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Original Article

Association of transport time interval with neurologic outcome in out-of-hospital cardiac arrest patients without return of spontaneous circulation on scene and the interaction effect according to prehospital airway management

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Objective This study analyzed the association of transport time interval (TTI) with survival rate and neurologic outcome in out-of-hospital cardiac arrest (OHCA) patients without return of spontaneous circulation (ROSC) and the interaction effect of TTI according to prehospital airway management.

Methods A retrospective observational study based on the nationwide OHCA database from January 2013 to December 2017 was designed. Emergency medical service (EMS)-treated OHCA patients aged ≥18 years were included. TTI was categorized into four groups of quartiles (≤4, 5–7, 8–11, ≥12 minutes). The primary outcome was favorable neurologic outcome at discharge. The secondary outcome was survival to discharge from the hospital. Multivariable logistic regression was used to analyze outcomes according to TTI. A different effect of TTI according to the administration of prehospital EMS advanced airway was evaluated.

Results In total, 83,470 patients were analyzed. Good neurologic recovery decreased as TTI increased (1.0% for TTI ≤4 minutes, 0.9% for TTI 5–7 minutes, 0.6% for TTI 8–11 minutes, and 0.5% for TTI ≥12 minutes; P for trend <0.05). The adjusted odds ratio of prolonged TTI (≥12 minutes) was 0.73 (95% confidence interval, 0.57–0.93; P<0.01) for good neurologic recovery. However, the negative effect of prolonged TTI on neurological outcome was insignificant when advanced airway or entotracheal intubation were performed by EMS providers (adjusted odds ratio, 1.17; 95% confidence interval, 0.42–3.29; P=0.76).

Conclusion EMS TTI was negatively associated with the neurologic outcome of OHCA without ROSC on scene. When advanced airway was performed on scene, TTI was insignificantly associated with the outcome.

Keywords Heart arrest; Emergency medical services; Intubation

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Capsule Summary

What is already known

In out-of-hospital cardiac arrest, patients that do not respond to field emergency medical service management should be transported to a hospital for advanced cardiac arrest care.

What is new in the current study

When no return of spontaneous circulation is achieved at the scene of an out-of-hospital cardiac arrest after emergency medical service management, minimizing hospital transport time is important for patient outcome. However, if transport time is suspected to be delayed, an advanced airway might be beneficial in good neurological outcome.

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains a primary public health problem because of the low survival rate and the unfavorable neurologic outcome.[1-3] Both prehospital resuscitation and hospital-based post-cardiac arrest care are emphasized to be important components in the chain of survival.[4,5] Emergency medical services (EMS) dispatched to the OHCA scene, perform prehospital management, including high-quality compression and airway management, and determine the mode for transporting the patient to the emergency medical center for adequate post-cardiac arrest treatment.[6,7]

The time for transporting the patient from on-scene departure to arrival at the emergency department (ED) is defined as the transport time interval (TTI).[8-12] Previous studies have shown that TTI does not have any significant effect on the survival outcome.[8,9,11] However, these studies were mainly conducted under a system wherein most patients were treated with the advanced cardiac life support (ACLS) system in the prehospital stage.[8,9,11,13] In an environment where EMS plays a limited role in the termination of resuscitation, OHCA patients without return of spontaneous circulation (ROSC) are transferred to the ED with ongoing resuscitation in the ambulance, which may interrupt high-quality cardiopulmonary resuscitation (CPR) and other interventions.[7,14-16] In addition, there have been no previous studies on the difference in TTI effects according to the interventions performed by the EMS on scene before the transport of the OHCA patient. Therefore, it is necessary to consider the impact of TTI on patient outcome in that OHCA patients without ROSC should be transferred to the center where suitable approaches for management are carried out in the appropriate time.[17]

The present study primarily aimed to evaluate the association of TTI with survival rate and neurologic outcome in OHCA patients without prehospital ROSC on scene. The secondary objective was to evaluate the interaction effect of TTI according to different types of prehospital airway management.

METHODS

Ethics statement

This study was approved by the institutional review board of Seoul National University Hospital (No. 1103–153-357), and the need for informed consent was waived for the present study due to minimal risk.

Study design and setting

This was a retrospective observational study based on the nationwide OHCA registry in Korea. The EMS of Korea is a single-tiered, government-based system. It is operated by 16 provincial headquarters of the National Fire Agency. Emergency medical technicians (EMTs) are divided into two levels: level 1 EMT and level 2 EMT. Level 1 EMTs are compatible with advanced EMTs in the United States, and level 2 EMTs are compatible with EMTs in the United States. Only level 1 EMTs can perform intravenous fluid resuscitation and prehospital airway management such as endotracheal intubation (ETI) or supraglottic airway (SGA), but they are restricted to administer epinephrine or other ACLS drugs during CPR even under direct medical supervision. They are also not allowed to discontinue CPR or declare death without ROSC at the scene. Thus, ACLS is available only in hospitals, which requires all OHCA patients to be transported to the ED regardless of their ROSC status. In the national EMS protocol, the transfer of OHCA patients is recommended to the nearest level 2 or higher EDs. EDs are designated by the government as levels 1 to 3 based on the availability of human resources, intensive care unit, and equipment. Level 1 EDs have the best facilities and resources, but these EDs must be covered by designated board-certified emergency physicians throughout (24 hours) a day.

Database

In 2006, the nationwide EMS-assessed OHCA registry was established by the Ministry of Health and Welfare of Korea. The Korea Centers for Disease Control and Prevention has managed the registry with financial support since 2007. The database consists of data on acute myocardial infarction and acute stroke from OHCA patients nationwide. The data of all OHCA cases assessed by the EMS are collected from the EMS run sheets containing demographic and Utstein information. The EMS run sheets are electronically stored in the server of EMS headquarters after the transportation of OHCA patients. The hospital electronic medical records were then reviewed to assess hospital resuscitation and postresuscitation care. Expert reviewers from the Korea Centers for Disease Control and Prevention visit the hospital where the OHCA patient was transported, and they investigate the medical records of the patient for collecting detailed clinical information and assessing outcomes using a structured survey form.

Study population

All adult OHCA patients who were treated by the EMS between January 2013 and December 2017 were included in the study. Patients were excluded if they were aged < 18 years or if the cause of arrest had a noncardiac origin. Patients who underwent prehospital ROSC by the EMS before hospital transport were excluded. Patients with unknown prehospital ROSC status and those with a TTI of longer than 60 minutes were also excluded.

Variables

The main exposure variable in this study was TTI. TTI was defined as the time between EMS scene departure and hospital arrival. TTI was categorized into four groups according to its distribution (≤ 4, 5–7, 8–11, and ≥ 12 minutes).

The methods of airway management were classified as ETI, SGA, or bag-valve mask ventilation. The EMT may carry out SGA or ETI at the scene or during the transportation, but only level 1 EMTs can perform ETI. EMTs may determine not to insert an ETI or SGA, thereby using only a bag-valve mask during CPR and transportation, or choose ETI or SGA by their preference or proficiency.

Data of patients' characteristics were obtained from the nationwide registry database. The information included age, sex, community urbanization (metropolitan area or not), arrest location (public, private, or other), witnessed status, bystander CPR, initial EMS rhythm, prehospital defibrillation, EMS response time interval, scene time interval, TTI, EMS advanced airway, EMS intravenous access, and level of EDs (level 1, 2, or 3).

Outcomes

The primary outcome in this study was good neurologic recovery, defined as Glasgow-Pittsburgh cerebral performance category score of 1 or 2 at hospital discharge. The secondary outcome was survival to discharge from the hospital.

Statistical analysis

Demographics, prehospital EMS interventions and outcomes were compared according to the TTI groups. Data of categorical variables were compared using the chi-square test, and data of continuous variables were compared using Student t-test and analysis of variance. We analyzed the association between TTI and neurologic outcome using multivariable logistic regression analysis adjusting for possible confounders such as age, sex, community urbanization, arrest location, witnessed status, bystander CPR, initial EMS rhythm, prehospital defibrillation, EMS response time interval, scene time interval, and EMS intravenous access. In the regression analysis, we divided the patients into two groups by a TTI of 12 minutes: the group with a TTI of more than 12 minutes and the group with a TTI of less than 12 minutes; the odds ratios (ORs) of both groups were calculated and compared. In addition, the OR was calculated when the TTI increased by 1 minute. Interaction analysis was performed to evaluate the different effects of TTI on outcomes according to whether the administration of prehospital advanced airway was performed by the EMS provider. All statistical analyses were performed using SAS ver. 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Demographics and outcomes according to TTI

In total, 137,268 patients with OHCA identified from the nationwide registry database were evaluated during the study period; 2,872 pediatric OHCA patients were excluded. Among 139,396 adult OHCA patients, we excluded 35,090 patients with noncardiac cause of arrest, 8,554 EMS-treated patients, 521 patients with TTI longer than 60 minutes, and 6,761 patients with prehospital ROSC or unknown ROSC status; finally, 83,470 OHCA patients without prehospital ROSC were enrolled (Fig. 1).

The enrolled patients were classified into four groups according to the TTI distribution. Demographic and patient characteristics are presented in Table 1. Among the total population, the number of patients who survived to discharge was 2,238 (2.7%) and the number of patients who showed a favorable neurological outcome was 636 (0.8%). Moreover, 18,455 patients were identified to have a TTI of more than 12 minutes, in which the rate of the metropolitan area was significantly lower than that in the other

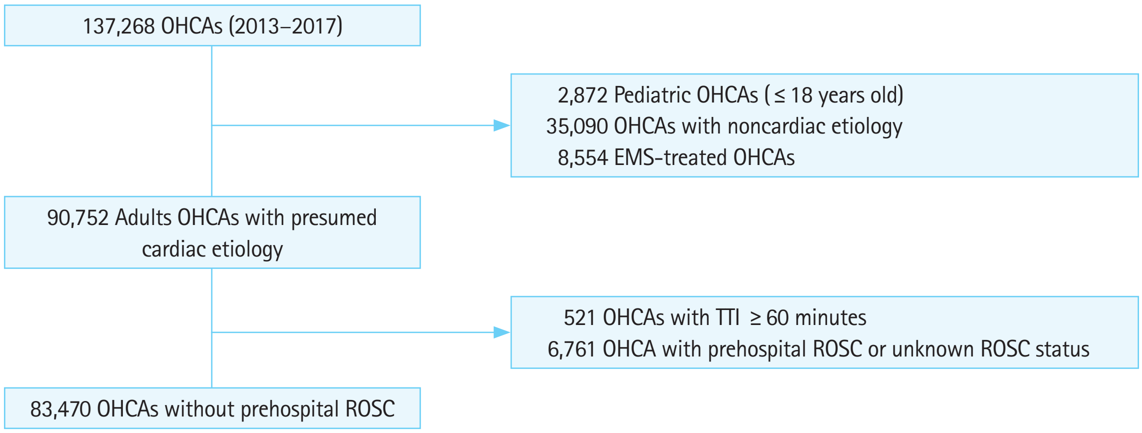

Fig. 1. Selection of the study population for analysis. OHCA, out-of-hospital cardiac arrest; EMS, emergency medical service; TTI, transport time interval; ROSC, return of spontaneous circulation.

Table 1. Characteristics of the study population based on transport time interval

Characteristic	Total (n = 83,470)	≤ 4 min (n = 22,322)	5–7 min (n = 25,357)	8–11 min (n = 17,336)	≥ 12 min (n = 18,455)	P-value
Year						< 0.01
2013	15,641 (18.7)	3,747 (16.8)	4,831 (19.1)	3,345 (19.3)	3,718 (20.1)	
2014	16,723 (20.0)	4,111 (18.4)	5,255 (20.7)	3,565 (20.6)	3,792 (20.5)	
2015	17,529 (21.0)	4,859 (21.8)	5,401 (21.3)	3,598 (20.8)	3,671 (19.9)	
2016	16,851 (20.2)	4,703 (21.1)	5,023 (19.8)	3,499 (20.2)	3,626 (19.6)	
2017	16,726 (20.0)	4,902 (22.0)	4,847 (19.1)	3,329 (19.2)	3,648 (19.8)	
Age (yr)	70.1 ± 15.1	69.8 ± 15.2	69.9 ± 15.2	70.6 ± 15.0	71.3 ± 14.6	< 0.01
Male sex	52,104 (62.4)	13,986 (62.7)	15,785 (62.3)	10,743 (62.0)	11,590 (62.8)	0.32
Time of day						< 0.01
0 a.m.–8 a.m.	21,113 (25.3)	6,041 (27.1)	6,492 (25.6)	4,257 (24.6)	4,323 (23.4)	
8 a.m.–4 p.m.	34,237 (41.0)	9,124 (40.9)	10,313 (40.7)	7,104 (41.0)	7,696 (41.7)	
4 p.m.–0 a.m.	28,120 (33.7)	7,157 (32.1)	8,552 (33.7)	5,975 (34.5)	6,436 (34.9)	
Location (metropolis)	34,624 (41.5)	10,287 (46.1)	13,157 (51.9)	7,492 (43.2)	3,688 (20.0)	< 0.01
Witnessed arrest	37,892 (45.4)	9,587 (42.9)	11,364 (44.8)	8,078 (46.6)	8,863 (48.0)	< 0.01
Initial EMS rhythm (shockable)	9,649 (11.6)	2,605 (11.7)	2,947 (11.6)	1,965 (11.3)	2,132 (11.6)	0.75
EMS defibrillation	15,755 (18.9)	3,840 (17.2)	4,584 (18.1)	3,319 (19.1)	4,012 (21.7)	< 0.01
EMS airway						< 0.01
Bag-valve mask	53,670 (64.3)	13,687 (61.3)	15,583 (61.5)	11,074 (63.9)	13,326 (72.2)	
Endotracheal intubation	4,433 (5.3)	1,277 (5.7)	1,447 (5.7)	865 (5.0)	844 (4.6)	
Supraglottic airway	25,367 (30.4)	7,358 (33.0)	8,327 (32.8)	5,397 (31.1)	4,285 (23.2)	
EMS time interval						
Response time interval (min)	7 (5–10)	6 (5–8)	7 (5–9)	7 (6–10)	10 (6–14)	< 0.01
Scene time interval (min)	11 (7–15)	11 (8–15)	11 (7–15)	10 (7–14)	10 (6–14)	< 0.01
EMS intravenous access	15,430 (18.5)	4,605 (20.6)	5,118 (20.2)	3,169 (18.3)	2,538 (13.8)	< 0.01
Emergency department level						< 0.01
1	11,713 (14.0)	2,841 (12.7)	3,814 (15.0)	2,593 (15.0)	2,465 (13.4)	
2	40,281 (48.3)	10,373 (46.5)	13,263 (52.3)	8,866 (51.1)	7,779 (42.2)	
3	31,476 (37.7)	9,108 (40.8)	8,280 (32.7)	5,877 (33.9)	8,211 (44.5)	
Survival outcome						
Survival to discharge	2,238 (2.7)	718 (3.2)	779 (3.1)	432 (2.5)	309 (1.7)	< 0.01
Good neurological outcome	636 (0.8)	220 (1.0)	219 (0.9)	106 (0.6)	91 (0.5)	< 0.01

Values are presented as number (%), mean ± standard deviation, or median (interquartile range).
EMS, emergency medical service.

Table 2. Association of transport time interval with survival rate and neurologic outcome

Variable	Unadjusted		Adjusted[a]		P-value
	OR	95% CI	OR	95% CI	
Survival to discharge					
TTI ≥ 12 min	0.56	0.49–0.63	0.71	0.61–0.80	< 0.01
TTI 1-min increase	0.96	0.95–0.98	0.98	0.96–0.99	< 0.01
Favorable neurologic outcome					
TTI ≥ 12 min	0.57	0.49–0.63	0.73	0.57–0.93	0.01
TTI 1-min increase	0.97	0.95–0.98	0.98	0.96–0.99	< 0.01

OR, odds ratio; CI, confidence interval; TTI, transport time interval; EMS, emergency medical service.
[a]Adjusted covariables: age, sex, community urbanization, arrest location, witnessed status, bystander cardiopulmonary resuscitation, initial EMS rhythm, prehospital defibrillation, EMS response time interval, scene time interval, EMS advanced airway, and EMS intravenous access.

three groups with a TTI of less than 12 minutes (n = 3,688, 20.0%, P < 0.01). In terms of the rate of advanced airway management, the longer the TTI, the lower the rate observed (38.7% vs. 38.5% vs. 36.1% vs. 27.8%, P < 0.01). The neurological outcome was significantly less favorable in the group with a longer TTI than in the group with a shorter TTI (3.2% vs. 3.1% vs. 2.5% vs. 1.7%, P < 0.01).

Multivariable logistic regression of the association between TTI and patient outcomes

Based on a TTI of less than 12 minutes, the ORs of the survival rate and neurological outcome in the group with a TTI of more than 12 minutes were compared. Using multivariable logistic regression analysis after adjustment for possible confounders, the adjusted OR (aOR) for favorable neurologic outcome was lower when the TTI was more than 12 minutes (0.73; 95% confidence interval [CI], 0.57–0.93; P = 0.01). It was also shown that the aOR when the TTI increased by 1 minute was decreased by 0.98 (95% CI, 0.96–0.99; P < 0.01). The aOR of the survival rate in the group with a TTI of more than 12 minutes was 0.71 (95% CI, 0.61–0.80; P < 0.01) (Table 2).

Interaction effect of prehospital airway management on the association between TTI and patient outcomes

The aOR for a TTI of 12 minutes was compared according to the type of prehospital airway placement. Although the aOR of the favorable neurologic outcome was 0.66 (95% CI, 0.499–0.872; P < 0.01), the aOR was insignificant in the group with a TTI of more than 12 minutes when prehospital advance airway placement was performed (0.98; 95% CI, 0.6–1.50; P = 0.92). When prehospital ETI was performed, the aOR of the neurologic outcome was not significant in the group with a TTI of more than 12 minutes (1.17; 95% CI, 0.42–3.29; P = 0.76). The aOR of the neurologic outcome was not significant, as the TTI increased by 1 minute if prehospital airway placement was performed (aOR of 1.00 for advanced airway; 95% CI, 0.97–1.02; P = 0.77; aOR of 1.01 for ETI; 95% CI, 0.97–1.06; P = 0.57). In the case of survival rate, the significant difference in the aOR according to TTI disappeared when ETI was performed (0.99; 95% CI, 0.58–1.68; P = 0.97) (Table 3).

Table 3. Interaction effect according to the type of prehospital airway placement on transport time interval and survival outcome

Variable	Adjusted OR	95% CI	P-value
Survival to discharge			
TTI ≥ 12 min (vs. TTI < 12 min)			
Advanced airway			
Not performed	0.71	0.61–0.82	< 0.01
Performed	0.73	0.57–0.93	< 0.01
ETI			
Not performed	0.70	0.61–0.80	< 0.01
Performed	0.99	0.58–1.68	0.97
TTI 1-min increase			
Advanced airway			
Not performed	0.99	0.98–0.99	< 0.01
Performed	0.98	0.97–0.99	0.02
ETI			
Not performed	0.98	0.97–0.99	< 0.01
Performed	1.01	0.99–1.03	0.45
Favorable neurologic outcome			
TTI ≥ 12 min (vs. TTI < 12 min)			
Advanced airway			
Not performed	0.66	0.50–0.87	< 0.01
Performed	0.98	0.64–1.50	0.92
ETI			
Not performed	0.72	0.56–0.92	< 0.01
Performed	1.17	0.42–3.29	0.76
TTI 1-min increase			
Advanced airway			
Not performed	0.97	0.96–0.99	< 0.01
Performed	1.00	0.97–1.02	0.77
ETI			
Not performed	0.98	0.96–0.99	< 0.01
Performed	1.01	0.97–1.06	0.57

OR, odds ratio; CI, confidence interval; TTI, transport time interval; ETI, endotracheal intubation; EMS, emergency medical service.
[a]Adjusted covariables: age, sex, community urbanization, arrest location, witnessed status, bystander cardiopulmonary resuscitation, initial EMS rhythm, prehospital defibrillation, EMS response time interval, scene time interval, and EMS intravenous access.

DISCUSSION

In this study, outcomes according to TTI were compared in OHCA patients who did not achieve prehospital ROSC, and as the TTI increased, the neurologic and survival outcomes at discharge tended to be unfavorable. As the association between TTI and the outcomes of OHCA patients without prehospital ROSC was analyzed using multivariable logistic regression adjusted for possible confounders, the aOR was found to be low in the patient group with a longer TTI. However, the effect of prolonged TTI on patient outcomes was insignificant when advanced airway management was performed.

Previous studies on TTI in OHCA have shown that TTI did not have a significant effect on patient outcome.[8,9,11] Therefore, there is evidence that with prolonged TTI it is more advantageous to transfer patients to a cardiovascular center of a higher level where appropriate treatment is possible, even for a long distance.[12,17] In most countries where previous studies were conducted, the EMS provider could perform ACLS for OHCA patients on scene.[8,9,11,13] However, in some countries, EMS providers are allowed to perform only limited interventions in the prehospital stage, which can lead to prolonged transport of OHCA patients without achieving ROSC.[6,7] There has been a lack of studies on the outcomes of patients who undergo long-distance transport without prehospital ROSC.[10]

When a patient is transferred before achieving prehospital ROSC, then high-quality CPR performed within the ambulance may be interrupted during the transport compared to the CPR executed on scene.[15,16,18] The effect of interrupted high-quality CPR ambulance on patient survival outcome is uncertain; however, the possibility of a deteriorating outcome is considered.[15,18,19]

Our result suggests that when EMS performed ETI before departure and decided to transfer the patient, the effect of TTI on outcomes might not be significant despite ROSC not being achieved. Our hypothesis is that chest compression can be sufficient only within a short period of arrest, but if it takes a longer time to transport the patient to an available ED, then the implementation of high-quality oxygen delivery procedure such as ETI would aid in oxygenation and ventilation in long-distance transport.[20-24]

Advanced airways are allowed only to a more educated and skilled EMT (level 1 EMT in Korea).[6,7] It is possible that, in OHCA, initial resuscitative management by the EMT, who can provide professional treatment, contributed to a favorable patient outcome. Therefore, performing advanced airway management before patient transport can indicate that sufficient prehospital treatment has been performed, and if adequate treatment is performed on-scene, then the outcome according to TTI may not be significantly different for patients who did not achieve ROSC. However, performing advanced medical procedures by the EMS provider is more difficult and sometimes delays the time to hospital arrival. The negative influence of delayed hospital transport time due to advanced airway management on-scene should also be considered.

In addition to cardiac arrest, patients with serious diseases such as critical trauma or stroke are transferred to a distant specialized center for regionalization, although the transport time is slightly longer.[25-27] In case of cardiac arrest without ROSC, it is necessary to carefully consider establishing a regional strategy for appropriate on-scene treatment and transport of the patient to a proper facility.

This study has several limitations. First, as this was a retrospective observational study and involved a multivariate analysis, it has limitations in adjusting for possible confounders compared to an intervention trial or a randomized controlled study. There are various factors affecting the outcome of OHCA. Because of the observational nature of the study and the presence of unmeasured potential confounding factors in this study, we could not conclude that a certain method or protocol is the best or the most optimal based on our study. Second, there is a possibility that TTI is not a result of the decision of EMS but a result of regional characteristics and cardiac arrest location. The proportion of metropolitan areas decreased as the TTI was longer in the study. Possible intervention variables were adjusted for; yet it is considered that other regional characteristics may have influenced the study results. Although the level of urbanization was included in the adjusted model, it might be debatable that urbanization is an appropriate variable for inclusion in adjustment because the level of urbanization might have already been included in the characteristics of EMS time variables such as TTI. Third, a longer TTI does not mean that the patients were transported to the higher level of ED. The current EMS protocol in Korea recommends transporting an OHCA patient without ROSC to the nearest ED available with prenotification to the hospital. Various factors may influence the selection of destination ED in cases of OHCA, such as the availability of ED, traffic status, and EMS resources.

In summary, hospital TTI was negatively associated with the neurologic outcome of OHCA without ROSC on scene. However, when ETI was performed on scene, TTI was insignificantly associated with the outcome. Performing advanced airway on scene may be considered when a longer hospital TTI is expected.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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