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Adjusting on-scene CPR duration based on transport time interval in out-of-hospital cardiac arrest: a nationwide multicenter study

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The optimal duration of on-scene cardiopulmonary resuscitation (CPR) for out-of-hospital cardiac arrest (OHCA) patients remains uncertain. Determining this critical time period requires outweighing the potential risks associated with intra-arrest transport while minimizing delays in accessing definitive hospital-based treatments. This study evaluated the association between on-scene CPR duration and 30-day neurologically favorable survival based on the transport time interval (TTI) in patients with OHCA. We retrospectively analyzed data from the Korean Cardiac Arrest Research Consortium registry of OHCA, comprising 65 participating hospitals in South Korea, between October 2015 and December 2021. We categorized the patients into Short-TTI (TTI < 10 min) and Long-TTI (TTI ≥ 10 min) groups. Differences in clinical features were adjusted for using propensity score matching (PSM) for TTI. The primary outcome was a 30-day neurologically favorable outcome, defined as cerebral performance category 1 or 2. Multivariable logistic regression was used to determine the variables associated with clinical outcomes. A generalized additive model based on a restricted cubic spline smooth function was utilized to infer the optimal cutoff point for on-scene CPR duration. Of the 6,345 patients, 5,844 PSM pairings were created (Short-TTI: 2,922; Long-TTI: 2,922). The primary outcome was achieved in 7.4% and 9.8% of the patients in Short-TTI and Long-TTI groups, respectively ($p = 0.001$). Increased on-scene CPR duration was associated with decreased neurologically favorable survival (adjusted odds ratio, 0.94; 95% confidence interval, 0.92–0.96). The optimal on-scene CPR durations in the overall PSM, Short-TTI, and Long-TTI groups were 5.1, 0, and 5.0 min, respectively. An adjusted on-scene CPR duration based on expected transport duration may be beneficial for favorable clinical outcomes in patients with OHCA.

Keywords Out-of-hospital cardiac arrest, Cardiopulmonary resuscitation, Emergency medical services, Survival

Abbreviations

CPR	Cardiopulmonary resuscitation
TTI	Transport time interval
OHCA	Out-of-hospital cardiac arrest
TOR	Termination of resuscitation
PSM	Propensity score matching
ECLS	Extracorporeal life support
EMS	Emergency medical services

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ER	Emergency room
ECG	Electrocardiography
ACLS	Advanced cardiac life support
CAG	Coronary angiography
TTM	Targeted temperature management
CPC	Cerebral performance category
TPT	Total prehospital time
RTI	Response time interval
STI	Scene time interval
ROSC	Return of spontaneous circulation
OR	Odds ratio
aOR	Adjusted odds ratio
CI	Confidence interval
GAM	Generalized additive model

Out-of-hospital cardiac arrest (OHCA) is a major global health concern. The survival to hospital discharge rate of patients with OHCA was approximately 10% in Europe and the United States, and was similar or lower in East Asia[1–6]. Despite the administration of high-quality on-scene cardiopulmonary resuscitation (CPR) by emergency medical services (EMS), 50–90% of patients with OHCA fail to achieve return-of-spontaneous-circulation (ROSC) on the scene[7,8].

The choice between "expedited transport" and "prolonged on-scene CPR" in patients experiencing refractory OHCA presents a prehospital dilemma[9]. The expedited transport approach aims to minimize delays in initiating advanced in-hospital therapies than providing prolonged on-scene resuscitation. However, several critical considerations should be addressed when implementing this strategy. Firstly, concerns have been noted regarding the potential deterioration in the quality of CPR when patients are transferred to ambulances or during transport itself. Lee et al. reported that the no-flow fraction was highest during the interval spanning 1 min before and 1 min after ambulance departure[10]. Similarly, Russi et al. demonstrated that both the depth and rate of chest compressions were significantly compromised during transport compared to on-site CPR, even when visual feedback technology was employed[11]. Secondly, the transport time interval (TTI) may play a crucial role in decision-making for transport following OHCA. However, its impact on the outcomes is inconclusive due to heterogeneous findings across EMS systems and geographical regions. Park et al. observed that a longer TTI was negatively associated with poor neurological outcomes in patients without prehospital ROSC[12]. In contrast, several studies, including a meta-analysis, have found no significant effect of TTI on patient outcomes[13,14]. Notably, these findings were primarily derived from studies conducted in regions with advanced EMS systems characterized by well-trained personnel and established protocols. Furthermore, the TTIs observed in these studies were relatively short and likely did not exceed a critical "threshold"—the duration beyond which delays in definitive care may negatively impact outcomes.

The EMS system in South Korea is distinct from that in other nations in two key aspects: advanced cardiac life support (ACLS) capabilities and termination-of-resuscitation (TOR) regulations. The highest certification level for emergency medical technicians (EMTs) in South Korea corresponds to the intermediate EMT level in the United States, and the scope of procedures they are authorized to perform on scene is limited. Additionally, unless patients exhibit obvious signs of death, such as rigor mortis, all patients with OHCA must be transported to the hospital regardless of ROSC, as prehospital TOR is prohibited. These aspects underscore the critical need to determine the optimal timing for transport during on-scene resuscitation to maximize the likelihood of favorable neurological outcomes.

Current guidelines provide various recommendations for on-scene CPR duration and when to transport patients with OHCA. The updated 2020 Korean national emergency care protocol for EMS personnel recommends 6–10 min of on-scene CPR before transporting the patient to the hospital[15]. The 2020 American Heart Association guidelines do not specify the number of CPR cycles to be performed on-scene before deciding to transport the patient in cases of refractory OHCA[4]. European guidelines recommend considering the distance to the hospital when deciding whether to transport the patient or continue on-scene CPR[16]. However, the guidelines do not provide specific instructions regarding on-scene CPR duration or the distance to the hospital. Given these disparities, the optimal duration of on-scene CPR remains unclear, making it challenging to balance the risks of resuscitation during intra-arrest transport with the prolonged periods spent in the prehospital setting.

Few studies have explored whether the optimal duration of on-scene CPR is affected by transportation time. We hypothesized that the optimal duration of on-scene CPR varies according to the transport duration. This study evaluated the association between on-scene CPR duration and 30-day neurologically favorable survival based on transport duration in patients with OHCA.

Methods

Study population and data collection

We conducted a retrospective analysis of the Korean Cardiac Arrest Research Consortium (KoCARC), a multicenter registry of OHCA encompassing 65 participating hospitals in the Republic of Korea (ClinicalTrials.gov, NCT03222999)[17]. The details of the participating hospitals have been provided in the Supplementary Table S1. This study was approved by the institutional review board of Samsung Medical Center (IRB number 2024-05-069). The ethics committee of Samsung Medical Center waived the requirement for informed consent owing to the retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations.

The KoCARC registry included patients who experienced OHCA of medical etiology and were transferred to the emergency room (ER) by the EMS after resuscitation efforts. The following patients were excluded: those who were pregnant; those with terminal illness or receiving hospice care; those experiencing OHCA due to non-medical causes such as trauma, drowning, poisoning, burn, asphyxia, or hanging; and those with advanced directive or documented 'do not resuscitate' orders. The quality management committee monitored the quality of the registry data.

We examined the data of all patients with OHCA in the KoCARC registry between October 2015 and December 2021. Patients who met the following criteria were excluded: (1) age ≤ 18 years, (2) missing time variables, (3) missing arrest location, (4) total prehospital time (TPT) ≥ 60 min, (5) low-flow time ≥ 120 min, and (6) scene time interval (STI) ≥ 40 min. We addressed the highly skewed distributions of the data for TTI, low-flow time, and STI, by establishing cutoff thresholds at the 98th percentile, excluding extreme outliers beyond these points.

A comprehensive list of variables collected from the KoCARC registry is available from a previously published article[17]. We extracted the following data from the registry: information on patient demographics such as age, sex, and comorbidities; arrest characteristics such as arrest location, witnessed arrest, bystander CPR, and initial electrocardiography (ECG) rhythm; EMS intervention such as prehospital defibrillation, prehospital epinephrine administration, prehospital advanced airway management, use of prehospital ACLS interventions, defined as advanced airway management and administration of vasoactive drugs, and implementation of mechanical CPR devices; laboratory data, including initial arterial pH and initial lactate measurement; time-stamped data on emergency call at dispatch center, EMS arrival on scene, EMS departure from scene, and arrival at the ER; low-flow time; in-hospital interventions such as coronary angiography (CAG), extracorporeal life support (ECLS), and targeted temperature management (TTM); and outcome measurements such as 30-day cerebral performance category (CPC) 1 or 2 survival, ROSC, and survival to hospital discharge.

Missing values for binary variables related to arrest characteristics (e.g., witnessed arrest, bystander CPR, shockable rhythm) and prehospital interventions (e.g., prehospital defibrillation, epinephrine administration, airway management, ACLS, mechanical CPR devices) were imputed based on the assumption that unrecorded data indicates the intervention was not performed or the characteristic was absent. Imputation was not performed for non-binary variables (i.e., time-related variables and arrest location data). Patients with missing values in these variables were excluded from the analysis (Fig. 1). Detailed number of measurements are provided in Supplementary Table S2.

Definitions

The response time interval (RTI) was defined as the time from the emergency call to EMS arrival at the scene. STI was the duration for which the EMS remained at the scene—which is the time between EMS arrival and departure —reflecting on-scene CPR duration. TTI was defined as the time interval between the EMS leaving the scene and their arrival at the ER. TPT was defined as the time between the emergency call at the dispatch center and the EMS arrival at the ER. We categorized patients into two groups: Short-TTI (TTI < 10 min) and Long-TTI (TTI ≥ 10 min) groups. This classification was determined based on the mean TTI of 10 min observed in the dataset. Low-flow time was defined as the time interval from the beginning of CPR by EMS personnel to ROSC or death.

EMS protocol in Korea

The OHCA protocol of EMS in Korea is based on the American Heart Association guidelines. ACLS, which includes advanced airway management and epinephrine administration during the prehospital period, is limited by the Korean EMS system[18]. Advanced prehospital airway management, such as endotracheal intubation, is allowed for level-1 EMTs only when directly ordered on telephone by an EMS physician on duty at a dispatcher center.

Measures

The primary outcome was survival at 30-days with neurologically favorable survival, defined as a CPC of 1 or 2. Secondary outcomes included ROSC and survival to hospital discharge.

Data analysis

The basic characteristics of the study population are summarized using the mean and standard deviation for continuous variables and using frequency and percentage for categorical variables. Inter-group differences in continuous and categorical variables were tested using t- and chi-square tests, respectively. The normality of each data distribution was assessed using quantile-quantile plots (QQ-plots) (Supplementary Fig. S1).

Propensity score matching (PSM) was performed to adjust for confounding factors to minimize potential selection bias. We have used probability values of the patient TTI being over the mean value (> 10 min) as the outcome to calculate the propensity score. Covariables related to the outcome were selected based on previous studies and expert opinions[19,20]. Age, sex, arrest location, witnessed arrest, bystander CPR, initial ECG rhythm, and prehospital ACLS were used to calculate the propensity score. The probability of being over the mean TTI based on the above covariables for balancing the other variable effects was calculated. Nearest score matching was performed with a 1:1 ratio.

After matching, univariable and multivariable logistic regression analyses were used to determine variables associated with the primary and secondary outcomes. The final model included the following variables: age, sex, witnessed arrest, bystander CPR, initial ECG rhythm, arrest location, prehospital ACLS, and STI. The odds ratios (OR) and adjusted odds ratios (aOR) were reported with 95% confidence intervals (CI).

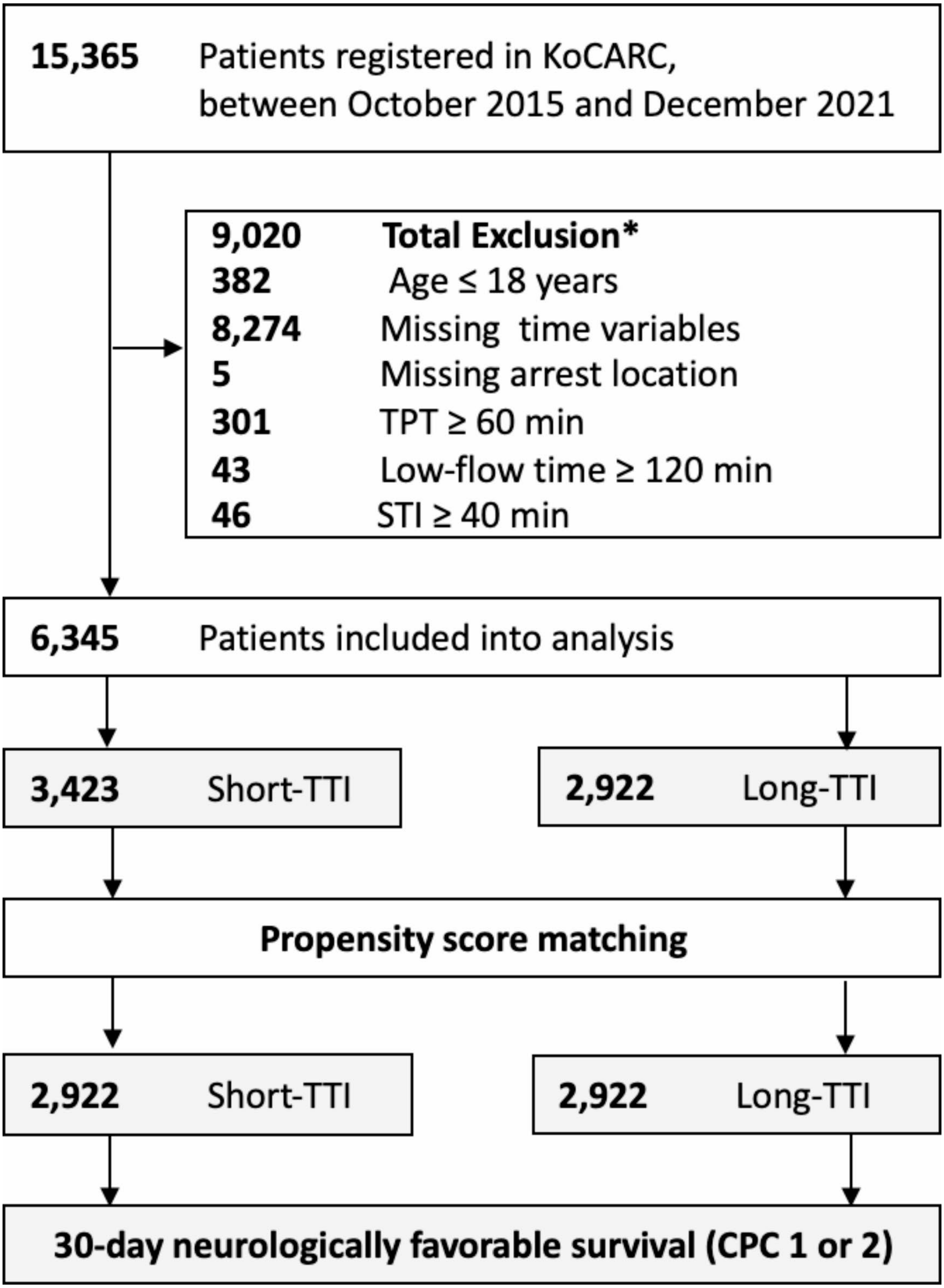

Fig. 1. Study flow. *Patients meeting multiple exclusion criteria were counted separately for each criterion. However, in the calculation of the total exclusion count, each patient was counted only once to avoid duplication. *KoCARC* Korean cardiac arrest research consortium, *TPT* total prehospital time defined as the time between the emergency call at the dispatch center and arrival at the emergency room, Low-flow time, defined as the time interval from the beginning of cardiopulmonary resuscitation by emergency medical services (EMS) personnel to return of spontaneous circulation or death; *STI* scene time interval defined as the time between EMS arrival at the scene and EMS departure, *TTI* transport time interval defined as the time interval between the EMS leaving the scene and their arrival at the emergency room, *CPC* cerebral performance category.

To identify the optimal cutoff point for STI, a multivariable generalized additive model (GAM) based on a restricted cubic spline smooth function was utilized for inference and visualization. For the multivariable GAM, age, sex, witnessed arrest, bystander CPR, initial ECG rhythm, arrest location, and prehospital ACLS were adjusted. The number of knots was chosen via generalized cross-validation (GCV)[21]. Compared to other linear models or generalized linear models which assume rigid linearity, non-linear relationships could be identified based on GAM with consideration of knots or smoothing functions. Moreover, unlike conventional "black-box" models, GAM can have interpretability of each predictor. The additive nature of the GAM allows for understanding of the contributions of each variable to the outcome.

In the subgroup analysis of shockable rhythms, adjustments were considered for all variables except those used to define the subgroups. Statistical significance was set at a p-value < 0.05. All statistical analyses were performed using the R software (version 4.3.0; Vienna, Austria; http://www.R-project.org/).

Results

Baseline characteristics

The KoCARC registry includes 15,365 patients. A total of 6,345 patients were included in the analysis after excluding 9,020 patients who were aged ≤ 18 years, missing at least one required time variable for assessing time interval, missing arrest location data, had a TPT ≥ 60 min, had low-flow time ≥ 120 min, or had a STI ≥ 40 min (Fig. 1).

The baseline characteristics of the unmatched cohort are presented in Table 1. The average age of the patients in this cohort was 68.3 ± 15.6 years, and 34.0% of them were female. The frequencies of witnessed arrest, bystander CPR, and initial shockable rhythm were 55.7, 60.3, and 19.6%, respectively. Prehospital ACLS was performed in 19.6% of the patients and the average low-flow time was 34.3 ± 21.3 min. A total of 3,423 (53.9%) and 2,922 (46.1%) patients were classified into the Short-TTI and Long-TTI groups, respectively. After PSM, 5,844 patients were selected (1-to-1 matching: Short-TTI group, N = 2,922 vs. Long-TTI group, N = 2,922) (Table 2). The PSM approach resulted in balanced grouping for the matching variables. Baseline characteristics of the excluded patients (age > 18 years) are given in Supplementary Table S2. The distributions of TTI and low-flow time in each group are presented in Supplementary Fig. S2 and Fig. S3, respectively.

Primary and secondary outcomes

The primary and secondary outcome measures are presented in Table 3. In the PSM cohort, 30-day neurologically favorable survival was lower in the Short-TTI group than in the Long-TTI group (7.4% vs. 9.8%, respectively, $p = 0.001$). The Short-TTI group exhibited a lower ROSC rate than the Long-TTI group (11.1% vs. 16.2%, $p < 0.001$). The survival to hospital discharge rate was also lower in the Short-TTI group than in the Long-TTI group (9.9% vs. 13.6%, $p < 0.001$).

Variables associated with primary and secondary outcomes in the PSM cohort

The results of the logistic regression analysis are presented in Table 4. Univariable logistic regression analysis revealed that STI was negatively associated with the 30-day neurologically favorable survival (overall PSM cohort: OR, 0.93; 95% CI, 0.92–0.95; Short-TTI group: OR, 0.92; 95% CI, 0.90–0.95; Long-TTI group: OR, 0.95; 95% CI, 0.93–0.97; all $p < 0.001$). Multivariable logistic regression analysis revealed that STI was associated with decreased probability of 30-day neurologically favorable survival (overall PSM cohort: aOR, 0.94; 95% CI, 0.92–0.96; Short-TTI group: aOR, 0.95; 95% CI, 0.92–0.99; Long-TTI group: aOR, 0.94; 95% CI, 0.92–0.97; all $p < 0.05$). Details of the univariable and multivariable logistic regression analyses of the unmatched cohort are presented in Supplementary Tables S3 and S4, respectively.

The restricted cubic spline smooth function was used to visualize the association between neurologically favorable survival and STI. Figure 2 shows the optimal STI for predicting neurologically favorable survival in the overall PSM cohort (5.1 min), the Short-TTI group (expedited transport, representing minimal on-scene time), and the Long-TTI group (5.0 min), after adjusting for covariates.

Results of the multivariable logistic regression analyses of the secondary outcomes of the PSM cohort are shown in Table 5. While STI was negatively associated with ROSC in the overall PSM cohort (aOR, 0.97; 95% CI, 0.96–0.98; $p < 0.001$) and the Long-TTI group (aOR, 0.98; 95% CI, 0.96–0.99; $p = 0.013$), it showed no association with ROSC in the Short-TTI group (aOR, 0.98; 95% CI, 0.96–1.00; $p = 0.09$). STI was associated with decreased survival to hospital discharge in the overall PSM cohort (aOR, 0.94; 95% CI, 0.92–0.96), and the Short-TTI (aOR, 0.95; 95% CI, 0.92–0.97), and Long-TTI (aOR, 0.94; 95% CI, 0.92–0.96) groups (all $p < 0.001$). Figure 3 shows the predicted probabilities of ROSC and survival to hospital discharge according to STI in the overall PSM cohort, and the Short-TTI and Long-TTI groups.

Subgroup analysis of optimal STI predicting neurologically favorable survival

Figure 4 illustrates the optimal STI for predicting neurologically favorable survival in patients with an initial shockable rhythm after adjusting for covariates within the PSM cohort. The optimal STI was 6.3 min for the entire PSM cohort. Notably, expedited transport was linked to improved neurologically favorable survival in the Short-TTI group, whereas the optimal STI in the Long-TTI group was 6.8 min.

Discussion

This study evaluated the association between on-scene CPR duration and 30-day neurologically favorable survival according to TTI in adult patients with OHCA. For patients with TTI < 10 min, expedited transport was associated with better neurological outcomes, whereas the optimal on-scene CPR duration was 5.0 min in patients with a relatively long TTI (TTI ≥ 10 min).

	Overall (N = 6,345)	Short-TTI group (N = 3,423)	Long-TTI group (N = 2,922)	p-value
Age, mean (SD), y	68.3 (15.6)	68.2 (15.7)	68.5 (15.5)	0.50
Sex, female, (%)	2,157 (34.0)	1,195 (34.9)	962 (32.9)	0.10
Underlying disease, N (%)				
Hypertension	2,511 (46.3)	1,338 (46.3)	1,173 (46.3)	1.00
Diabetes	1,650 (30.6)	853 (29.7)	797 (31.5)	0.16
Arrest characteristics, N (%)				
Arrest location,public place	2,126 (33.5)	1,161 (33.9)	965 (33.0)	0.47
Witnessed arrest	3,537 (55.7)	1,905 (55.7)	1,632 (55.9)	0.89
Bystander CPR	3,828 (60.3)	2,048 (59.8)	1,780 (60.9)	0.39
Shockable rhythm	1,241 (19.6)	658 (19.2)	583 (20.0)	0.49
EMS intervention, N (%)				
Prehospital defibrillation	1,603 (25.3)	854 (24.9)	749 (25.6)	0.55
Prehospital epinephrine given	1,280 (20.2)	736 (21.5)	544 (18.6)	0.005
Prehospital airway	5,573 (87.8)	3,052 (89.2)	2,521 (86.3)	0.001
Prehospital ACLS	1,244 (19.6)	718 (21.0)	526 (18.0)	0.003
Mechanical CPR devices	1,722 (27.1)	916 (26.8)	806 (27.6)	0.48
Laboratory data				
Initial pH, mean (SD)	6.93 (0.20)	6.93 (0.19)	6.93 (0.21)	0.71
Initial lactate, mean (SD), mmol/L	12.6 (5.1)	12.6 (4.9)	12.6 (5.2)	0.73
EMS time interval, minutes				
RTI, mean (SD)	8.0 (3.8)	7.7 (3.6)	8.4 (4.0)	< 0.001
STI, mean (SD)	14.0 (6.7)	15.3 (6.4)	12.6 (6.8)	< 0.001
TTI, mean (SD)*	10.2 (5.8)	6.3 (2.2)	14.8 (5.3)	< 0.001
TPT, mean (SD)	32.3 (8.6)	29.3 (7.5)	35.8 (8.6)	< 0.001
Low-flow time, mean (SD)**	34.3 (21.3)	34.9 (20.6)	33.7 (22.0)	0.031
In-hospital intervention, N (%)				
CAG	779 (12.3)	385 (11.2)	394 (13.5)	0.008
ECLS	140 (2.2)	81 (2.4)	59 (2.0)	0.39
TTM	556 (8.8)	300 (8.8)	256 (8.8)	1.00

Table 1. Baseline characteristics of the unmatched cohort. *Distribution of TTI in each group is presented in Supplementary Fig. S2. **Distribution of low-flow time in each group is presented in Supplementary Fig. S3. *TTI* transport time interval defined as the time interval between the EMS leaving the scene and their arrival at the emergency room, *SD* standard deviation, *CPR* cardiopulmonary resuscitation, *EMS* emergency medical services, *ACLS* advanced cardiac life support, *RTI* response time interval defined as the time from the emergency call to EMS arrival at the scene, *STI* scene time interval defined as the time between EMS arrival at the scene and EMS departure, *TPT* total prehospital time defined as the time between the emergency call at the dispatch center and arrival at the emergency room; Low-flow time, defined as the time interval from the beginning of CPR by EMS personnel to return of spontaneous circulation or death, *CAG* coronary angiography, *ECLS* extracorporeal life support, *TTM* targeted temperature management.

The clinical relevance of our findings stems from the possibility that the TTI could be a significant component in establishing the optimal on-scene CPR duration to maximize neurologically favorable survival. In South Korea and Japan, EMS personnel lack the authority to determine the TOR point, and transportation of the patient to a hospital is mandatory at some point during on-scene CPR, irrespective of whether ROSC is achieved. Early hospital transport may be advantageous in such situations, so that patients can receive definitive care immediately and EMS resources are used more efficiently. However, CPR administered during transportation may be of low quality, thereby negatively affecting patient outcomes[10,11]. These conflicting priorities make prehospital transport decisions challenging for EMS personnel. Thus, establishing an optimal time for transportation is crucial for making appropriate decisions. Our study suggests that adjusting the STI based on the TTI may be beneficial in patients with OHCA. This approach is feasible because transport time can be estimated using data such as the distance from the scene to the hospital and real-time traffic conditions provided by map applications.

Previous studies have shown inconsistent findings regarding the impacts of TTI and STI on the clinical outcomes in OHCA. The Ontario Prehospital Advanced Life Support (OPALS) study showed no association between TTI and survival ($N = 15{,}559$; OR, 1.01; 95% CI, 0.99–1.05)[14]. The OPALS study population exhibited relatively short TTI (median TTI, 4.2 min; IQR, 3.0–6.2). Chien et al. showed that the probability of neurologically favorable survival was < 10% in cases where the TTI was > 14 min[22]. Expedited transport in refractory OHCA

	Overall (N = 5,844)	Short-TTI group (N = 2,922)	Long-TTI group (N = 2,922)	p-value	SMD
Age, mean (SD), y	68.6 (15.4)	68.7 (15.3)	68.5 (15.5)	0.47	0.019
Sex, female, (%)	1,942 (33.2)	980 (33.5)	962 (32.9)	0.64	0.013
Underlying disease, N (%)					
Hypertension	2,342 (46.7)	1,169 (47.0)	1,173 (46.3)	0.63	0.014
Diabetes	1,545 (30.9)	748 (30.3)	797 (31.5)	0.37	0.026
Arrest characteristics, N (%)					
Arrest location, public place	1,925 (32.9)	960 (32.9)	965 (33.0)	0.91	0.004
Witnessed arrest	3,266 (55.9)	1,634 (55.9)	1,632 (55.9)	0.98	0.001
Bystander CPR	3,568 (61.1)	1,788 (61.2)	1,780 (60.9)	0.85	0.006
Shockable rhythm	1,133 (19.4)	550 (18.8)	583 (20.0)	0.29	0.029
EMS intervention, N (%)					
Prehospital defibrillation	1,462 (25.0)	713 (24.4)	749 (25.6)	0.29	0.028
Prehospital epinephrine given	1,089 (18.6)	545 (18.7)	544 (18.6)	1.00	0.001
Prehospital airway	5,126 (87.7)	2,605 (89.2)	2,521 (86.3)	0.001	0.088
Prehospital ACLS	1,053 (18.0)	527 (18.0)	526 (18.0)	1.00	0.001
Mechanical CPR devices	1,585 (27.1)	779 (26.7)	806 (27.6)	0.44	0.021
Laboratory data					
Initial pH, mean (SD)	6.93 (0.20)	6.93 (0.19)	6.93 (0.21)	0.81	0.008
Initial lactate, mean (SD), mmol/L	12.6 (5.0)	12.6 (4.8)	12.6 (5.2)	0.81	0.008
EMS time interval, minutes					
RTI,mean (SD)	8.0 (3.8)	7.7 (3.6)	8.4 (4.0)	<0.001	0.186
STI, mean (SD)	13.9 (6.6)	15.1 (6.2)	12.6 (6.8)	<0.001	0.389
TTI, mean (SD)*	10.5 (5.8)	6.3 (2.1)	14.8 (5.3)	<0.001	2.120
TPT,mean (SD)	32.4 (8.6)	29.1 (7.3)	35.8 (8.6)	<0.001	0.840
Low-flow time, mean (SD)**	34.3 (21.3)	34.9 (20.6)	33.7 (22.0)	0.037	0.055
In-hospital intervention, N (%)					
CAG	719 (12.3)	325 (11.1)	394 (13.5)	0.007	0.072
ECLS	125 (2.1)	66 (2.3)	59 (2.0)	0.59	0.017
TTM	498 (8.5)	242 (8.3)	256 (8.8)	0.54	0.017

Table 2. Baseline characteristics of the PSM cohort. *Distribution of TTI in each group is presented in Supplementary Fig. S2. *Distribution of low-flow time in each group is presented in Supplementary Fig. S3. PSM, propensity score-matched; *TTI* transport time interval defined as the time interval between the EMS leaving the scene and their arrival at the emergency room, *SMD* standardized mean difference, *SD* standard deviation, *CPR* cardiopulmonary resuscitation, *EMS* emergency medical service, *ACLS* advanced cardiac life support, *RTI* response time interval defined as the time from the emergency call to EMS arrival at the scene, *STI* scene time interval defined as the time between EMS arrival at the scene and EMS departure, *TPT* total prehospital time defined as the time between the emergency call at the dispatch center and arrival at the emergency room; Low-flow time, defined as the time interval from the beginning of CPR by EMS personnel to return of spontaneous circulation or death; CAG, coronary angiography; *ECLS* extracorporeal life support, *TTM* targeted temperature management.

was reported to be associated with a lower probability of survival to hospital discharge compared to prolonged on-scene CPR in an analysis of 43,969 patients from 10 North American sites (4.0% vs. 8.5%, respectively)[23]. Kurosaki et al. recommended that the decision to initiate transport should be made approximately 8–10 min after on-scene CPR[24]. The geographical location is an essential variable to consider in interpreting these findings. A recent systematic review and meta-analysis produced inconclusive results on the effectiveness of expedited transport compared to continuous on-scene resuscitation for refractory OHCA[25]. This review indicated that geographical location is a key variable contributing to heterogeneity, which can be attributed to diverse EMS protocols.

Few studies have investigated the relationship between on-scene CPR duration and TTI. Our findings are consistent with those of previous studies, suggesting that STI and TTI should be considered in cases of refractory OHCA that involve transport. In a previous study analyzing 57,822 patients with OHCA, a longer TTI was significantly associated with a lower likelihood of good neurological recovery, with this effect being more pronounced in the short STI group[26]. Using a short TTI (1–5 min) as reference, intermediate (6–10 min) and long (≥ 11 min) TTIs had aORs of 0.46 (95% CI, 0.32–0.67) and 0.31 (95% CI, 0.17–0.55), respectively. In the long STI (≥ 6 min) group, intermediate and long TTIs had aORs of 0.72 (95% CI, 0.59–0.89) and 0.49 (95%

	Unmatched cohort				PSM cohort				
	Overall (*N* = 6,345)	Short-TTI group (*N* = 3,423)	Long-TTI group (*N* = 2,922)	*p*-value	Overall (*N* = 5,844)	Short-TTI group (*N* = 2,922)	Long-TTI group (*N* = 2,922)	*p*-value	SMD
Primary outcome									
30-day neurologically favorable survival, N (%)	548 (8.6)	261 (7.6)	287 (9.8)	0.002	504 (8.6)	217 (7.4)	287 (9.8)	0.001	0.085
Secondary outcomes									
ROSC, N (%)	876 (13.8)	404 (11.8)	472 (16.2)	< 0.001	795 (13.6)	323 (11.1)	472 (16.2)	< 0.001	0.149
Survival discharge, N (%)	748 (11.8)	352 (10.3)	396 (13.6)	< 0.001	685 (11.7)	289 (9.9)	396 (13.6)	< 0.001	0.114

Table 3. Primary and secondary outcomes of the unmatched cohort and the PSM cohort. *PSM* propensity score-matched, *TTI* transport time interval defined as the time interval between the emergency medical services leaving the scene and their arrival at the emergency room; *SMD* standardized mean difference, *ROSC* return of spontaneous circulation.

CI, 0.37–0.65), respectively. These findings emphasize the importance of considering STI and TTI in choosing a hospital for transporting patients with OHCA without prehospital ROSC.

It is generally assumed that prolonged TTIs result in longer durations of inadequate CPR and poorer clinical outcomes. However, our findings revealed that the Short-TTI group demonstrated worse clinical outcomes than the Long-TTI group. One potential explanation for this result is that the Long-TTI group experienced shorter low-flow times than the Short-TTI group. Several studies have reported that prolonged low-flow time is significantly associated with decreased survival rates in patients with OHCA[27]. Another possible explanation is that a higher proportion of patients in the Long-TTI group received coronary angiography compared to that in the Short-TTI group, suggesting that the former may have included a greater proportion of patients with cardiac-related OHCA. This finding is consistent with those from previous studies that indicate that patients with cardiac-related OHCA exhibit higher survival-to-discharge rates than those with noncardiac-related OHCA[27].

Subgroup analysis of patients with an initial shockable rhythm revealed that the optimal STI varied between the groups. Expedited transport was associated with neurologically favorable survival in the Short-TTI group and an optimal STI of 6.8 min in the Long-TTI group. In a study with patients with OHCA and an initial shockable rhythm, Park et al. found that if TTI is > 10 min, the aOR for a favorable neurological outcome in the group with STI ≥ 15 min (vs. those with an STI < 15 min) was 0.10 (95% CI, 0.02–0.55)[28]. While the authors suggested that field resuscitation should be shortened if TTI is > 10 min, they did not provide an optimal STI for either TTIs > or < 10 min. In the Short-TTI group, it would be practical to anticipate an improvement in a favorable neurological prognosis by receiving timely invasive therapy, such as ECLS and percutaneous coronary intervention, through expedited transport following initial defibrillation in the field[29]. In the long-TTI group with initial shockable rhythm, the patients who may not be eligible for ECLS would be diminished because of extended transport durations[30,31]. These patients would benefit more from relatively prolonged high-quality pre-hospital ACLS, which would include more accurate initial rhythm analysis, defibrillation, and airway management, compared to expedited transport[26,32].

Patient outcomes may be significantly affected by not only the time to definitive care but also by the type of prehospital interventions—particularly ACLS vs. BLS. For instance, extended ACLS using a treatment algorithm similar to that used in hospitals, may offer clinical benefits that justify delays in definitive care. However, previous studies have found conflicting results on ACLS vs. BLS in prehospital settings. Sanghavi et al. found that 1,643 BLS-treated participants had better survival to hospital discharge rates than 31,292 ACLS-treated subjects (13.1% vs. 9.2% for ACLS; 3.9 [95% CI, 2.3–5.7] percentage point difference)[33]. Kurz et al. evaluated 35,065 OHCA cases using Resuscitation Outcomes Consortium data, categorizing them as BLS-only, BLS + late ACLS (> 6 min after CPR initiation), BLS + early ACLS (≤ 6 min after CPR initiation), or ACLS-first[34]. They found that ACLS care was associated with improved survival to hospital discharge when provided initially or within six minutes of BLS arrival. However, ACLS care was not associated with better functional outcomes. A meta-analysis comparing ACLS and BLS for patients with non-traumatic cardiac arrest showed that ACLS care increases the probability of survival to hospital discharge compared to BLS care; however, these findings are limited by significant heterogeneity in the research design and EMS system configurations[35]. Since the primary aim of our study was to identify the optimal STI while adjusting for confounding variables, including the type of care provided (ACLS or BLS), we did not directly compare the effectiveness of ACLS and BLS. Further studies focusing on the optimal STI based on the type of prehospital intervention and TTI are needed.

Limitations

Our study has several limitations. First, this study is not exempt from the inherent limitations of a retrospective analysis of multicenter registry data. Data were collected based on the Utstein-style guidelines, and efforts were made to reduce potential biases through quality control. We performed PSM analysis to minimize inherent biases associated with the study design. Second, the generalizability of findings to EMS systems under different authorities such as TOR or physician-based EMS is limited. Third, a substantial number of patients were excluded due to missing time data, which may have impacted the results. To address missing values for binary variables, we assumed that unrecorded data indicated that the intervention was not performed or the arrest characteristics were absent. We acknowledge that this approach could influence the data distribution or lead to

	Univariable logistic regression						Multivariable logistic regression					
	Overall (N = 5,844)		Short-TTI (N = 2,922)		Long-TTI (N = 2,922)		Overall (N = 5,844)		Short-TTI (N = 2,922)		Long-TTI (N = 2,922)	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Age	0.95 (0.94–0.95)	< 0.001	0.95 (0.94–0.95)	< 0.001	0.95 (0.94–0.96)	< 0.001	0.96 (0.95–0.96)	< 0.001	0.95 (0.94–0.96)	< 0.001	0.96 (0.95–0.97)	< 0.001
Sex,female	0.43 (0.34–0.54)	< 0.001	0.41 (0.28–0.58)	< 0.001	0.44 (0.32–0.59)	< 0.001	1.07 (0.80–1.43)	0.63	1.35 (0.86–2.1)	0.19	0.91 (0.62–1.33)	0.64
Witnessed arrest	4.73 (3.72–6.09)	< 0.001	4.33 (3.04–6.34)	< 0.001	5.10 (3.69–7.2)	< 0.001	2.64 (2.00-3.53)	< 0.001	2.63 (1.72–4.11)	< 0.001	2.73 (1.88–4.03)	< 0.001
Bystander CPR	1.81 (1.48–2.23)	< 0.001	1.64 (1.22–2.24)	0.001	1.96 (1.5–2.6)	< 0.001	1.35 (1.05–1.73)	0.020	1.27 (0.87–1.85)	0.22	1.43 (1.02–2.01)	0.038
Shockable rhythm	30.02 (23.68–38.45)	< 0.001	38.59 (26.36–58.34)	< 0.001	25.44 (18.81–34.93)	< 0.001	18.01 (13.90-23.54)	< 0.001	23.97 (15.83–37.39)	< 0.001	15.17 (10.89–21.42)	< 0.001
Arrest location, public place	3.65 (3.03–4.41)	< 0.001	3.52 (2.65–4.69)	< 0.001	3.77 (2.94–4.86)	< 0.001	1.76 (1.39–2.22)	< 0.001	1.57 (1.10–2.25)	0.013	1.96 (1.44–2.68)	< 0.001
Prehospital ACLS	0.34 (0.24–0.47)	< 0.001	0.29 (0.16–0.49)	< 0.001	0.37 (0.23–0.56)	< 0.001	0.37 (0.25–0.56)	< 0.001	0.30 (0.15–0.56)	< 0.001	0.41 (0.24–0.67)	< 0.001
STI	0.93 (0.92–0.95)	< 0.001	0.92 (0.9–0.95)	< 0.001	0.95 (0.93–0.97)	< 0.001	0.94 (0.92–0.96)	< 0.001	0.95 (0.92–0.99)	0.006	0.94 (0.92–0.97)	< 0.001

Table 4. Univariable and multivariable logistic regression analyses of 30-day neurologically favorable survival of the PSM cohort. *PSM* propensity score-matched, *TTI* transport time interval defined as the time interval between the emergency medical services (EMS) leaving the scene and their arrival at the emergency room, *OR* odds ratio, *CI* confidence interval, *aOR* adjusted odds ratio, *CPR* cardiopulmonary resuscitation, *ACLS* advanced cardiac life support, *STI* scene time interval defined as the time between EMS arrival at the scene and EMS departure.

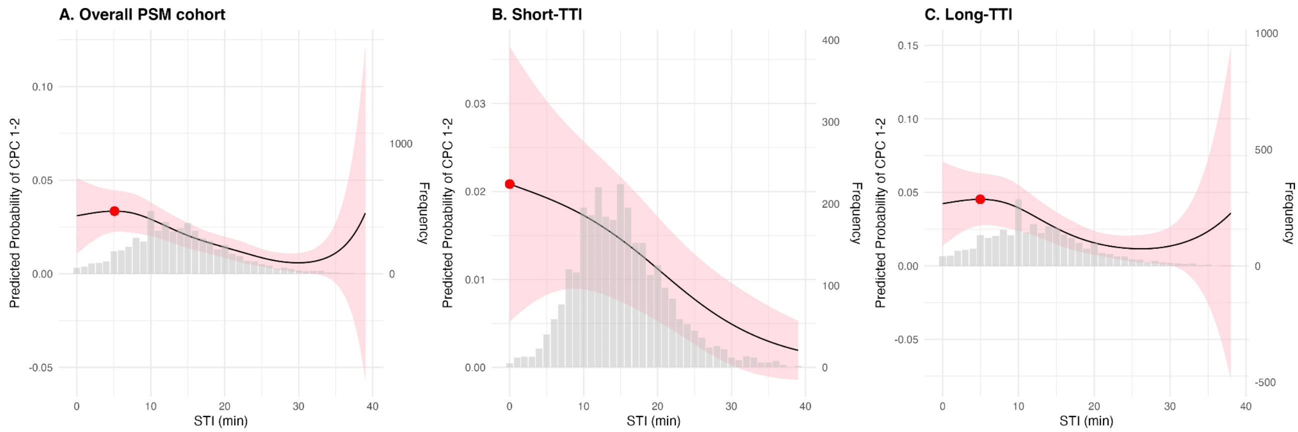

Fig. 2. Restricted cubic spline curve demonstrating predicted probability of CPC 1 or 2 according to the STI and distribution of STI in the PSM cohort. (**a**) Overall PSM cohort. (**b**) Short-TTI group. (**c**) Long-TTI group. Black line: restricted cubic spline curve of predicted probability of CPC 1 or 2; Red point: Optimal STI; Pink shade: 95% CI, Grey bar: Frequency of STI. *CPC* cerebral performance category, *STI* scene time interval defined as the time between emergency medical services (EMS) arrival at the scene and EMS departure; *PSM* propensity score matched, *TTI* transport time interval defined as the time interval between the EMS leaving the scene and their arrival at the emergency room,*CI* confidence interval.

	Overall (*N* = 5,844)		**Short-TTI, (*N* = 2,922)**		**Long-TTI, (*N* = 2,922)**	
	aOR (95% CI)	***p*-value**	**aOR (95% CI)**	***p*-value**	**aOR (95% CI)**	***p*-value**
ROSC						
Age	0.97 (0.97–0.98)	< 0.001	0.98 (0.97–0.98)	< 0.001	0.97 (0.97–0.98)	< 0.001
Sex,female	1.10 (0.89–1.34)	0.38	1.10 (0.8–1.51)	0.55	1.08 (0.83–1.41)	0.56
Witnessed arrest	2.35 (1.93–2.87)	< 0.001	1.93 (1.43–2.62)	< 0.001	2.73 (2.10–3.58)	< 0.001
Bystander CPR	1.05 (0.88–1.27)	0.58	1.02 (0.78–1.35)	0.88	1.07 (0.83–1.37)	0.60
Shockable rhythm	7.95 (6.62–9.57)	< 0.001	8.93 (6.74–11.9)	< 0.001	7.54 (5.91–9.65)	< 0.001
Arrest location, public place	1.54 (1.29–1.84)	< 0.001	1.55 (1.18–2.04)	0.002	1.58 (1.24-2.00)	< 0.001
Prehospital ACLS	2.00 (1.58–2.54)	< 0.001	1.87 (1.29–2.7)	< 0.001	1.95 (1.42–2.67)	< 0.001
STI	0.97 (0.96–0.98)	< 0.001	0.98 (0.96-1.00)	0.09	0.98 (0.96–0.99)	0.013
Survival to hospital discharge						
Age	0.96 (0.96–0.97)	< 0.001	0.97 (0.96–0.98)	< 0.001	0.96 (0.96–0.97)	< 0.001
Sex, female	1.02 (0.81–1.28)	0.90	1.08 (0.76–1.53)	0.66	0.96 (0.70–1.30)	0.77
Witnessed arrest	2.53 (2.03–3.19)	< 0.001	2.2 (1.58–3.11)	< 0.001	2.82 (2.08–3.85)	< 0.001
Bystander CPR	1.08 (0.88–1.33)	0.44	1.03 (0.76–1.39)	0.86	1.13 (0.86–1.49)	0.38
Shockable rhythm	9.56 (7.82–11.73)	< 0.001	10.21 (7.53–13.95)	< 0.001	9.29 (7.10-12.22)	< 0.001
Arrest location, public place	1.69 (1.39–2.06)	< 0.001	1.59 (1.18–2.13)	0.002	1.84 (1.41–2.39)	< 0.001
Prehospital ACLS	0.59 (0.43–0.81)	0.001	0.58 (0.35–0.93)	0.028	0.56 (0.36–0.84)	0.007
STI	0.94 (0.92–0.96)	< 0.001	0.95 (0.92–0.97)	< 0.001	0.94 (0.92–0.96)	< 0.001

Table 5. Multivariable logistic regression analyses of the secondary outcomes in the PSM cohort. *PSM* propensity score-matched, *TTI* transport time interval defined as the time interval between the emergency medical services (EMS) leaving the scene and their arrival at the ER, *aOR* adjusted odds ratio, *ROSC* return of spontaneous circulation, *CPR* cardiopulmonary resuscitation, *ACLS* advanced cardiac life support, *STI* scene time interval defined as the time between EMS arrival at the scene and EMS departure.

an underestimation of interventions, thereby introducing potential bias into the outcomes. Alternative methods, such as imputation, might have yielded different results and potentially mitigated these limitations. Fourth, we arbitrarily defined TTIs based on the observed distribution within our dataset. As there is no universally accepted standard for distinguishing short TTIs from long TTIs, their definition varies across studies and is often determined by the specific context and data characteristics of each analysis. Finally, the study findings may have been influenced by several factors that are not accounted for. The dataset lacked indices necessary for directly evaluating CPR quality. Additionally, the use of mechanical CPR devices was not included in the

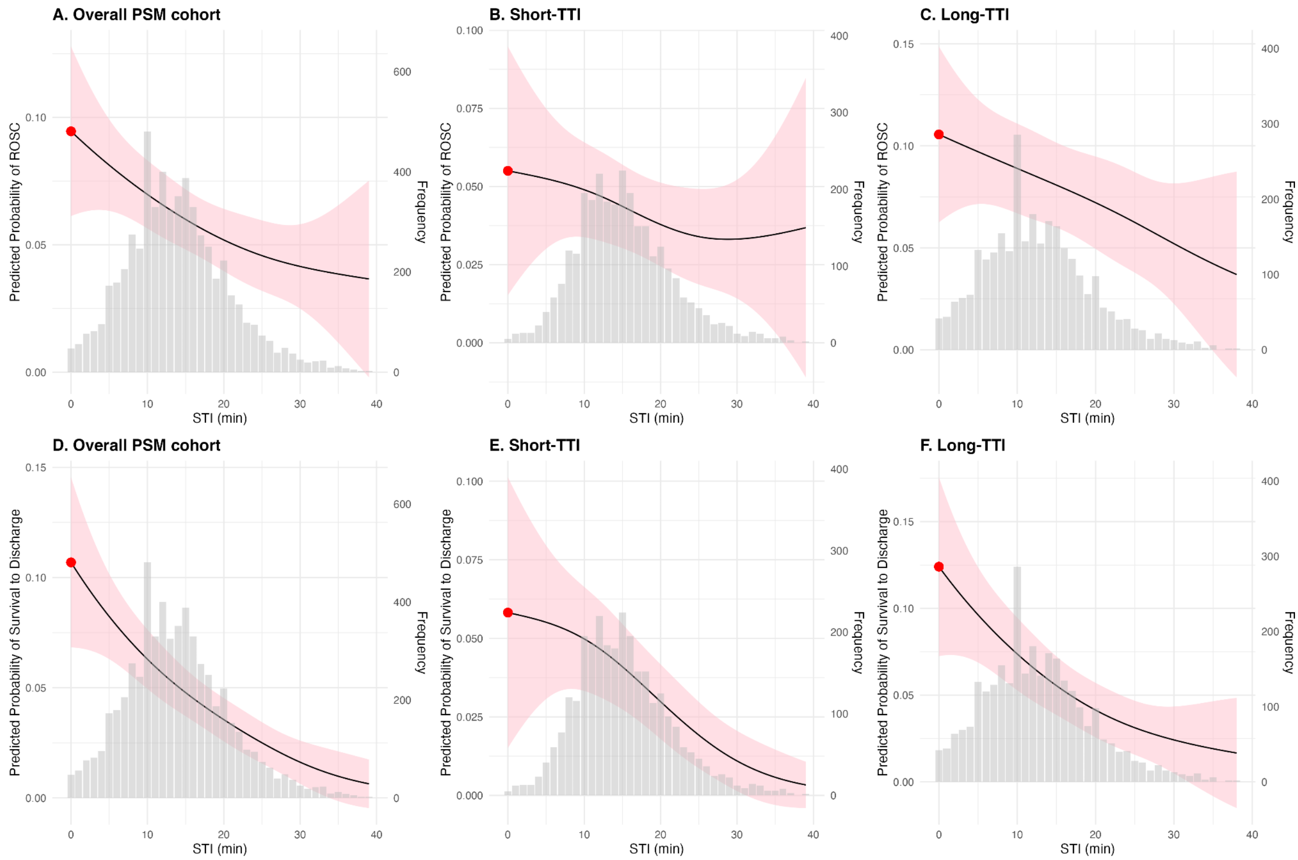

Fig. 3. Restricted cubic spline curve demonstrating predicted probability of secondary outcomes according to the STI and distribution of STI in the PSM cohort. (**a**) Predicted probability of ROSC in the overall PSM cohort. (**b**) Predicted probability of ROSC in the Short-TTI group. (**c**) Predicted probability of ROSC in the Long-TTI group. (**d**) Predicted probability of survival discharge in the overall PSM cohort. (**e**) Predicted probability of survival discharge in the Short-TTI group. (**f**) Predicted probability of survival discharge in the Long-TTI group. Black line: restricted cubic spline curve of predicted probability of secondary outcomes; Red point: Optimal STI; Pink shade: 95% CI; Grey bar: Frequency of STI. PSM, propensity score matched; *TTI* transport time interval defined as the time interval between the emergency medical services (EMS) leaving the scene and their arrival at the emergency room, *STI* scene time interval defined as the time between EMS arrival at the scene and EMS departure, *ROSC* return of spontaneous circulation, *CI* confidence interval.

analysis. These devices offer a consistent and effective method for delivering chest compressions, particularly in challenging scenarios such as patient transport in a moving ambulance[36]. While evidence regarding their efficacy in improving patient outcomes remains inconclusive, their potential impact on the study results should be taken into consideration[37]. Furthermore, although the study accounted for whether bystander CPR was initiated prior to EMS arrival, it did not consider the duration of CPR performed by bystanders or the interval between the initial notification to the dispatch center and the first medical contact. Including these time intervals may potentially affect the study findings.

Conclusion
This study showed that the optimal duration of on-scene CPR varies according to transport duration. Adjusted on-scene CPR duration based on the expected duration of transport would be beneficial for clinical outcomes in patients with OHCA. These findings suggest that EMS protocols may benefit from incorporating transport duration as a critical factor in the decision-making process for determining the optimal timing for patient transport. Further research is required to refine these guidelines and assess their impact on patient outcomes.

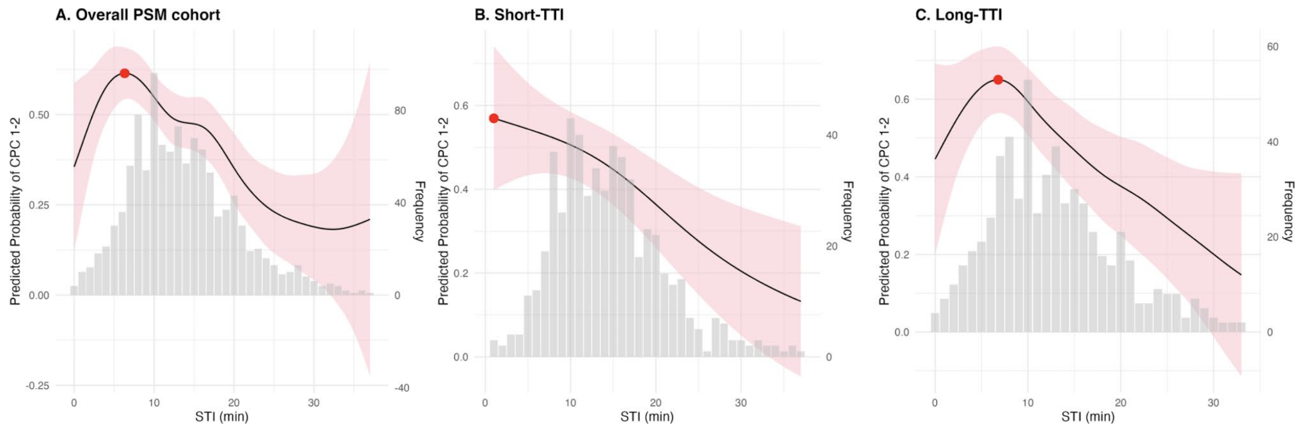

Fig. 4. Subgroup analysis of optimal STI predicting CPC 1or 2. Panels **A–C** show the predicted probability of CPC 1 or 2 in patients with shockable rhythm. Black line: restricted cubic spline curve of predicted probability of CPC 1 or 2; Red point: Optimal STI; Pink shade: 95% CI; Grey bar: Frequency of STI. PSM, propensity score matching; TTI, transport time interval defined as the time interval between the emergency medical services (EMS) leaving the scene and their arrival at the emergency room; STI, scene time interval defined as the time between EMS arrival at the scene and EMS departure; CPC, cerebral performance category; CI, confidence interval.

Data availability

All data used to support the findings of this study are available from the corresponding author upon request.

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Author contributions
DJ, JYY, DSK, MK, and GTL performed data analysis and drafted the manuscript. SDS, DJ, and SYH acquired data and made critical revisions to the manuscript. DJ, JYY, and SYH managed the data and revisions to the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing interests
The authors declare no competing interests.

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