Outcomes in Acute Ischemic Stroke Patients Undergoing Air Versus Ground Interhospital Transport in Suburban and Rural Areas: A Comparative Study

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ABSTRACT

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Background and Purpose: Rapid transport is crucial for effective treatment of acute ischemic stroke patients, particularly given the 4.5-hour window for thrombolytic therapy administration. This study aimed to compare treatment outcomes between helicopter emergency medical services (HEMS) and ground emergency medical services (GEMS) for interhospital transfer in suburban and rural areas.

Methods: The study included 182 patients (91 HEMS, 91 GEMS) matched by propensity score, who were transferred to a tertiary care center in a rural area between July 2013 and June 2021. We analyzed rates of thrombolytic therapy, thrombectomy, neurological outcomes (NIHSS, mRS), transport times, and hospital stay durations. A subgroup analysis was performed for patients arriving at the first hospital within 2 hours of symptom onset.

Results: The HEMS group showed significantly shorter "door-in-door-out" time (60 vs. 83 minutes, p=0.004), interhospital transfer time (39 vs. 51 minutes, p=0.000), and symptom onset to receiving hospital arrival time (204 vs. 289 minutes, p=0.02). While rates of thrombolytic therapy (15.4% vs. 11.0%) and thrombectomy (11.0% vs. 5.5%) were higher in the HEMS group, these differences were not statistically significant. The main reason for not administering thrombolytic therapy was exceeding the 4.5-hour time limit, which occurred more frequently in the GEMS group (72.8% vs. 42.9%, p=0.0001). There were no significant differences in NIHSS score changes (GEMS 1.38±5.83 vs. HEMS 1.89±7.66, p=0.27), mRS score changes (GEMS 0.34±1.12 vs. HEMS 0.52±1.27, p=0.61), or mortality rates (4.4% in both groups, p=1.000).

Conclusions: While HEMS significantly reduced transport times and enabled more patients to arrive within the therapeutic window, these temporal advantages did not necessarily translate to better clinical outcomes. This may be attributed to potentially higher initial severity in the HEMS group, treatment limitations due to various contraindications for thrombolytic therapy, and the study's limited sample size. Future large-scale prospective studies are needed to clearly determine the effectiveness of HEMS and establish patient selection criteria for optimal air transport utilization.

Key words: Acute ischemic stroke, Helicopter emergency medical services, Ground emergency medical services, Thrombolytic therapy, Thrombectomy, Neurological outcome

1. Introduction

According to the Global Burden of Disease, Injuries, and Risk Factors Study, stroke is largely preventable and its incidence has been decreasing globally. However, as of 2019, stroke still remains the third leading cause of disability and death worldwide[1]. In South Korea, stroke was the second most common cause of death after cancer in 2015[2]. According to a 2018 report by the Epidemiologic Research Committee of the Korean Stroke Society, cerebrovascular diseases accounted for 29.6 deaths per 100,000 population, with ischemic stroke causing 9.1 deaths per 100,000 population[3].

When a cerebral blood vessel is obstructed, blood flow is interrupted, leading to ischemic damage to brain cells. Therefore, the primary goal of acute ischemic stroke treatment is to promptly restore blood flow by minimizing the time from symptom onset to diagnosis and treatment. In particular, recombinant tissue plasminogen activator (rtPA) must be administered within 4.5 hours of symptom onset in patients with ischemic stroke[4, 5], making rapid transport during the pre-hospital phase critically important. There is a previous study indicating that for every 1-minute delay in transport, the likelihood of receiving intra-arterial thrombolytic therapy decreases by 2.5%[6]. However, according to the 2018 Stroke Statistics in Korea by J.Y. Kim and colleagues, the average time from symptom onset to hospital arrival for stroke patients in Korea was 6.2 hours, which is longer than the 2.8 hours reported in the United States. Furthermore, only 10.7% of all patients were eligible for tPA treatment[3].

To facilitate the timely administration of thrombolytic therapy or when appropriate treatment is not available at a primary hospital, helicopter emergency medical services (HEMS) may be utilized to transfer stroke patients to a stroke center[6]. Several studies have reported advantages of air transport. For instance, it has been shown that 96.4% of acute ischemic stroke patients transported by air arrive at the final hospital within two hours[7], and the use of interhospital air transport has been associated with increased rates of thrombolytic therapy administration[8]. Additionally, a domestic study comparing the outcomes of ischemic stroke patients transported by air and by ground found that air transport was associated with shorter hospital stays and reduced mortality rates[9]. However, there are also numerous studies that do not support these findings. For example, in a study conducted by Funder K.S. et al., which compared the outcomes of stroke unit patients transported by physician-staffed helicopters versus those transported by ground, the cumulative mortality rate was similar between the two groups, with 9.04 deaths per 100 patients in the ground transport group and 9.71 deaths per 100 patients in the air transport group[10]. Moreover, a study conducted in Denmark reported that the "door to needle time," which refers to the time from emergency department arrival to tPA(tissue plasminogen activator) administration, was actually faster in the ground transport group, with no significant differences in neurological outcomes or short- and longterm mortality between the air and ground transport groups[11]. Consequently, the debate remains as to whether air transport for acute ischemic stroke patients contributes to better outcomes, with potential differences influenced by regional variations in HEMS operations or transport protocols.

There has been one report in Korea suggesting that air transport reduces mortality in acute ischemic stroke patients. However, no study has yet analyzed the factors that may influence patient outcomes during air transport in stroke patients. Therefore, this study aims to compare the rates of thrombolytic therapy administration and neurological outcomes between acute ischemic stroke patients undergoing air versus ground transport for interhospital transfer and to identify the factors that may affect these outcomes.

2. Methods

This study was conducted at a single tertiary medical institution located in a rural area, focusing on patients who visited the emergency center via interhospital transfer due to acute ischemic stroke. The study period spanned from July 2013 to June 2021, and it was a retrospective observational study that divided patients into two groups based on the mode of transport: air transport and ground transport. The composition of personnel responsible for interhospital transport differs between transport methods. For interhospital air transport, the HEMS team consists of two medical personnel: one emergency medicine specialist and one paramedic or nurse. In contrast, interhospital ground transport is primarily handled by either hospital ambulances or private transport services, with patient care during transport typically managed by a single paramedic or nurse.

The inclusion criteria for this study were patients aged 18 years or older who were diagnosed with acute ischemic stroke, classified under ICD-I63, and were transferred between hospitals using either air or ground transport. To reflect the operating hours of air transport in Korea and the minimum distance required for air transport eligibility, only patients who were transferred from a referring hospital located more than 30 km from the emergency medical facility were included in the study. Additionally, only transfers that occurred during the operational hours of air transport, which is from sunrise to sunset, were considered. Exclusion criteria were as follows: patients who had more than 24 hours between the onset of neurological symptoms and hospital arrival, those diagnosed with transient ischemic attacks, cases where ICD-I63 was assigned due to sequelae rather than a diagnosis of acute ischemic stroke, insufficient medical records, and cases of stroke occurring within a medical facility. The analysis included demographic and clinical data such as age, sex, stroke risk factors, NIHSS (National Institutes of Health Stroke Scale), mRS (modified Rankin Scale), time of symptom onset, time of arrival at the referring hospital, time of arrival at the primary hospital, transport time, rates of thrombolytic therapy and thrombectomy. Neurological outcomes were measured using mRS and NIHSS, with a good neurological outcome defined as an mRS score of 2 or less. Data for air-transported patients were collected from the HEMS team's air transport records and hospital records (electronic medical records), while data for ground-transported patients were collected from hospital records (electronic medical records) and interhospital transfer records.

Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. To compare the GEMS(Ground emergency medical services) group and the HEMS group, normality and homogeneity of variance tests were performed on continuous variables. Based on these tests, either an independent samples t-test or Wilcoxon rank-sum test was conducted, as appropriate. For categorical variables, chi-square tests or Fisher's exact tests were used. All statistical analyses were conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). Propensity Score Matching was applied to the GEMS and HEMS groups, considering the variables 'Age', 'Sex', and 'Hospital'. The matching process was performed using the 'MatchIt' package version 4.5.5 in R version 4.3.1. Statistical significance was set at $P < 0.05$.

This study was approved by the Institutional Review Board of Yonsei University Wonju Severance Christian Hospital (CR323109), and informed consent was waived by the board due to the retrospective nature of the study.

3. Result

From July 2013 to June 2023, 351 patients who were diagnosed with cerebral infarction after interhospital transfer, either by air transport or ground transport, were included in the study. After excluding patients with diagnoses other than acute cerebral infarction, such as sequelae of cerebral infarction, and applying 1:1 propensity score matching based on age, sex, and hospital, a final total of 91 patients in the ground transport group and 91 patients in the air transport group were included in the analysis (Figure 1).

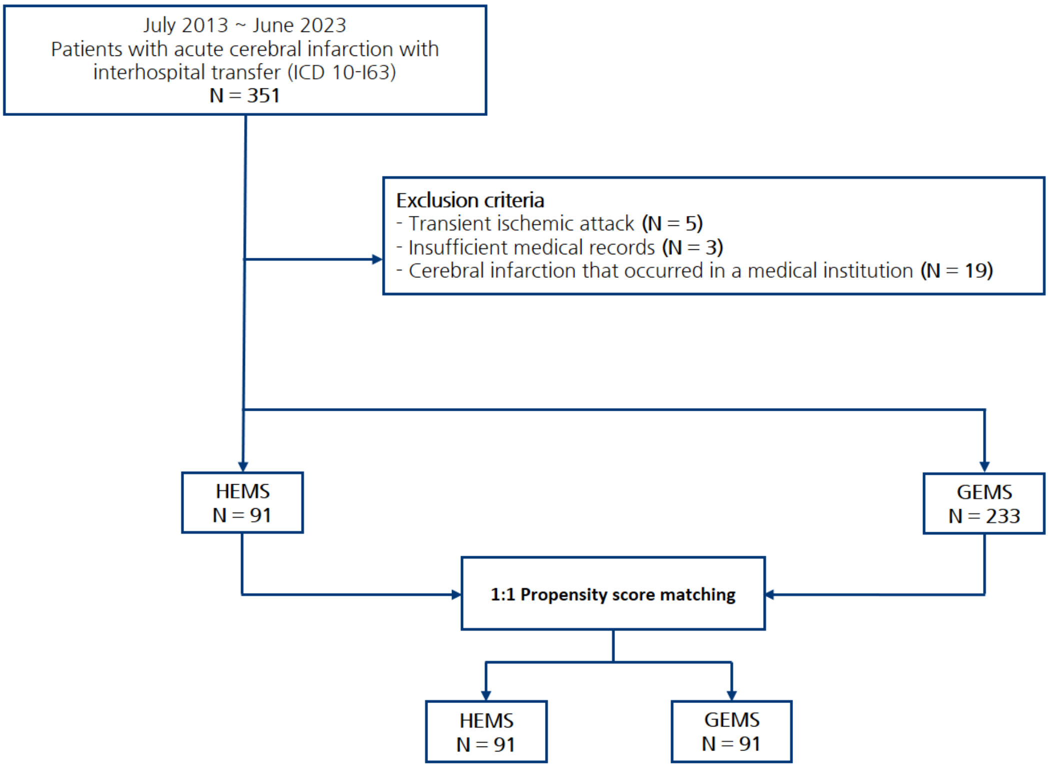

Figure 1. Flowchart of patients who met inclusion/exclusion criteria

Of the total patients, 102 (56%) were male, and the mean age was 71.91 years (±10.13). There were no significant differences between the HEMS and GEMS groups in terms of past medical history, including hypertension, diabetes, dyslipidemia, heart failure, ischemic heart disease, atrial fibrillation, history of stroke, and kidney disease. However, the percentage of current smokers was higher in the HEMS group at 29.7% compared to 15.4% in the GEMS group (p=0.02) (Table 1). In the ground transport group, there were no transfers from Taebaek Hospital and Chungju Medical Center, but the proportion of referral hospitals between the groups did not differ significantly, and the median transport distance was the same at 65 km for both groups (Table 2).

Table 2. Characteristics of patients in the GEMS and HEMS group after PSM

	GEMS (N=91)	HEMS (N=91)	All patients (N=182)	p-value
Sex				1.0000
Male	51 (56.0)	51 (56.0)	102 (56.0)	
Female	40 (44.0)	40 (44.0)	80 (44.0)	
Age	71.65 ± 9.24	72.16 ± 10.99	71.91 ± 10.13	0.5599
History				
Hypertension	50 (54.9)	61 (67.0)	111 (61.0)	0.0946
Diabetes mellitus	33 (36.3)	24 (26.4)	57 (31.3)	0.1503
Dyslipidemia	13 (14.3)	8 (8.8)	21 (11.5)	0.2460
Heart failure	6 (6.6)	3 (3.3)	9 (4.9)	0.4967
Ischemic heart disease	13 (14.3)	6 (6.6)	19 (10.4)	0.0897
Atrial fibrillation	12 (13.2)	9 (9.9)	21 (11.5)	0.4864
Stroke	17 (18.7)	25 (27.5)	42 (23.1)	0.1593
Current smoker	14 (15.4)	27 (29.7)	41 (22.5)	0.0211
Kidney disease	3 (3.3)	2 (2.2)	5 (2.7)	1.0000

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as *n* (%). GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM: Propensity Score Matching.

Table 3. Patient transfer rate by transfer request institution in the GEMS and HEMS group after PSM

	GEMS (N=91)	HEMS (N=91)	All patients (N=182)	p-value
Referral Hospital				
Jecheon Seoul Hospital	11 (12.1)	7 (7.7)	18 (9.9)	0.3206
Sokcho Medical Center	2 (2.2)	1 (1.1)	3 (1.6)	1.0000
Yeongwol Medical Center	27 (29.7)	29 (31.9)	56 (30.8)	0.7481
Gangneung Asan Hospital	3 (3.3)	1 (1.1)	4 (2.2)	0.6208
Konkuk University Chungju Hospital	4 (4.4)	3 (3.3)	7 (3.8)	1.0000
Icheon Medical Center	2 (2.2)	1 (1.1)	3 (1.6)	1.0000
Jeongseon Hospital	7 (7.7)	14 (15.4)	21 (11.5)	0.1044
Taebaek Hospital	0 (0.0)	2 (100.0)	2 (1.1)	0.4972
Myongji Hospital	27 (29.7)	20 (22.0)	47 (25.8)	0.2358
Yeongju RedCross Hospital	1 (1.1)	2 (2.2)	3 (1.6)	1.0000
Jeongseon County Hospital	2 (2.2)	4 (4.4)	6 (3.3)	0.6822
Chungju Medical Center	0 (0.0)	1 (100.0)	1 (0.5)	1.0000
Pyeongchang Medical Center	5 (5.5)	6 (6.6)	11 (6.0)	0.7558
Distance, km	67.9 ± 25.8	60.6 ± 18.8	64.3 ± 22.8	0.0352
Median [IQR]	65.0 [48.2-76.4]	65.0 [40.0-72.0]	65.0 [47.2-76.4]	

Continuous variables are presented as mean ± standard deviation along with median [IQR]. Categorical variables are presented as *n* (%). GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM: Propensity Score Matching.

The rate of tPA administration in acute ischemic stroke patients at both the referring hospitals and the receiving hospital was slightly higher in the HEMS group compared to the GEMS group, but the difference was not statistically significant. Similarly, the rate of thrombectomy was approximately twice as high in the HEMS group compared to the GEMS group (11.0% vs. 5.5%), although this difference was also not statistically significant. Among the reasons for not administering rtPA, failure to administer the drug within the 4.5-hour window was more common in the GEMS group with 59 cases (72.8%) compared to 33 cases (42.9%) in the HEMS group, and this difference was statistically significant (Table 3).

Table 2. Rates of rtPA administration and thrombectomy in the GEMS and HEMS group after PSM

	GEMS (N=91)	HEMS (N=91)	All patients (N=182)	p-value
rtPA use (referral hospital)	(N=89)	(N=91)	(N=180)	0.4448
Yes	6 (6.7)	9 (9.9)	15 (8.3)	
No	83 (93.3)	82 (90.1)	165 (91.7)	
rtPA use (receiving hospital)				0.3809
Yes	10 (11.0)	14 (15.4)	24 (13.2)	
No	81 (89.0)	77 (84.6)	158 (86.8)	
Reason for not rtPA use	(N=81)	(N=77)	(N=158)	
Cannot administer within 4.5 hours	59 (72.8)	33 (42.9)	92 (58.2)	0.0001
INR>1.7 or PT>15 second	1 (1.2)	1 (1.3)	2 (1.3)	1.0000
History of head trauma or ischemic stroke within 3 months	1 (1.2)	1 (1.3)	2 (1.3)	1.0000
Slight neurologic disorder	12 (14.8)	22 (28.6)	34 (21.5)	0.0354
Administration in former hospital	6 (7.4)	8 (10.4)	14 (8.9)	0.5097
Brain hemorrhage or Over 1/3 definite low density in brain hemi-sphere	2 (2.5)	8 (10.4)	10 (6.3)	0.0522
Anticoagulation within 48 hours	0 (0.0)	2 (2.6)	2 (1.3)	0.2359
Under 6 months life expectancy	0 (0.0)	1 (1.3)	1 (0.6)	0.4873
Over 80 years	0 (0.0)	1 (1.3)	1 (0.6)	0.4873
For ruling out other disease	0 (0.0)	0 (0.0)	0 (0.0)	-
Thrombectomy				0.1777
Yes	5 (5.5)	10 (11.0)	15 (8.2)	
No	86 (94.5)	81 (89.0)	167 (91.8)	

Categorical variables are presented as *n* (%). rtPA: recombinant tissue Plasminogen Activator. GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM: Propensity Score Matching. INR: Internatinal normalized ratio. PT: Prothrombin time.

The mean NIHSS score at admission was 8.34 (±7.85) in the GEMS group and 9.68 (±7.86) in the HEMS group. At discharge, the mean NIHSS score was 5.67 (±8.16) in the GEMS group and 6.79 (±9.37) in the HEMS group. Although the NIHSS Difference, which compares the NIHSS scores at admission and discharge, showed a greater decrease in the HEMS group compared to the GEMS group, this difference was not statistically significant. There were no significant differences between the groups in terms of mRS scores at admission and discharge, mRS Difference (GEMS 0.34±1.12, HEMS 0.52±1.27, p=0.61), or mortality rates (Table 4).

Table 4. Neurologic outcome and mortality in the GEMS and HEMS group after PSM

	GEMS (N=91)	HEMS (N=91)	All patients (N=182)	p-value
NIHSS (admission)	8.34 ± 7.85	9.68 ± 7.86	9.01 ± 7.86	0.1395
NIHSS (discharge)	5.67 ± 8.16 (N=61)	6.79 ± 9.37 (N=72)	6.28 ± 8.82 (N=133)	0.4645
NIHSS Difference (admission-discharge)	1.38 ± 5.83 (N=61)	1.89 ± 7.66 (N=72)	1.65 ± 6.86 (N=133)	0.2668
mRS (admission)	3.41 ± 1.43	3.67 ± 1.44	3.54 ± 1.44	0.1654
≤ 2	28 (30.8)	19 (20.9)	47 (25.8)	0.1274
> 2	63 (69.2)	72 (79.1)	135 (74.2)	
mRS (discharge)	3.07 ± 1.69	3.15 ± 1.73	3.11 ± 1.70	0.6900
≤ 2	41 (45.1)	35 (38.5)	76 (41.8)	0.3671
> 2	50 (54.9)	56 (61.5)	106 (58.2)	
mRS Difference (admission-discharge)	0.34 ± 1.12	0.52 ± 1.27	0.43 ± 1.20	0.6127
Death (discharge)	4 (4.4)	4 (4.4)	8 (4.4)	1.0000

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as *n* (%). GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM: Propensity Score Matching. NIHSS: National Institute of Health Stroke Scale. mRS: modified Rankin Score.

"Door in Door out" refers to the time a patient spends in the emergency department at the referring hospital, from the time of arrival until the time of departure. The median [interquartile range] for the GEMS group was 83 minutes [67.0-122.0], while it was 60 minutes [43.0-83.2] for the HEMS group, indicating that the HEMS group had a shorter time by approximately 20 minutes (p=0.004). The median interhospital transport time was 51 minutes [43.0-63.0] for the GEMS group and 39 minutes [32.0-48.0] for the HEMS group (p=0.000). Similarly, the median time from symptom onset to arrival at the receiving hospital's emergency department was 289 minutes [185.0-534.0] for the GEMS group and 204.0 minutes [143.0-303.0] for the HEMS group, showing that the HEMS group was approximately 85 minutes faster (p=0.02).

"Onset to injection," which represents the time from symptom onset to tPA administration, showed no significant difference between the two groups at both the referring and receiving hospitals.

"Onset to groin," the time from symptom onset to the start of thrombectomy, was shorter in the HEMS group at 313 minutes [235-340] compared to 410 minutes [405.0-500.0] in the GEMS group, with a difference of about 97 minutes (p=0.02). Additionally, the time from arrival at the receiving hospital's emergency department to the start of thrombectomy, referred to as "ED to groin," was significantly shorter in the HEMS group at 111 minutes [92.0-159.0] compared to 262 minutes [251.0-284.0] in the GEMS group (p=0.01) (Table 5). Moreover, when analyzing only the patients who received rtPA at the receiving hospital and comparing the "ED to groin" time, the median [interquartile range] was 273 minutes [256.5-328.0] for the GEMS group and 102 minutes [92.5-162.5] for the HEMS group, indicating that the HEMS group started thrombectomy approximately 2 hours and 50 minutes earlier (p=0.03) (Table S1).

Table 5. Time based on events in the GEMS and HEMS group after PSM

		GEMS (N=91)	HEMS (N=91)	All patients (N=182)	p-value
Door in Door out	N	31	43	74	
	Median [IQR]	83.0 [67.0-122.0]	60.0 [43.0-82.0]	68.0 [52.0-91.0]	0.0046
Transfer time	N	31	43	74	
	Median [IQR]	51.0 [43.0-63.0]	39.0 [32.0-48.0]	44.5 [35.0-59.0]	0.0004
Onset to ED (referral hospital)	N	39	54	93	
	Median [IQR]	169.0 [49.0-447.0]	98.5 [47.0-194.0]	108.0 [47.0-236.0]	0.2540
Onset to ED (receiving hospital)	N	91	91	182	
	Median [IQR]	289.0 [185.0-534.0]	204.0 [143.0-303.0]	243.0 [153.0-416.0]	0.0046
Onset to injection (referral hospital)	N	5	9	14	
	Median [IQR]	120.0 [80.0-147.0]	150.0 [123.0-200.0]	141.0 [93.0-176.0]	0.2033
Onset to injection (receiving hospital)	N	10	14	24	
	Median [IQR]	212.5 [180.0-268.0]	170.0 [165.0-190.0]	182.5 [167.0-241.5]	0.1968
Onset to groin (receiving hospital)	N	5	9	14	
	Median [IQR]	410.0 [405.0-500.0]	313.0 [235.0-340.0]	342.5 [277.0-410.0]	0.0233
ED to injection (receiving hospital)	N	10	14	24	
	Median [IQR]	41.0 [35.0-52.0]	40.5 [27.0-50.0]	41.0 [34.0-51.0]	0.4611
ED to groin (receiving hospital)	N	5	9	14	
	Median [IQR]	262.0 [251.0-284.0]	111.0 [92.0-159.0]	148.5 [93.0-251.0]	0.0164

Continuous variables are presented as median [IQR] along with the number of observed values. GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM: Propensity Score Matching. ED: Emergency Department.

A subgroup analysis was conducted on patients who arrived at the first hospital within 2 hours from symptom onset. A total of 50 patients were included in the analysis, with 18 in the GEMS group and 32 in the HEMS group. Among all patients, 29 (58%) were male, and the mean age was 71.78 (± 8.78) years. There were no significant differences in past medical history or transport distance between the two groups (Tables 6, 7). There were also no differences in the rates of rtPA administration and thrombectomy between the two groups. However, among the reasons for not administering rtPA, failure to administer within the 4.5-hour window occurred in 4 cases (30.8%) in the GEMS group compared to 1 case (4.0%) in the HEMS group (p=0.03) (Table 6).

To compare neurological outcomes between the GEMS and HEMS groups, the mean NIHSS and mRS scores at admission and discharge were examined, but no significant differences were found between the groups (Table 7). The "Door in Door out" time was 86 minutes [77.0-126.0] in the GEMS group and 62 minutes [43.0-82.0] in the HEMS group, indicating that the HEMS group was faster (p=0.01). However, the transport time was about 10 minutes longer in the HEMS group (p=0.009). The "Onset to groin" time, which reflects the time from symptom onset to the start of thrombectomy, was 405 minutes [370.0-410.0] in the GEMS group and 256 minutes [220.0-313.0] in the HEMS group, showing that thrombectomy was performed more quickly in the HEMS group (p=0.005). Similarly, the "ED to groin" time was also shorter in the HEMS group compared to the GEMS group (GEMS vs HEMS group; 251 [134.0-262.0] vs 102 [92.0-138.0], p=0.01) (Table 8).

Table 6. Rate of rtPA administration and thrombectomy visits within 2 hours of symptom onset in the GEMS and HEMS groups after PSM.

	GEMS (N=18)	HEMS (N=32)	All patients (N=50)	p-value
rtPA use (referral hospital)				0.4945
Yes	5 (27.8)	6 (18.8)	11 (22.0)	
No	13 (72.2)	26 (81.2)	39 (78.0)	
rtPA use (receiving hospital)				0.7349
Yes	5 (27.8)	7 (21.9)	12 (24.0)	
No	13 (72.2)	25 (78.1)	38 (76.0)	
Reason for not rtPA use	(N=13)	(N=25)	(N=38)	
Cannot administer within 4.5 hours	4 (30.8)	1 (4.0)	5 (13.2)	0.0382
INR>1.7 or PT>15 second	1 (7.7)	0 (0.0)	1 (2.6)	0.3421
History of head trauma or ischemic stroke within 3 months	0 (0.0)	1 (4.0)	1 (2.6)	1.0000
Slight neurologic disorder	3 (23.1)	9 (36.0)	12 (31.6)	0.4859
Administration in former hospital	5 (38.5)	6 (24.0)	11 (28.9)	0.4573
Brain hemorrhage or Over 1/3 Definite low density in brain hemisphere	0 (0.0)	6 (24.0)	6 (15.8)	0.0764
Anticoagulation within 48 hours	0 (0.0)	0 (0.0)	0 (0.0)	-
Under 6 months life expectancy	0 (0.0)	1 (4.0)	1 (2.6)	1.0000
Over 80 years	0 (0.0)	1 (4.0)	1 (2.6)	1.0000
For ruling out other disease	0 (0.0)	0 (0.0)	0 (0.0)	-
Thrombectomy				1.0000
Yes	3 (16.7)	6 (18.8)	9 (18.0)	
No	15 (83.3)	26 (81.2)	41 (82.0)	

Categorical variables are presented as *n* (%). rtPA: recombinant tissue Plasminogen Activator. GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM, Propensity Score Matching. INR: Internatinal normalized ratio. PT: Prothrombin time.

Table 7. Neurologic outcome and mortality in patients visiting within 2 hours of symptom onset in the GEMS and HEMS groups after PSM.

	GEMS (N=18)	HEMS (N=32)	All patients (N=50)	p-value
NIHSS (admission)	10.50 ± 9.00	10.91 ± 8.67	10.76 ± 8.71	0.8474
NIHSS (discharge)	7.00 ± 7.19 (N=14)	4.83 ± 6.55 (N=23)	5.65 ± 6.78 (N=37)	0.2497
NIHSS Difference (admission-discharge)	3.36 ± 6.37 (N=14)	4.09 ± 6.14 (N=23)	3.81 ± 6.15 (N=37)	0.4027
mRS (admission)	3.89 ± 1.13	3.88 ± 1.45	3.88 ± 1.33	0.6382
≤ 2	2 (11.1)	6 (18.8)	8 (16.0)	0.6939
> 2	16 (88.9)	26 (81.2)	42 (84.0)	
mRS (discharge)	3.50 ± 1.58	3.25 ± 1.76	3.34 ± 1.69	0.6189
≤ 2	6 (33.3)	11 (34.4)	17 (34.0)	0.9405
> 2	12 (66.7)	21 (65.6)	33 (66.0)	
mRS Difference (admission-discharge)	0.39 ± 1.24	0.63 ± 1.41	0.54 ± 1.34	0.5562
Death (discharge)	1 (5.6)	1 (3.1)	2 (4.0)	1.0000

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as *n* (%). GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM, Propensity Score Matching. NIHSS: National Institute of Health Stroke Scale. mRS: modified Rankin Score.

Table 8. Time to event those who visited within 2 hours of symptom onset in the GEMS and HEMS groups after PSM.

		GEMS (N=18)	HEMS (N=32)	All patients (N=50)	p-value
Door in Door out	N	13	25	38	
	Median [IQR]	86.0 [77.0-126.0]	62.0 [43.0-82.0]	73.0 [45.0-102.0]	0.0111
Transfer time	N	13	25	38	
	Median [IQR]	51.0 [44.0-63.0]	39.0 [30.0-47.0]	43.5 [35.0-55.0]	0.0097
Onset to ED (referral hospital)	N	18	32	50	
	Median [IQR]	46.0 [25.0-62.0]	50.5 [31.5-85.5]	48.5 [29.0-80.0]	0.1447
Onset to ED (receiving hospital)	N	18	32	50	
	Median [IQR]	191.5 [151.0-271.0]	173.0 [139.5-205.5]	181.0 [141.0-216.0]	0.0955
Onset to injection (referral hospital)	N	4	6	10	
	Median [IQR]	113.5 [55.0-161.5]	136.5 [93.0-167.0]	135.0 [80.0-167.0]	0.5033
Onset to injection (receiving hospital)	N	5	7	12	
	Median [IQR]	180.0 [180.0-240.0]	188.0 [170.0-190.0]	184.0 [170.0-215.0]	0.4041
Onset to groin (receiving hospital)	N	3	6	9	
	Median [IQR]	405.0 [370.0-410.0]	256.0 [220.0-313.0]	313.0 [235.0-370.0]	0.0050
ED to injection (receiving hospital)	N	5	7	12	
	Median [IQR]	41.0 [36.0-49.0]	41.0 [25.0-45.0]	41.0 [29.5-47.0]	0.3331
ED to groin (receiving hospital)	N	3	6	9	
	Median [IQR]	251.0 [134.0-262.0]	102.0 [92.0-138.0]	134.0 [93.0-159.0]	0.0151

Continuous variables are presented as median [IQR] along with the number of observed values. GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. PSM, Propensity Score Matching. ED: Emergency Department.

4. Discussion

This study compared the rates of thrombolytic therapy (tPA) administration, thrombectomy, and neurological outcomes between helicopter emergency medical services (HEMS) and ground emergency medical services (GEMS) for interhospital transport of acute ischemic stroke patients. Results demonstrated that air transport significantly reduced time to arrival at the definitive treatment hospital for acute ischemic stroke patients, as well as the in-hospital time to tPA administration and thrombectomy. Although tPA administration and thrombectomy rates were somewhat higher in the HEMS group compared to the GEMS group, the difference was not statistically significant. Similarly, no statistically significant differences were observed in neurological outcomes and mortality rates between the HEMS and GEMS groups, including among patients who arrived at the referring hospital within two hours of symptom onset. In acute ischemic stroke, timely administration of thrombolytics like tPA and performing thrombectomy are critical to enhancing neurological recovery[4, 5]. One of the most crucial aspects of treating ischemic stroke is minimizing brain injury through prompt reperfusion following symptom onset. Although this study did not show statistically significant differences, the higher rates of tPA administration and thrombectomy observed in the HEMS group provide clinically relevant insights, suggesting that the time advantage associated with HEMS could be beneficial. Previous literature supports these findings; for instance, Funder et al. (2017) reported that HEMS reduces transport time, facilitating faster treatment for acute stroke patients[10]. Additionally, a South Korean study by Lee et al. (2020) noted that HEMS could reduce time to hospital arrival, potentially decreasing patient mortality rates[9]. Air transport offers the advantage of quickly transferring patients over greater distances, which may be especially beneficial in remote or geographically challenging regions where access to medical care is limited.

This study did not identify statistically significant differences in revascularization outcomes between the HEMS and GEMS groups, despite differences in transport modes. Diaz et al. (2005) suggested that although helicopter transport might reduce prehospital time, delays within the hospital could offset the time gained during transport. Regenhardt et al. (2018) also reported that air transport does not always correlate with improved clinical outcomes, indicating that transport mode alone does not guarantee a better prognosis[12, 13]. The results of this study may be explained by several factors. First, although tPA administration and thrombectomy rates were higher in the HEMS group, the differences were not statistically significant, potentially due to variations in the severity of cases between groups. The NIHSS score, a measure of stroke severity, was slightly higher on average in the HEMS group (9.68) than in the GEMS group (8.34), although not statistically significant. Since HEMS is typically employed for more severe cases, the HEMS group may have included patients in more critical conditions, impacting the observed treatment outcomes. As reported by Regenhardt et al. (2018), the quality of in-hospital care may affect outcomes more than transport time for patients with higher stroke severity[12]. The higher NIHSS score in the HEMS group may have contributed to the lack of substantial differences in neurological outcomes between the two groups. Secondly, among the transported patients, the number of those eligible for definitive treatment was limited due to contraindications for thrombolytic therapy. Even though a relatively higher number of patients in the HEMS group arrived within the treatment window, the overall rate of tPA administration or thrombectomy post-transport was approximately 15%. Moreover, a notable 42.9% of patients arrived after the 4.5-hour window for tPA administration, while others had contraindications such as mild neurological deficits or intracerebral hemorrhage, accounting for about 10.4% each (Table 3). The higher frequency of contraindications, especially among patients transported by HEMS, suggests that faster transport may not translate to clinical benefit if contraindications restrict therapeutic intervention. This finding highlights the need for selective HEMS use based on eligibility for tPA and other treatments. Utilizing HEMS for patients with contraindications might lead to inefficiencies, as it involves considerable resource expenditure compared to GEMS[14]. Chalela et al. (1999) reported that while air transport is generally safe post-tPA, contraindications can limit its benefits. Additionally, a significant number of patients transported for mechanical thrombectomy may ultimately be diagnosed with conditions other than true ischemic stroke[15, 16]. If the use of HEMS does not significantly improve outcomes for patient ineligible for tPA, careful selection of candidates for HEMS transport may be warranted. Conroy et al. (1999) recommended implementing remote telemedicine protocols and prehospital screening systems to minimize treatment delays and improve candidate selection, while Tal et al. suggested that HEMS should be selectively utilized where specific advantages are evident[14, 17]. In other words, efficient preselection of patients eligible for thrombolytic therapy and their strategic routing to specialized centers is essential for improving outcomes[8]. Thirdly, the limitations of this study's sample, which included only interhospital transfers and not initial scene transports, may have contributed to the lack of significant differences in outcomes between the two groups. Prabhakaran et al. (2011) noted that interfacility transfers could introduce additional delays, potentially impacting patients who require time-sensitive interventions[6]. Lastly, the lack of differences in outcomes may be due to the limited sample size. The statistical power of this study may not have been sufficient to detect differences between the HEMS and GEMS groups. Larger-scale studies are necessary to determine whether HEMS significantly impacts tPA and thrombectomy rates, offering a clearer understanding of HEMS's role in stroke transport.

The lack of significant differences in neurological outcomes and mortality between the HEMS and GEMS groups is particularly notable. Despite the critical importance of time in the treatment of acute ischemic stroke, patients transported by HEMS did not demonstrate better outcomes than those transported by ground, which may be attributable to several factors. Previous studies suggest that regional characteristics or hospital protocols may account for such results. For example, even if patients arrive faster via HEMS, delays in administering tPA or performing thrombectomy within the hospital could influence outcomes, regardless of transport mode. Funder et al. (2017) reported that in some cases, patients transported by GEMS had a shorter time to tPA administration after hospital arrival than those transported by HEMS, emphasizing that shorter transport times do not always translate to improved outcomes[10]. However, since the in-hospital care processes in the HEMS group were conducted more swiftly in this study, it is difficult to conclude that differences in hospital protocols significantly influenced outcomes. In fact, our findings indicate that not only was the overall transport time shorter for the HEMS group, but the 'door-in-door-out' time, 'onset-to-injection' time, and 'onset-to-groin' time were all significantly reduced in the HEMS group as well. Similarly, a Danish study reported that the DIDO time and initiation of thrombectomy were faster for the HEMS group than for the GEMS group. The authors attributed this to pre-arrival coordination and dispatch that allowed hospital teams to activate stroke protocols promptly[11]. A similar mechanism may have been at play in our study as well, though further research is needed to verify the specific in-hospital care processes. Despite faster transport and expedited post-transfer care in the HEMS group, several factors may explain the lack of significant differences in outcomes between the HEMS and GEMS groups. First, HEMS patients receiving tPA or undergoing thrombectomy may have had higher initial severity of illness. Second, it is possible that HEMS patients who ultimately received definitive treatment might have shown better outcomes, but this could not be confirmed in the current study due to the absence of subgroup analysis for these patients. Future research focusing on patients who received definitive care could further clarify the impact of HEMS on outcomes in this population.

This study was designed as a retrospective observational analysis, and several limitations stem from this approach. First, as patients were not randomly assigned to HEMS or GEMS, there may be an inherent selection bias, with the choice of transport potentially influenced by the patient's initial condition. In this study, we restricted the subjects to inter-hospital transfers and aimed to standardize transport distances between the two groups as much as possible to reduce heterogeneity. However, the factors mentioned above may still act as confounding factors when interpreting differences in outcomes between the two groups. Future studies employing randomized controlled trials would be beneficial to minimize these biases and produce clearer conclusions. Florez-Perdomo et al. (2022) also highlighted in a systematic review that multiple critical variables impact patient transfer, emphasizing the need for multi-center, prospective studies that incorporate various contextual factors[18]. Second, this study did not account for the qualitative differences in medical care provided during transport. Olson et al. (2012) found that the quality of care administered by HEMS personnel could significantly influence neurological outcomes[19]. In Korea, HEMS teams are frequently staffed by emergency medicine specialists, offering higher levels of care during transit, whereas GEMS teams often consist of paramedics or nurses. Assessing the impact of different transport team compositions on treatment outcomes is crucial. Additionally, evaluating how in-transit care affects subsequent in-hospital treatment outcomes is an important area for future research. Finally, the study's relatively small sample size limits the statistical power to detect significant differences between groups. Larger-scale studies with greater sample sizes are necessary to provide a more precise understanding of treatment outcomes between HEMS and GEMS, enabling a more robust assessment of the clinical efficacy of each transport modality.

This study provides valuable insights into the potential role of Helicopter Emergency Medical Services (HEMS) in inter-hospital transfers for acute ischemic stroke patients. HEMS currently facilitates acute stroke care for approximately 20% of the U.S. population, and in our study, more than half of the patients transported received thrombolytic therapy following air transfer. Although there were no statistically significant differences in tPA administration rates and thrombectomy rates between the HEMS and Ground Emergency Medical Services (GEMS) groups, HEMS's ability to enable more timely therapeutic intervention holds clinical significance. In settings like Korea, where access to medical resources varies greatly between regions, HEMS can play a particularly essential role. In geographically isolated or underserved regions with limited hospital accessibility, HEMS may be critical for providing prompt reperfusion therapy, thereby improving neurological outcomes through optimal patient selection for air transfer. Future studies should aim to clarify therapeutic differences between HEMS and GEMS, with further assessment of patient selection criteria and the operational efficiency of HEMS across diverse regional settings. This evidence could inform policy recommendations to maximize HEMS's contribution within the Korean emergency medical system.

Appendices

Table S1. Characteristics of rtPA patients in the GEMS and HEMS group after PSM

		GEMS (N=10)	HEMS (N=14)	All patients (N=24)	*p-value*
Door in Door out	N	2	7	9	0.0972
	Median [IQR]	88.5 [86.0-91.0]	43.0 [23.0-66.0]	44.0 [41.0-86.0]	
Transfer time	N	2	7	9	0.5435
	Median [IQR]	65.5 [40.0-91.0]	43.0 [40.0-47.0]	43.0 [40.0-47.0]	
Onset to ED (referral hospital)	N	5	8	13	0.1069
	Median [IQR]	34.0 [31.0-49.0]	53.5 [41.5-79.0]	49.0 [34.0-59.0]	
Onset to ED (receiving hospital)	N	10	14	24	0.2185
	Median [IQR]	166.5 [128.0-216.0]	136.5 [127.0-152.0]	141.5 [127.5-193.5]	
Onset to injection (receiving hospital)	N	10	14	24	0.1968
	Median [IQR]	212.5 [180.0-268.0]	170.0 [165.0-190.0]	182.5 [167.0-241.5]	
Onset to groin (receiving hospital)	N	4	4	8	0.0061
	Median [IQR]	455.0 [390.0-500.0]	274.0 [227.5-316.5]	345.0 [274.0-455.0]	
ED to injection (receiving hospital)	N	10	14	24	0.4611
	Median [IQR]	41.0 [35.0-52.0]	40.5 [27.0-50.0]	41.0 [34.0-51.0]	
ED to groin (receiving hospital)	N	4	4	8	0.0304
	Median [IQR]	273.0 [256.5-328.0]	102.0 [92.5-162.5]	232.5 [102.0-273.0]	

Continuous variables are presented as median [IQR] along with the number of observed values. rtPA: recombinant tissue Plasminogen Activator. GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. ED: Emergency Department.

Table S2. Characteristics of patients visited within 2 hours from onset in the GEMS and HEMS group after PSM.

	GEMS (N=18)	HEMS (N=32)	All patients (N=50)	p-value
Sex				0.7928
Male	10 (55.6)	19 (59.4)	29 (58.0)	
Female	8 (44.4)	13 (40.6)	21 (42.0)	
Age	72.17 ± 8.96	71.56 ± 8.81	71.78 ± 8.78	0.7691
History				
Hypertension	10 (55.6)	24 (75.0)	34 (68.0)	0.1571
Diabetes Mellitus	7 (38.9)	10 (31.3)	17 (34.0)	0.5842
Dyslipidemia	3 (16.7)	4 (12.5)	7 (14.0)	0.6915
Heart failure	0 (0.0)	0 (0.0)	0 (0.0)	-
Ischemic heart disease	2 (11.1)	3 (9.4)	5 (10.0)	1.0000
Atrial fibrillation	2 (11.1)	2 (6.3)	4 (8.0)	0.6123
Stroke	6 (33.3)	6 (18.8)	12 (24.0)	0.3088
Current smoker	4 (22.2)	10 (31.3)	14 (28.0)	0.4950
Kidney disease	0 (0.0)	2 (6.3)	2 (4.0)	0.5298

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as *n* (%). GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. ED: Emergency Department.

Table S3. Percentage of patient transfers by transport requesting hospital visited within 2 hours of symptom onset in the GEMS and HEMS groups after PSM.

	GEMS (N=18)	HEMS (N=32)	All patients (N=50)	p-value
Hospital				
Jecheon Seoul Hospital	3 (16.7)	5 (15.6)	8 (16.0)	1.0000
Sokcho Medical Center	1 (5.6)	0 (0.0)	1 (2.0)	0.3600
Yeongwol Medical Center	2 (11.1)	8 (25.0)	10 (20.0)	0.2947
Gangneung Asan Hospital	2 (11.1)	1 (3.1)	3 (6.0)	0.2914
Konkuk University Chungju Hospital	1 (5.6)	3 (9.4)	4 (8.0)	1.0000
Jeongseon Hospital	1 (5.6)	4 (12.5)	5 (10.0)	0.6418
Taebaek Hospital	0 (0.0)	1 (3.1)	1 (2.0)	1.0000
Myongji Hospital	8 (44.4)	8 (25.0)	16 (32.0)	0.1571
Yeongju RedCross Hospital	0 (0.0)	2 (6.3)	2 (4.0)	0.5298
Distance, km	69.97 ± 35.87	56.02 ± 17.75	60.32 ± 26.06	0.0811
Median [IQR]	48.2 [48.2-76.4]	52.5 [40.0-68.5]	48.2 [40.0-72.0]	

Continuous variables are presented as mean ± standard deviation along with median [IQR]. Categorical variables are presented as *n* (%). GEMS: Ground Emergency Medical Service. HEMS: Helicopter Emergency Medical Service. ED: Emergency Department.

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Abstract in Korean

교외 및 농촌 지역에서 급성 허혈성 뇌졸중 환자의 병원 간 이송 시 항공 이송과 지상 이송의 예후 비교

배경 및 목적: 급성 허혈성 뇌졸중 환자의 효과적인 치료를 위해서는 신속한 이송이 중요하다. 특히 증상 발현 후 4.5 시간 이내에 혈전용해제를 투여해야 하는 치료 특성상, 환자의 신속한 이송은 치료 성공률에 직접적인 영향을 미친다. 본 연구는 교외 및 농촌 지역에서 병원 간 이송 시 항공 이송과 지상 이송의 치료 결과와 예후를 비교 분석하고자 하였다.

방법: 2013 년 7 월부터 2021 년 6 월까지 도서산간 지역 3 차의료기관의 응급의료센터로 전원 된 급성 허혈성 뇌졸중 환자 중 성향 점수 매칭을 통해 선정된 182 명(항공 이송 91 명, 지상 이송 91 명)을 대상으로 하였다. 두 군의 혈전용해제 사용률, 혈전제거술 시행률, 신경학적 예후(NIHSS, mRS), 이송 시간을 비교 분석하였으며, 증상 발현 후 2 시간 이내 도착 환자군에 대한 하위 분석도 시행하였다.

결과: 항공 이송군에서 'Door in Door out' 시간(60 분 vs 83 분, p=0.004), 병원 간 이송 시간(39 분 vs 51 분, p=0.000), 증상 발현부터 수용 병원 도착까지의 시간(204 분 vs 289 분, p=0.02)이 모두 유의하게 단축되었다. 혈전용해제 사용률과 혈전제거술 시행률은 항공 이송군에서 각각 15.4%(vs 11.0%), 11.0%(vs 5.5%)로 더 높았으나 통계적 유의성은 없었다. 혈전용해제 투여 제한 사유 중 4.5 시간 초과는 지상 이송군(72.8%)이 항공 이송군(42.9%)보다 유의하게 높았다(p=0.0001).

결론: 항공 이송은 급성 허혈성 뇌졸중 환자의 병원 전 단계 및 병원 간 이송 시간을 유의하게 단축시키고, 더 많은 환자가 치료 적정 시간 내에 도착할 수 있게 하는 것으로 나타났다. 그러나 이러한 시간적 이점이 반드시 더 나은 임상 결과로 이어지지는 않았다. 이는 항공 이송군의 초기 중증도가 더 높았을 가능성, 혈전용해제의 다양한 금기증으로 인한 치료 제한, 그리고 연구의 제한된 표본 크기 등이 영향을 미쳤을 것으로 추정된다. 향후 항공 이송의 효과를 명확히 규명하기 위해서는 더 큰 규모의 전향적 연구와 함께, 항공 이송이 효과적일 수 있는 환자군 선별 기준의 확립이 필요할 것으로 보인다.

핵심되는 말: 급성 허혈성 뇌졸중, 항공 이송, 지상 이송, 혈전용해제, 혈전제거술, 신경학적 예후