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Effect of Emergency Medical Services Use on Mortality and Disability in Acute Hemorrhagic Stroke

급성 출혈성 뇌졸중에서 응급의료서비스의 이용이 사망 및 장애에 미치는 효과

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김 솔 아

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Effect of Emergency Medical Services Use on Mortality and Disability in Acute Hemorrhagic Stroke

by
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A thesis submitted to the Department of Clinical Medical Sciences in partial fulfillment of the requirements for the Degree of Master of Science in Clinical Medical Sciences at Seoul National University College of Medicine

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Abstract

Introduction: It is unclear whether the use of emergency medical services (EMS) is associated with enhanced survival and decreased disability after hemorrhagic stroke and whether the effect size of EMS use differs according to the length of stay (LOS) in emergency department (ED).

Methods: Adult patients (19 years and older) with acute hemorrhagic stroke who survived to admission at 29 hospitals between 2008 and 2011 were analyzed, excluding those who had symptom-to -ED arrival time of 3 hours or greater, received thrombolysis or craniotomy before inter-hospital transfer, or had experienced cardiac arrest before ED arrival, had unknown information about ambulance use and outcomes. Exposure variable was EMS use. Endpoints were survival at discharge and worsened modified Rankin Scale (W-MRS) defined as 3 or greater points difference between pre- and post-event MRS. Adjusted odds ratios (AORs) with 95% confidence intervals (95% CIs) for the outcomes were calculated, including potential confounders (demographic, socioeconomic status, clinical parameter, comorbidity, behavior, and time of event) in the final model and stratifying patients by inter-hospital transfer and by time interval from symptom to ED arrival (S2D). ED LOS, classified into short (<120 minutes) and long (≥120 minutes), was added to the final model for testing of the interaction model.

Results: A total of 2,095 hemorrhagic strokes were analyzed in which 75.6% were transported by EMS. For outcome measures, 17.4% and 41.4% were dead and had worsened MRS, respectively. AORs (95%

CIs) of EMS were 0.67 (0.51-0.89) for death and 0.74 (0.59-0.92) for W-MRS in all patients. The effect size of EMS, however, was different according to LOS in ED. AORs (95% CIs) for death were 0.74 (0.54-1.01) in short LOS and 0.60 (0.44-0.83) in long LOS group. AORs (95% CIs) for W-MRS were 0.76 (0.60-0.97) in short LOS and 0.68 (0.52-0.88) in long LOS group.

Conclusions: EMS transport was associated with lower hospital mortality and disability after acute hemorrhagic stroke. Effect size of EMS use for mortality was significant in patients with long ED LOS.

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Keywords: Emergency Medical Service, Hemorrhagic Stroke, Mortality, Disability
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INTRODUCTION

The global burden of hemorrhagic stroke increased significantly between 1990 and 2010 in terms of the absolute number of people with incident hemorrhagic stroke (47% increase), number of deaths (20% increase) and disability-adjusted life years lost (14% increase). (1) A study reported that the range in early (21-day to 1-month) case fatality due to hemorrhagic stroke is between 25% and 35%.(2) Every year, approximately 105,000 people in Korea experience new or recurrent stroke, and more than 26,000 die of stroke, which indicates that every 5 minutes stroke attacks someone and every 20 minutes stroke kills someone.(3) Incidence rate of hemorrhagic stroke in the above study was 54 per 100,000 person-years (2006) which slightly decreased from 123 in 1995 and 106 in 2003 in 35-74 aged population.

Presentations of hemorrhagic stroke are various in severity and mortality. One third of patients die within one month after onset, and most surviving patients are left with disability.(4) The Korean Center for Disease Control reported that 1-month case fatality rate of hemorrhagic stroke was 35.0% in 2006 which was 2.4 fold higher than that of ischemic stroke.(3) Blood pressure control, intracerebral pressure control, and surgical operation in hemorrhagic stroke have been investigated as optimal therapeutic tools, but evidence are weak whether the treatments are associated with improved clinical outcomes or not.(5) There had been no change in one month case-fatality rate of hemorrhagic stroke during the last four decades.(2) Novel risk factors

associated with survival outcomes after hemorrhagic stroke are age, Glasgow Coma Scale, location and volume of intracerebral hemorrhage, and intraventricular extension.(6)

Hemorrhagic stroke results in neurological deterioration due to irreversible secondary injury caused by an increase in intracranial pressure and brain edema in early phase of the disease progress.(7) To minimize the secondary injury of brain parenchyma, emergency care for early diagnosis and treatment is an essential component of stroke care system. To provide early diagnosis and treatment, suspected patients should be promptly transported to emergency department where brain computed tomography (CT) or magnetic resonance image (MRI) are available.

Use of emergency medical services (EMS) has been known to be related with shortening the time from symptom onset to provision of definitive care in hemorrhagic stroke(8). It is unclear, however, whether EMS use is associated with survival and disability after hemorrhagic stroke, and whether the effect size of EMS use is different according to the length of stay (LOS) in emergency department (ED), which is regarded as a proxy measure of the time interval from ED arrival to provision of definitive care. This study aims to test the effect of EMS use on hospital outcomes of hemorrhagic stroke according to the length of stay in ED.

MATERIALS AND METHODS

The study received ethical clearance from the Institutional Review Board of the study institution, and the Korea Centers for Disease Control and Prevention (CDC) approved the data analysis and publication.

1. Study setting and design

A cross-sectional observational study was performed using a cardiovascular disease database collected from 29 teaching and tertiary hospital EDs. Each hospital has more than 30,000 ED visitors annually and has departments of emergency medicine, neurology, and neurosurgery, and radiology. All hospitals have emergency medicine physicians available 24 hours and 365 days a year to provide acute stroke care. CTs and MRIs are also available in all EDs as routine emergency practices at all times. The hospitals have their own stroke care protocol on the basis of the national recommendation guideline provided by the Ministry of Health and Welfare, which had been revised from the international academic society recommendations(5). Every year, all designated EDs should be reviewed by the audit process of the government for its quality of care according to the Emergency Medical Services Act.

Prehospital ambulance services are tax-based and are operated by the national fire department. Service level in Korea is comparable to the intermediate level of EMS provided in North America. When a patient with symptoms of stroke

calls 119 ambulance services, a single-tiered ambulance service responds and transports the patient to ED based on the national stroke protocol. There is no regionalized program available for stroke care. The EMS protocol mandates that when a patient is suspected of having a stroke, the EMS providers should transport the patient to the nearest ED. Inter-hospital transport services are provided by hospital ambulance system or commercial ambulance companies.

The study received ethical clearance from the Institutional Review Board of the study institution, and the Korea Centers for Disease Control and Prevention (CDC) approved the data analysis and publication.

2. Data source

The Cardiovascular Disease Surveillance (CAVAS) project, sponsored by the Korean CDC and the National Emergency Management Agency since 2008, is a nationwide, observational database of all EMS assessed out-of-hospital cardiac arrests (OHCAs) and acute cardiovascular and cerebrovascular diseases diagnosed in EDs within 1 week of symptom onset.(9-12) Data of patients admitted or discharged with acute cardiovascular and cerebrovascular disease (ICD-10 codes: I21.0~I21.9, I60.0~I60.9, I61.0~I61.9, I63.0~I63.9, I64) from 29 participating EDs in 12 cities and provinces were prospectively collected through an in-depth cardiovascular disease registry and medical record review process. Trained reviewers abstracted data from medical records. Through medical record review, demographic data (age, gender, and address), socioeconomic data (insurance status, education, and occupation), and information about risk factors (hypertension, diabetes, dyslipidemia,

chronic renal failure, cardiovascular and cerebrovascular disease, smoking and alcohol use) were collected. Time variables for symptom onset, EMS call and arrival, ED arrival, transfer, and treatment as well as information on initial diagnostic information including brain imaging, treatments, and in-hospital outcomes were also collected.

3. Study population

Adult patients who were 18 years or older between November 2008 and December 2011 were included if diagnosed with acute hemorrhagic stroke within 3 hours of admission at ED. The definition of hemorrhagic stroke was the diagnosis code of international classification of disease (ICD) 10th edition I61.0-I61.9 at hospital discharge. For this analysis, we excluded patients if they were discharged or transferred to EDs of other hospitals, had less than 3 hours of symptom to ED arrival time, received thrombolysis or craniotomy at prior hospital before inter-hospital transfer, had cardiac arrest in prehospital stage or in ED, or had unknown information about ambulance use and outcomes.

4. Variables

Patients were divided into 2 groups according to EMS use. EMS use was defined if a patient was directly transported by ambulance from field and were not transferred from other medical facilities. We assessed for the differences between groups with EMS use and those without EMS use in their age, gender,

urbanization level, education level, occupation and insurance type, behavioral and risk factors (exercise, smoking, alcohol use), season, day of week, time of day, co-morbidities (diabetes, hypertension, dyslipidemia, chronic renal failure, cardiovascular disease, and cerebrovascular disease), transfer, and ED LOS from arrival to ED to discharge or admission. If information was unobtainable from medical records, the variables were considered unknown.

5. Outcomes

The primary and secondary outcomes were hospital mortality and worsened disability at hospital discharge measured by 3 or greater points difference between pre-event and post-event modified Rankin Scale (W-MRS). The MRS has seven ordinal scores of disability ranging from normal condition (0), mild to severe disabled (1 to 5), and death (6).(13) Coordinators were educated and trained on how to measure the MRS using discharge medical records. For pre-event MRS, emergency physicians routinely asked patients directly or family members and guardians during history-taking, and describe the disability status according to registry and data variable dictionary. Discharge summary, which is the core manuscript about hospital care for reimbursement from the national health insurance program, mostly described patients' disability status after stroke at discharge. Study coordinators collected pre-event information from emergency department medical records and collected post-event MRS from discharge summary record. When coordinators could not extract the exact MRS score due to incomplete information available, the case was regarded as unknown MRS.

6. Statistical analysis

Descriptive statistics for categorical variables (percentages) and continuous variables (median and interquartile ranges (IQR)) were reported. Differences in the distribution of demographic, medical history, and clinical factors were examined using chi-square for discrete variables and Wilcoxon rank sum tests for continuous variables. A multivariable logistic regression model was used to examine the associations between exposure variable and outcomes, adjusted odds ratios (AORs) and 95% confidence intervals (95% CIs) were calculated after controlling age, gender, urbanization level, education level, occupation, insurance type, behavioral and risk factors (exercise, smoking, alcohol use), season, day of week, time of day, and comorbidities (diabetes, hypertension, dyslipidemia, chronic renal failure, cardiovascular disease, and cerebrovascular disease) for all patients and also stratified by inter-hospital transfer and by time interval from symptom to ED arrival (S2D<60, $60 \leq$ S2D ≤ 120, and S2D ≥ 120 minutes). To compare the effect size of EMS use for outcomes by ED LOS, AORs (95% CIs) were calculated using short and long ED LOS (<120 and ≥ 120 minutes, respectively) in the interaction model with an interaction term (EMS*ED LOS).

RESULTS

Demographic findings

Of 5588 eligible hemorrhagic stroke, a total of 2095 cases were analyzed, excluding cases with longer symptom onset to ED arrival time of 3 hours or greater (n=2719), those that were discharged or transferred in ED (n=610), those who had received thrombolysis, anticoagulation, antiplatelet, coiling at other hospital (n=135), pediatric patients younger than 18 (n=5), cases that had cardiac arrest in prehospital stage (n=23), and those with incomplete information on EMS use or inter-hospital transfer (n=73).

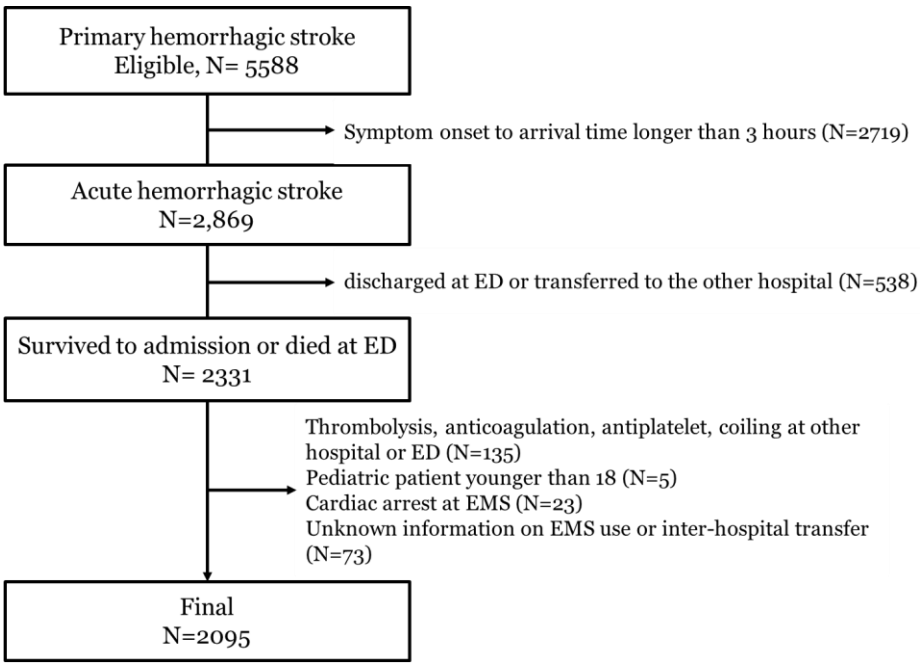

Figure 1. Study Population

Descriptive characteristics of the patients are summarized in Table 1. The median age of the patients was 61 years, and 54.7% were male. Inter-hospital transfer was 25.9% in the EMS group and 77.0% in the Non-EMS group ($p<0.01$). Proportions of patients with ED LOS less than 2 hours were 34.4% in the EMS group and 29.1 % in the Non-EMS group ($p=0.03$). The EMS group showed significantly higher levels of urbanization and education, while the non-EMS group showed less exercise behavior.

	Total		EMS		Non-EMS		P-value
	N	%	N	%	N	%	
Total	2095	100	1583	100	512	100	
Age							0.11
Median (IQR)	61	(51-71)	61	(51-71)	60	(50-70)	
Gender							0.32
Male	1145	54.7	875	55.3	270	52.7	
Female	950	45.3	708	44.7	242	47.3	
Urbanization							<0.01
Urban	720	34.4	597	37.7	123	24.0	
Suburban	491	23.4	344	21.7	147	28.7	
Rural	159	7.6	71	4.5	88	17.2	
Other and Unknown	725	34.6	571	36.1	154	30.1	
Level of Education							<0.01
< High School	991	47.3	724	45.7	267	52.1	
>= High School	955	45.6	759	47.9	196	38.3	
Unknown	149	7.1	100	6.3	49	9.6	
Occupation Class							0.13
Non-Physical	109	5.2	81	5.1	28	5.5	
Physical	671	32.0	487	30.8	184	35.9	
Military/Student/House-wife	342	16.3	262	16.6	80	15.6	
Unemployed	808	38.6	632	39.9	176	34.4	
Other and Unknown	165	7.9	121	7.6	44	8.6	
Insurance							0.01
National health insurance	1965	93.8	1498	94.6	467	91.2	
Medical Aid	107	5.1	72	4.5	35	6.8	
Other and Unknown	23	1.1	13	0.8	10	2.0	
Underlying Risk Factors							

Lack of exercise	1513	72.2	1118	70.6	395	77.1	<0.01
Smoking	442	21.1	338	21.4	104	20.3	0.26
Alcohol use	741	35.4	556	35.1	185	36.1	0.68
Season							0.46
Spring (Mar-May)	580	27.7	447	28.2	133	26.0	
Summer (Jun-Aug)	414	19.8	309	19.5	105	20.5	
Autumn (Sep-Nov)	523	25.0	384	24.3	139	27.1	
Winter (Dec-Feb)	578	27.6	443	28.0	135	26.4	
Day of Week							0.41
Sun	287	13.7	215	13.6	72	14.1	
Mon	321	15.3	245	15.5	76	14.8	
Tue	313	14.9	221	14.0	92	18.0	
Wed	300	14.3	232	14.7	68	13.3	
Thu	317	15.1	247	15.6	70	13.7	
Fri	285	13.6	219	13.8	66	12.9	
Sat	272	13.0	204	12.9	68	13.3	
Hour of day							0.30
0-6	293	14.0	225	14.2	68	13.3	
6-12	594	28.4	463	29.2	131	25.6	
12-18	742	35.4	547	34.6	195	38.1	
18-24	466	22.2	348	22.0	118	23.0	
Transfer							<0.01
Yes	804	38.4	410	25.9	394	77.0	
No	1291	61.6	1173	74.1	118	23.0	
ED LOS							0.03
<2 hours	694	33.1	545	34.4	149	29.1	
>=2 hours	1401	66.9	1038	65.6	363	70.9	

EMS: emergency medical services
ED LOS: Emergency department length of stay

Table 1. Demographic characteristics of the study population by EMS use

The EMS group showed significantly higher proportions of hypertension and cerebrovascular disease (Table 2). Time interval from symptom to arrival at destination ED was significantly different between the EMS and non-EMS groups 51 (82-144) and 119 minutes (31-86) ($p<0.001$). Median LOS in ED (time from ED arrival to admission) was shorter in the EMS (150 minutes (106-316)) than non-EMS group (169 minutes (103-272)) ($p<0.01$). Total

median time interval from symptom to admission at destination hospital were significantly greater in the non-EMS group (286 minutes) than in the EMS group (220 minutes) (p 0.04).

	Total		EMS		Non-EMS		P-value
	N	%	N	%	N	%	
Total	2095	100	1583	100	512	100	
SBP presenting at ED							<0.01
SBP<180	1051	50.2	749	47.3	302	59.0	
SBP>=180	1044	49.8	834	52.7	210	41.0	
MBP presenting at ED							<0.01
MBP<130	1239	59.1	897	56.7	342	66.8	
MBP>=130	856	40.9	686	43.3	170	33.2	
Co-morbidity							
Diabetes	372	17.8	277	17.5	95	18.6	<0.01
Hypertension	1400	66.8	1077	68.0	323	63.1	<0.01
Dyslipidemia	85	4.1	68	4.3	17	3.3	<0.01
Chronic renal disease	132	6.3	102	6.4	30	5.9	<0.01
Cardiovascular disease	147	7.0	121	7.6	26	5.1	<0.01
Cerebrovascular disease	342	16.3	283	17.9	59	11.5	<0.01
Time interval							
Symptom to destination ED	62	(36-116)	51	(82-144)	119	(31-86)	<0.01
Destination ED arrival to admission	154	(103-285)	150	(106-316)	169	(103-272)	<0.01
Symptom to admission at destination hospital	240	(168-374)	220	(220-436.5)	286	(155-352)	0.04

SBP: systolic blood pressure, MBP: mean blood pressure, ED: emergency department, EMS: emergency medical services

Table 2. Clinical information of the study population

The median days of duration (IQR) for measuring MRS between pre-event and post-event was 20 (9-40) days. Of total patients, most (77.7% with MRS 0 and 9.4% with MRS 1) were initially not disabled; after the event, however,

only 19.8% remained without moderate to severe disability (Table 3). In the EMS and non-EMS groups, worsened disability, defined as 3 or greater points difference between pre- and post-MRS, were observed in 39.7% and 46.5%, respectively ($p<0.01$). EMS group also showed significantly lower hospital mortality (16.3%) than non-EMS group (20.9%) ($p=0.02$).

	Total		EMS use		Non-EMS use		p-value
	N	%	N	%	N	%	
Total	2095	100	1583	100	512	100	
Pre-event MRS							<0.01
0	1628	77.7	1220	77.1	408	79.7	
1	196	9.4	168	10.6	28	5.5	
2	107	5.1	76	4.8	31	6.1	
3	54	2.6	45	2.8	9	1.8	
4	55	2.6	37	2.3	18	3.5	
5	43	2.1	27	1.7	16	3.1	
Unknown	12	0.6	10	0.6	2	0.4	
Post-event MRS							0.03
0	133	6.3	106	6.7	27	5.3	
1	282	13.5	217	13.7	65	12.7	
2	291	13.9	227	14.3	64	12.5	
3	251	12.0	202	12.8	49	9.6	
4	457	21.8	349	22.0	108	21.1	
5	553	26.4	391	24.7	162	31.6	
6	50	2.4	33	2.1	17	3.3	
Unknown	78	3.7	58	3.7	20	3.9	
Difference of MRS							<0.01
0	201	9.6	154	9.7	47	9.2	
1	281	13.4	217	13.7	64	12.5	
2	302	14.4	235	14.8	67	13.1	
3	275	13.1	223	14.1	52	10.2	
4	424	20.2	327	20.7	97	18.9	
5	407	19.4	279	17.6	128	25.0	
6	169	8.1	125	7.9	44	8.6	
Unknown	36	1.7	23	1.5	13	2.5	
W-MRS							<0.01
Yes	867	41.4	629	39.7	238	46.5	
No	1059	50.5	829	52.4	230	44.9	
Unknown	169	8.1	125	7.9	44	8.6	
Mortality							0.02
Yes	365	17.4	258	16.3	107	20.9	

No	1730	82.6	1325	83.7	405	79.1

MRS; modified Rankin Scale,
W-MRS is defined as the difference is greater than 3 between pre-event MRS and post-event MRS.

Table 3. Mortality and disability by the Modified Rankin Scale

Main analysis

Multivariable logistic regression analyses were conducted to test the associations between EMS use and outcomes after adjusting for the confounders. In the final model for all patients group, the AORs (95% CIs) were 0.67 (0.51-0.89) for death and 0.74 (0.59-0.92) for W-MRS (Table 4).

	Mortality				W-MRS			
	Total	Yes		AOR (95% CI)	Total	Yes		AOR (95% CI)
	N	n	%		N	n	%	
Total	2095	365	17.4		1926	867	45.0	
Non-EMS	512	107	20.9	1.00	468	238	50.9	1.00
EMS	1583	258	16.3	0.67 (0.51-0.89)	1458	629	43.1	0.74 (0.59-0.92)
Inter-hospital transfer (+)								
Non-EMS	394	71	18.0	1.00	355	169	47.6	1.00
EMS	410	39	9.5	0.50 (0.31-0.79)	374	100	26.7	0.39 (0.27-0.54)
Inter-hospital transfer (-)								
Non-EMS	118	36	30.5	1.00	113	69	61.1	1.00
EMS	1173	219	18.7	0.47 (0.30-0.74)	1084	529	48.8	0.63 (0.41-0.95)
0 ≤ S2D < 60 min								
Non-EMS	57	12	21.1	1.00	51	22	43.1	1.00
EMS	902	158	17.5	0.61 (0.30-1.26)	839	391	46.6	1.07 (0.58-1.97)

60 ≤ S2D < 120 min								
Non-EMS	200	49	24.5	1.00	186	94	50.5	1.00
EMS	447	77	17.2	0.51 (0.32-0.81)	411	169	41.1	0.72 (0.49-1.06)
S2D ≥ 120 min								
Non-EMS	255	46	18.0	1.00	231	122	52.8	1.00
EMS	234	23	9.8	0.40 (0.21-0.77)	208	69	33.2	0.46 (0.30-0.70)

EMS: emergency medical services;, MRS; modified Rankin Scale; AOR; adjusted odds ratio; 95% CI; 95% confidence interval, S2D: symptom to ED arrival

W-MRS is defined as the difference is greater than 3 between pre-event MRS and post-event MRS.

Adjusted for age, gender, urbanization level, blood pressure presenting at emergency department, education level, job, insurance, exercise, smoking, alcohol, diabetes, hypertension, dyslipidemia, chronic kidney disease, coronary heart disease, cerebrovascular disease, season, week, and hour of the event.

Table 4. Multivariable logistic regression model for examining the association between EMS use and mortality in all patients and in stratified groups

We performed stratified analysis by inter-hospital transfer and time interval from symptom to ED arrival (S2D). The AORs (95% CIs) for death were 0.50 (0.31-0.79) in patients that utilized inter-hospital transfer and 0.47 (0.30-0.74) in those that did not; in terms of S2D, the estimates were 0.61 (0.30-1.26) in short S2D group (S2D<60 minutes), 0.51 (0.32-0.81) in middle S2D group (60≤S2D<120 minutes), 0.40 (0.21-0.77) in long S2D group (S2D≥120 minutes), respectively. The AORs (95% CIs) for W-MRS were 0.39 (0.27-0.54) in inter-hospital transfer group and 0.63 (0.41-0.95) in non-transfer

group, 1.07 (0.58-1.97) in short S2D group (S2D<60 minutes), 0.72 (0.49-1.06) in middle S2D group (60≤S2D<120 minutes), 0.46 (0.30-0.70) in long S2D group (S2D≥120 minutes), respectively. (Table 5)

	Mortality				W-MRS			
	Total	Yes		AOR (95% CI)	Total	Yes		AOR (95% CI)
	N	n	%		N	n	%	
Short ED LOS								
Non-EMS	149	22	14.8	1.00	137	67	48.9	1.00
EMS	545	88	16.1	0.74 (0.54-1.01)	511	237	46.4	0.76 (0.60-0.97)
Long ED LOS								
Non-EMS	363	85	23.4	1.00	331	171	51.7	1.00
EMS	1038	170	16.4	0.60 (0.44-0.83)	947	392	41.4	0.68 (0.52-0.88)

EMS: emergency medical services; ED LOS: emergency department length of stay, MRS; modified Rankin Scale; AOR; adjusted odds ratio; 95% CI; 95% confidence interval

W-MRS is defined as the difference is greater than 3 between pre-event MRS and post-event MRS.

Adjusted for age, gender, urbanization level, blood pressure presenting at ED, education level, job, insurance, exercise, smoking, alcohol, diabetes, hypertension, dyslipidemia, chronic kidney disease, coronary heart disease, cerebrovascular disease, season, week, and hour of the event, ED length of stay (LOS), and interaction term (EMS use* ED LOS).

Table 5. Interaction model for examining the association of emergency medical service use and LOS in ED with mortality and worsened disability

The effect size of EMS use on mortality was significantly different by ED LOS (<120 versus ≥120 minutes) (Table 5). The AOR in the long ED LOS

group showed significant effects for reducing mortality (0.60 (0.44-0.83)) whereas in the short ED LOS group, the effects disappeared (0.74 (0.54-1.01)). For worsened disability, the effects of EMS in both short and long ED LOS groups were significant (0.76 (0.60-0.97) vs. 0.68 (0.52-0.88)).

DISCUSSION

Previous studies have shown that in settings where acute stroke patients were transferred to another hospital, the transfer was independently associated with poorer outcome at hospital discharge (14, 15). However, the association between EMS transport and mortality and disability after hemorrhagic stroke was unclear. In this study we found a strong effect of EMS use for saving more lives and reducing disability in all patients, and also for decreased mortality after acute hemorrhagic stroke in patients with greater than 2 hours of ED LOS.

The rationale of reduced mortality and disability in the EMS-use group is that EMS transportation can reduce the time interval from symptom onset to provision of definitive care (admission in this study). Short time interval can minimize secondary brain injury such as edema, swelling, hypoperfusion, and hypoxia. This study substantiated the effects of EMS use on reducing time interval from symptom onset to definitive care after hemorrhagic stroke.(8) In our study, we found that the reduced time interval from symptom to definitive care was about 66 minutes; 220 minutes (IQR 220-437 minutes) in the EMS group and 286 minutes (IQR 286-352 minutes) in the non-EMS group (p =0.04)).

Another rationale may be related to much higher proportion of direct visit to the destination hospital in the EMS group without inter-hospital transport. EMS providers are also expected to understand the value of optimal

emergency care at hospitals for hemorrhagic stroke than laypersons do. Therefore, EMS use can link patients to definitive emergency care more quickly. Through stratified analysis, our data showed the benefit of EMS use for reduced mortality and disability in both transfer and no-transfer group.

Stratified analysis by time interval from symptom to ED arrival (S2D) showed different results. When patients use EMS, those with S2D greater than 1 hour significantly benefited from reduced mortality, and those with S2D greater than 2 hours had significantly reduced disability.

In order to shorten the time interval from symptom to definitive care, it is important for EMS providers to clearly suspect of stroke in prehospital stage. Our EMS operates under the national standards and uses prehospital stroke scale without any regionalized system or bypassing protocol. Therefore, inter-hospital transfer may occur frequently. In this study, 61% was transported from other hospitals which attributed to increased total time interval from symptom to definitive care. If the national protocol were to encourage providers to bypass community hospital EDs for designated hospital EDs, the S2D would become much smaller. However, a previous study showed lower sensitivities of the National Institute of Health Stroke Scale or Cincinnati Prehospital Stroke Scale (CPSS) for detecting stroke. The ability of EMS providers to identify stroke patients in the study was relatively low. About 50% were missed by EMS for stroke (false negatives), and 3.5% were falsely considered to have stroke by EMS (false positives). The study was done in a hospital-based ambulance service in North America where CPSS was

educated and trained for stroke protocol, but the documentation protocol varied by local EMS authorities.(16)

To minimize S2D, the EMS protocol recommends that scene time interval should be kept under 10 minutes for providing stroke care procedure in the field. A study from North America analyzed the association between scene time intervals for stroke patients and the extent of stroke protocols for limiting scene time intervals. In the study, scene time interval was reduced when EMS operated under a specific prehospital stroke care protocol that limits scene time interval to be kept under a specific threshold.(17) Our EMS protocol has no specific time limits for stroke care, and EMS providers thus freely provide basic services, such as basic airway, oxygen therapy if needed, intravenous fluid therapy for shock, and ECG monitoring. Scene time intervals are usually kept less than 6 to 10 minutes. In Asian EMS systems with intermediate service levels like those in South Korea, Japan, and Taiwan, there are no designated centers available for patients with suspected hemorrhagic stroke or receiving transfer patients from other hospitals for definitive care.(18) In the Korean EMS system, emergency medical technicians evaluate the patients and quickly transport them to the nearest ED where emergency physicians provide emergency services. In this non-regionalized system, it is in the ED that the diagnosis and decision to provide definitive care or to transfer the patients to another hospital are made.

Some reported that longer stay in ED had increased hospital mortality of patients with hemorrhagic stroke,(19) but others reported that LOS in ED is not associated with poor neurologic outcomes(20). The associations between

LOS in ED and outcomes at hospital discharge are unclear. In demographic findings, the ED LOS in EMS group was significantly shorter than non-EMS group. In the interaction model, the effect size of EMS transport on mortality were significantly different between short and long LOS in ED. In patients who stayed less than 120 minutes in ED, EMS use did not change the odds for death, while it significantly decreased the odds for death by 0.60 (0.44-0.83) in patients who stayed for longer than 120 minutes in ED. From this finding, we assume the short LOS group would be too critical in condition to be saved than in the long LOS group. Simply reducing the time interval from symptom to admission was not effective in these patients group. Rapid deterioration or increase in intracranial pressure cannot be controlled by reducing only a few minutes by EMS transport.

Limitations

This is not a randomized controlled trial. Therefore we could not control for other hidden confounders which are potentially related with outcomes. We did not measure the amount of hemorrhage related with severity, change of mental status and presented symptoms. We use MRS at hospital discharge to measure disability. MRS is widely used in stroke patients, but it is more reliable for long term outcome. We enrolled patients who had less than 3 hour intervals from symptom onset to ED arrival. Stroke protocol and guidelines are focusing acute status to provide brain salvage procedure which should be done within 3 to 6 hours. The patients with longer interval from symptom onset to ED arrival were excluded (48.7%). Therefore the study results should

be carefully interpreted for this acute hemorrhagic stroke. EMS care during EMS use was not fully evaluated in this study. The EMS protocol in our study setting allows EMS providers to perform basic procedures only such as basic airway, oxygen, and fluid therapy. Due to limited information, we could not fully collect information on prehospital care and procedures. This study was performed in Korea where very limited advanced life support by EMS crew and non-standardized care by hospital providers are given. Regionalized networks of care for hemorrhagic stroke patients are not yet implemented. Generalization of our findings can be limited to the countries which has similar EMS system.

Conclusions

EMS transport was associated with significantly lower hospital mortality and disability for all study population and for patient subgroups with longer symptom to ED arrival times in those with acute adult hemorrhagic stroke. In particular, the patients group with longer LOS in ED then 2 hours showed significantly higher survival rates.

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국문 초록

서론: 출혈성 뇌졸중에서 응급의료서비스의 이용이 생존율을 증가시키고, 장애를 감소시키는 지와 이러한 응급의료서비스의 이용으로 인한 효과의 크기가 응급실 체류시간에 따라서 달라지는지는 명확히 알려져 있지 않다.

방법: 2008 년부터 2011 년까지 응급실로 내원한 19 세 이상의 성인 출혈성 뇌졸중 환자 중 살아서 입원한 환자를 대상으로 분석하였고, 증상발생부터 응급실 도착까지 3 시간 이상 소요되었거나 병원간 이송 전에 혈전용해제 투여 혹은 개두술을 받은 경우, 혹은 병원 도착 전 심정지가 발생한 경우 및 응급의료서비스 이용여부 및 병원결과에 대하여 알 수 없는 환자들은 분석에서 제외하였다. 독립변수는 응급의료서비스의 이용으로 설정하였고, 1 차결과는 생존 퇴원과, 뇌졸중 발생 전과 후 3 이상의 수정 Rankin 장애척도 (mRS)의 차이로 설정하였다. 인구통계학적 혹은 사회경제적 상태, 임상적 수치, 이환율, 습관, 발생과 같은 예상되는 교란변수를 보정하여 결과값의 보정된 오즈비 (adjusted odds ratio)와 95% 신뢰구간 (confidence interval)이 계산되었고 최종 분석모형에서는 환자를 병원간 전원 여부 및 증상발생부터 응급실 도착까지의 시간에 따라 층화분석하였다. 120 분을 기준으로 짧은 응급실 체류시간 긴 응급실 체류기간이 마지막 상호작용모형에 추가되었다.

결과: 총 2,095 명의 출혈성 뇌졸중 환자를 분석하였고, 그 중 75.6%가 응급의료서비스를 이용하였다. 17.4%가 사망하였고, 41.4%가 수정 Rankin 장애척도의 악화를 보였다. 응급의료서비스를

이용한 환자는 그렇지 않은 환자에 비하여 사망률이 0.67 배로 낮았고, (보정된 오즈비 0.67, 95% 신뢰구간 0.51-0.89), mRS 의 악화는 0.74 배로 낮았다. (보정된 오즈비 0.74, 95% 신뢰구간 0.59-0.92) 응급의료서비스의 이용에 따른 효과의 크기는 응급실 체류시간에 따라 차이를 보였다. 2 시간이내로 응급실 체류한 환자들의 사망에 대한 보정된 오즈비는 0.74, 95% 신뢰구간은 0.54-1.01 이었고, 2 시간 이상 체류한 환자들의 사망에 대한 보정된 오즈비는 0.60, 95% 신뢰구간은 0.44-0.83 이었다. mRS 의 악화에 대한 보정된 오즈비와 신뢰구간은 2 시간 이내 체류환자에서 0.76 (0.60-0.97), 2 시간 이상 체류환자에서 0.68 (0.52-0.88) 이었다.

결론: 결론적으로 응급의료서비스의 이용은 급성 출혈성 뇌졸중에서 낮은 사망율과 장애율과 연관을 보였다. 이런 효과의 크기는 응급실 체류시간이 긴 환자들에서 더 유의한 차이를 보였다.

주요어 : 응급의료서비스, 출혈성 뇌졸중, 사망율, 장애율

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