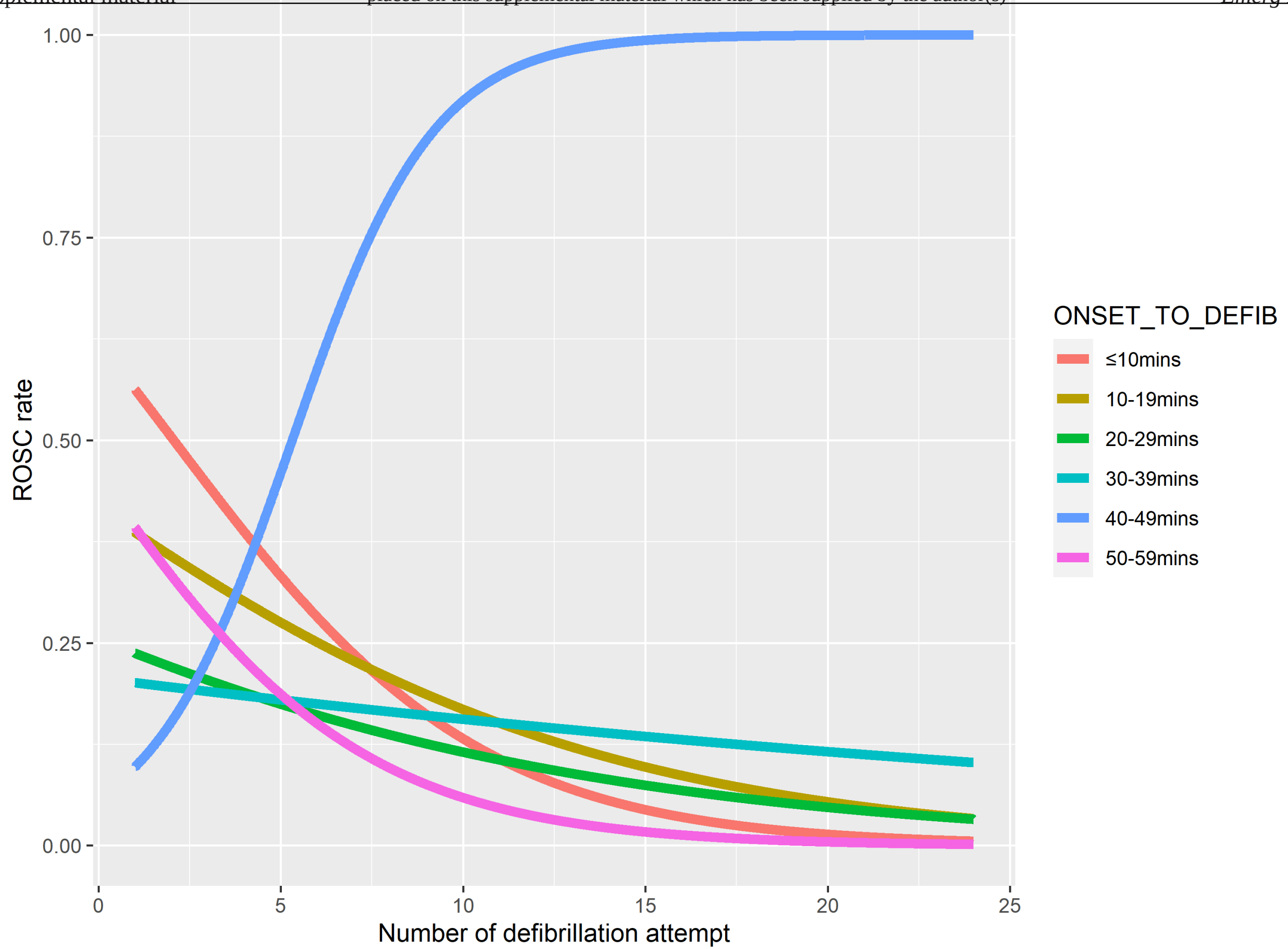
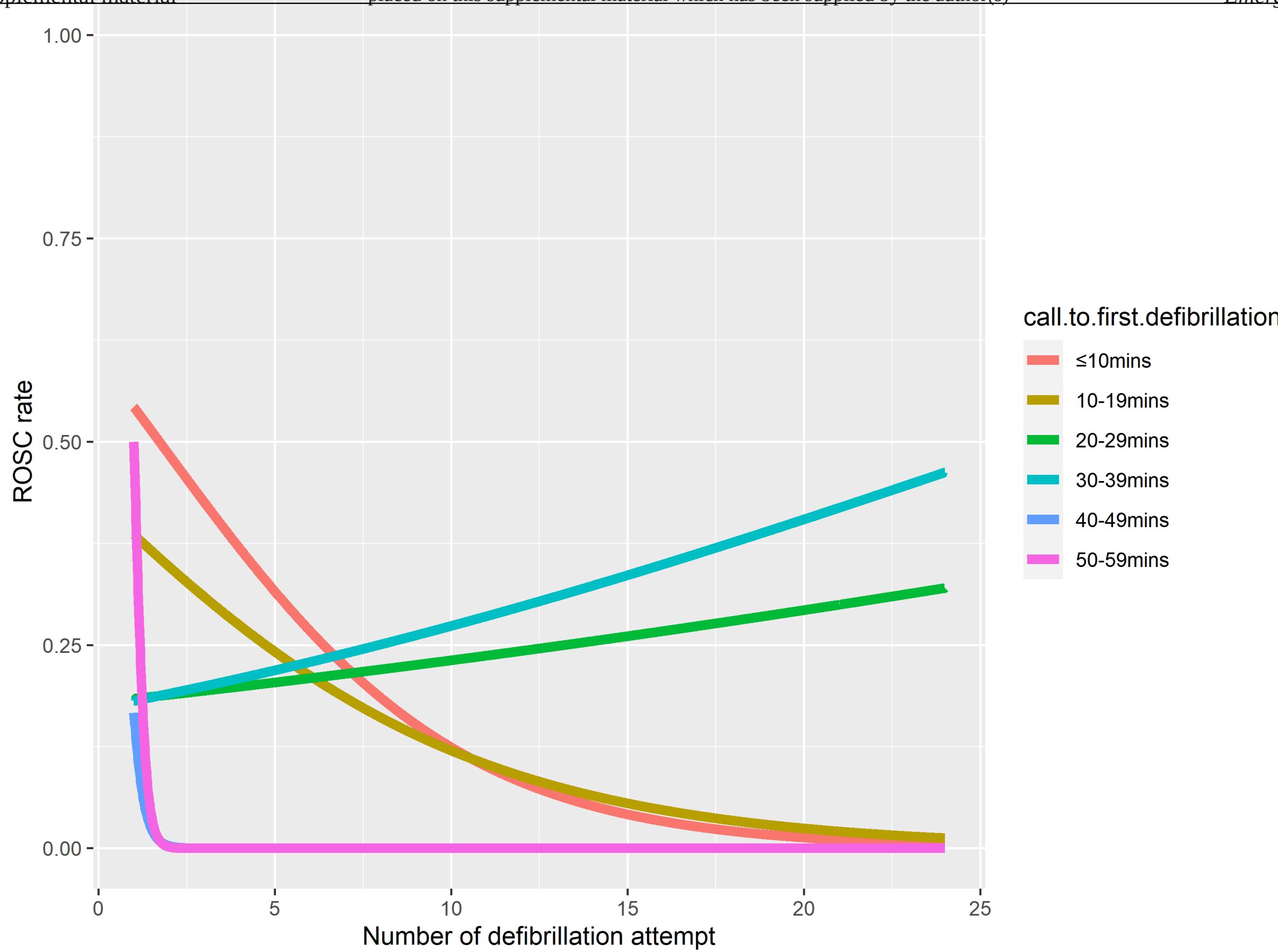


ROSC	16	11	7	5	3	1	0	0	0	0	0	0	0	0	0	0
95% CI Lower	14	10	5	4	2	1	0	0	0	0	0	0	0	0	0	0
95% CI Upper	18	13	8	6	4	2	1	1	1	1	0	0	0	0	0	0



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Cumulative good neurologic outcome rate	11	18	22	25	26	27	27	27	27	28	28	28	28	28	28	28	28	28	28	28	28	28	28	28
95% CI Lower	10	17	21	23	24	25	25	25	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26
95% CI Upper	13	20	24	27	28	29	29	29	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30


1.00
0.75
0.50
0.25
0.00
ROSC rate
0
5
10
15
20
25
Number of defibrillation attempt
ONSET_TO_DEFIB
≤10mins
10-19mins
20-29mins
30-39mins
40-49mins
50-59mins



ROSC rate
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
25
Number of defibrillation attempt
call.to.first.defibrillation
≤10mins
10-19mins
20-29mins
30-39mins
40-49mins
50-59mins

Supplementary table 1 Demographic and prehospital characteristics of included and excluded subjects

Characteristics	Included subjects (N = 1,983)	Excluded subjects (N=172)	P value
Demographics			
Age, years, median (IQR), y	61(61-72)	61 (52-73)	0.67
Male, n (%)	1553 (78.3%)	132 (76.7%)	0.7
History, n (%)			
Hypertension	725 (36.6%)	69 (40.1%)	0.348
Diabetes mellitus	400 (20.2%)	37 (21.5%)	0.413
Dyslipidemia	102 (5.1%)	13 (7.6%)	0.274
Cardiac arrest-related factors			
Initial shockable rhythm, n (%)	1535 (77.4%)	109 (63.7%)	<0.001
Witnessed by bystander, n (%)	1459 (73.6%)	121 (70.3%)	0.78
Bystander CPR, n (%)	1210 (61%)	75 (52.1%)	0.069
Defibrillation number, median (IQR)	2 (1-4)	2 (1-4)	0.757
Drug administration by EMS personnel, n (%)	351 (17.7%)	39 (22.9%)	0.008
Prehospital advanced airway, n (%)	1558 (81.1%)	108 (78.3%)	0.433
Time variables			
Arrest time to 1st defibrillation, median (IQR), minutes	10 (7-15)	12 (8-22)	0.011
Response time, median (IQR), minutes	7 (5-9)	7 (6-11)	0.076
Scene time, median (IQR), minutes	12 (9-18)	12 (7-17)	0.064
Transport time, median (IQR), minutes	9 (6-14)	13 (8-64)	<0.001
Outcomes			
Survival to hospital discharge, n (%)	659 (33.2%)	48 (27.9%)	0.215
Good neurologic outcome at hospital discharge, n (%)	549 (27.7%)	43 (25%)	0.477

CPR, cardiopulmonary resuscitation; EMS, emergency medical services; IQR, interquartile range; ROSC, return of spontaneous circulation.

Supplementary table 2 Utstein standardized template for reporting outcomes from out-of-hospital cardiac arrest.

Patient outcomes Reporting population		Any ROSC		Survived event		Survival^{dc} or survival^{30d}		Fav neurological^{dc} CPC≤2 or MR≤ 3	
		Yes	Unknown	Yes	Unknown	Yes	Unknown	Yes	Unknown
EMS witnessed included	All EMS Treated Arrests	N=47	N=0	N=41	N=52	N=48	N=52	N=42	N=56
EMS witnessed excluded	Shockable bystander witnessed	N=488	N=0	N=452	N=17	N=443	N=465	N=376	N=18
	Shockable bystander CPR	N=944	N=75	N=556	N=23	N=547	N=617	N=461	N=666
	Non-Shockable witnessed	N=39	N=0	N=31	N=12	N=28	N=165	N=18	N=172

CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; IQR, interquartile range; MR, modified rankin scale; ROSC, return of spontaneous circulation.