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The Relationship between Clinical Outcome in Subarachnoidal Hemorrhage Patients with Emergency Medical Service Usage and Interhospital Transfer

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Prompt diagnosis and appropriate transport of patients with subarachnoid hemorrhage (SAH) is critical. We aimed to study differences in clinical outcomes by emergency medical services (EMS) usage and interhospital transfer in patients with SAH. We analyzed the CAVAS (CArdioVAscular disease Surveillance) database which is an emergency department-based, national cohort of cardiovascular disease in Korea. Eligible patients were adults with non-traumatic SAH diagnosed between January 2007 and December 2012. We excluded those whose EMS use and intershopital transfer data was unknown. The primary and secondary outcomes were mortality and neurologic status at discharge respectively. We compared the outcomes between each group using multivariable logistic regressions, adjusting for sex, age, underlying disease, visit time and social history. Of 5,461 patients with SAH, a total of 2,645 were enrolled. Among those, 258 used EMS and were transferred from another hospital, 686 used EMS only, 1,244 were transferred only, and 457 did not use EMS nor were transferred. In the regression analysis, mortality was higher in patients who used EMS and were transferred (OR 1.40, 95% CI 1.02-1.92), but neurologic disability was not meaningfully different by EMS usage and interhospital transfer. In Korea, SAH patients' mortality is higher in the case of EMS use or receiving interhospital transfer.

Keywords: Subarachnoid Haemorrhage; Emergency Medical Services; Interhospital Transfer; Mortality

INTRODUCTION

Subarachnoid hemorrhage (SAH) is a critical disease with high mortality despite a relatively low incidence (1,2). According to the World Health Organization, the age-standardized incidence rates of hemorrhage from a ruptured aneurysm ranges from 2 to 22.5 per 100,000 (3). Furthermore, approximately 10% to 15% of patients with SAH from a ruptured aneurysms die before hospital arrival, and the overall mortality rate is about 40%. Surviving patients of SAH suffer from degradation of long-term cognitive ability and function, resulting in a quality of life of approximately 46% (4-6).

Various methods to enhance the clinical outcomes of SAH have been studied. Treatment of SAH patients at high-volume hospitals improves outcomes likely due to the availability of specialized equipment and experienced clinicians (7-9). An important risk factor associated with SAH morbidity and mortality is rebleeding which can occur due to delayed patient transport or blood pressure fluctuations (10). Rebleeding has recently been shown to be more frequent when systolic blood pressure is over 160 mmHg (11-13).

Considering the evidences, it is possible that transferring patients with SAH will have an unfavorable effect on clinical outcomes, especially when the transfer delays the delivery of timely treatment.

The objective of this study was to investigate the relationship between patient transfer and clinical outcomes in patients with non-traumatic SAH.

MATERIALS AND METHODS

Study design and setting

This is a retrospective observational study of patients with SAH presenting to the emergency departments of 29 institutions participating in the CArdioVAscular disease Surveillance (CAVAS) network. CAVAS is a national, emergency department-based, cardiovascular surveillance project sponsored by the Korea Centers for Disease Control and Prevention. Data was collected from January 2007 to December 2012.

CAVAS network is composed of 18 secondary and 11 tertiary hospitals in Korea. These hospitals oversee the emergency medical services (EMS) in their regions. These hospitals have the fa-

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cilities and physician experience to provide care to a variety of serious injuries and illnesses including patients with SAHs.

The Korean EMS system is organized by 16 municipal and provincial governments. This national EMS system provides medical treatment and transfer services at emergencies for the population of 50 million, and basic to intermediate level of medical treatment can be provided.

Study population

The study population included all patients over 18 yr of age with SAHs identified in the emergency departments of the 29 participating hospitals in the CAVAS project. Patients were considered to have a SAH if their ICD-10 code was I60.0-I60.8. The diagnosis of SAH was made by clinical presentation and verified by hemorrhage in the subarachnoid space on computed tomography (CT) or cerebrospinal fluid examination demonstrating RBCs with no clearing of blood in serial tube, or abnormal xanthochromia. All patients were classified into four groups depending on the EMS utilization and interhospital transfer. These four groups included: used EMS and interhospital transferred group, used EMS and not transferred group, not used EMS and interhospital transferred group, not used EMS and not transferred group.

Exclusion

Patients were excluded if any of the following variables were missing: interhospital transfer status, or outcome at hospital discharge. Patients who arrived at the emergency department after 24 hr from symptom onset were excluded.

Data collection

Data was derived from patient records. Interhospital transfer was defined as transfer of a patient to another medical institution for subsequent hospitalization. Additional variables collected included gender, age, normal exercise, associated disease history, smoking history, alcohol consumption, early symptoms, presence of cardiac arrest and clinical severity.

Outcome measurement

The primary outcome was in-hospital mortality. The secondary outcome was disability measured at the time of hospital discharge. Disability was measured by the modified Rankin Scale at the time of hospital discharge. Patients were considered to have disability if his or her modified Rankin Scale was below 3.

Statistical analysis

Continuous variables were reported as median and interquartile range (IQR). Student's *t*-tests were used to compare normally distributed continues variables and Wilcoxon Rank sum test was used to compare non-normally distributed data. Categorical variables were compare using Fisher's exact test. *P* values less than 0.05 were defined as statistical significance, and all statistical analyses were performed using SAS (version 9.1).

The impact of interhospital transfer and EMS transport was assessed by a multivariable logistic regression with propensity score matched subsets. The propensity score is the clinical factors of each case related to the prognosis. The matched variables were age, sex, education level, visit time at emergency departments, day of the week, past medical history, health behavior including smoking, alcohol consumption, etc. In addition, we performed an interaction model analysis to test the interhospital transfer effect for each EMS utilization group.

Ethics statement

The study was reviewed and approved by institutional review board in Seoul National University Hospital (IRB No. 1012-134-346).

RESULTS

During the 6-yr study period, 5,461 patients diagnosed with SAHs were identified. After eliminating the 2,612 patients with exclusion criteria, 2,849 patients were included in the study sample for analysis (Fig. 1).

These 2,849 patients were classified into four groups in accordance with EMS utilization and interhospital transfer. Baseline characteristics and demographic distribution of the four

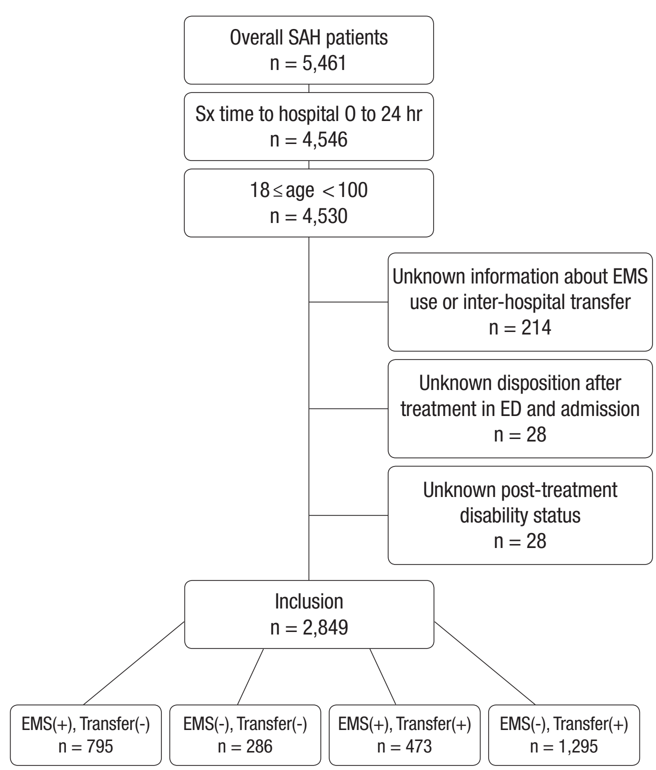

Fig. 1. Study population and their group.

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groups are provided in Table 1. The average age of patients in the four groups was in the range of 52 to 55 yr. EMS use increased as age increased, however, interhopital transfer did not change based on patient's age. More females than males were identified in this study population, but no statistically significant difference was observed by gender on EMS utilization or interhospital transfer. Rate of EMS utilization was increased in patients with higher educational background. More patients with SAHs presented on weekdays, and a higher proportion of interhospital transfers were performed. 1,105 (38.8%) of all patients had hypertension.

Mortality rates were higher in patients who used EMS or underwent interhospital transfer. Patients who did not use EMS or interhospital transfer had lower rates of disability at discharge (P < 0.001). Educational background was also an influential factor such that patients with educational background of high school or higher had lower odds of disability and mortality at discharge (P < 0.001). Mortality and disability rates were higher in patients who presented to the emergency department during nighttime hours (P = 0.003). Patients who exercise regularly had lower rates of mortality and disability. In patients with underlying diseases such as diabetes, hypertension, heart disease, and stroke, the rates of mortality and disability were higher. Furthermore, a shorter arrival time to the final hospital disposition was associated with a higher mortality rate (P < 0.001) (Table 2).

In order to identify the associations of clinical outcomes with EMS utilization and interhospital transfer, propensity score matching and logistic regression analysis were performed. Table 3

Table 1. Baseline characteristics and demographics by eligible patients

Characteristics	Total		EMS (+)				EMS (-)				*P* value
			Direct		Transfer		Direct		Transfer		
	No.	%	No.	%	No.	%	No.	%	No.	%	
Total	2,849		795		286		473		1,295		
Gender											0.428
Male	1,179	41.4	311	39.1	126	44.1	199	42.1	543	41.9	
Female	1,670	58.6	484	60.9	160	55.9	274	57.9	752	58.1	
Age											0.061
≤ 40	402	14.1	98	12.3	37	12.9	76	16.1	191	14.7	
41-60	1,544	54.2	413	51.9	153	53.5	255	53.9	723	55.8	
61-	903	31.7	284	35.7	96	33.6	142	30.0	381	29.4	
Median (IQR)	53 (45-63)		55 (46-66)		54 (46-65)		53 (45-63)		52 (45-62)		< 0.001
Time symptom onset to destination hospital (min)											< 0.001
Median (IQR)	135 (60-297)		45 (29-89)		178.5 (119-358)		117 (47-296)		195 (120-385)		
ED visit time											0.025
6PM-6AM	1,297	45.5	356	44.8	146	51.0	191	40.4	604	46.6	
6AM-6PM	1,552	54.5	439	55.2	140	49.0	282	59.6	691	53.4	
Week											0.033
Weekday	2,061	72.3	557	70.1	205	71.7	328	69.3	971	75.0	
Weekend	788	27.7	238	29.9	81	28.3	145	30.7	324	25.0	
Education											< 0.001
< High school	1,046	36.7	281	35.3	118	41.3	172	36.4	475	36.7	
≥ High school	1,419	49.8	429	54.0	141	49.3	256	54.1	593	45.8	
Unknown	384	13.5	85	10.7	27	9.4	45	9.5	227	17.5	
Health behavior											
Exercise	547	19.2	155	19.5	54	18.9	82	17.3	256	19.8	0.707
Current smoker	752	26.4	197	24.8	84	29.4	121	25.6	350	27.0	0.475
Ex-smoker	174	6.1	46	5.8	19	6.6	36	7.6	73	5.6	
Alcohol	982	34.5	258	32.5	122	42.7	145	30.7	457	35.3	0.004
Past medical history											
DM	220	7.7	68	8.6	24	8.4	42	8.9	86	6.6	0.265
Hypertension	1,105	38.8	357	44.9	117	40.9	188	39.7	443	34.2	< 0.001
Dyslipidemia	83	2.9	27	3.4	9	3.1	15	3.2	32	2.5	0.633
Chronic kidney disease	84	2.9	31	3.9	10	3.5	21	4.4	22	1.7	0.004
Heart disease	113	4.0	45	5.7	5	1.7	27	5.7	36	2.8	< 0.001
Stroke	173	6.1	54	6.8	18	6.3	40	8.5	61	4.7	0.022
Treatment											0.119
Coiling	591	20.7	153	19.2	70	24.5	110	23.3	258	19.9	
Post-stroke status											< 0.001
No disability	1,280	44.9	281	35.3	106	37.1	275	58.1	618	47.7	
Disability	807	28.3	210	26.4	58	20.3	133	28.1	406	31.4	
Death	762	26.7	304	38.2	122	42.7	65	13.7	271	20.9	

EMS, emergency medical service; ED, emergency department; DM, diabetes mellitus.

Table 2. Demographics of total study population by hospital outcomes

Characteristics	Total	No disability		Disability		Death		*P* value
	No.	No.	%	No.	%	No.	%	
Total	2,849	1,280		807		762		
Gender								0.203
Male	1,179	515	43.7	328	27.8	336	28.5	
Female	1,670	765	45.8	479	28.7	426	25.5	
Age								< 0.001
≤ 40	402	223	55.5	100	24.9	79	19.7	
41-60	1,544	785	50.8	423	27.4	336	21.8	
61-	903	272	30.1	284	31.5	347	38.4	
Median (IQR)	53 (45-63)	50 (44-59)		54 (46-65)		58.5 (48-70)		< 0.001
EMS and transfer								< 0.001
EMS and direct	795	281	35.3	210	26.4	304	38.2	
EMS and transfer	286	106	37.1	58	20.3	122	42.7	
Non-EMS and direct	473	275	58.1	133	28.1	65	13.7	
Non-EMS and transfer	1,295	618	47.7	406	31.4	271	20.9	
Time symptom onset to destination hospital (min)								< 0.001
Median (IQR)	135 (60-297)	157 (65-360)		144 (65-300)		106.5 (42-208)		
ED visit time								0.003
6PM-6AM	1,297	540	41.6	379	29.2	378	29.1	
6AM-6PM	1,552	740	47.7	428	27.6	384	24.7	
Week								0.184
Weekday	2,061	905	43.9	590	28.6	566	27.5	
Weekend	788	375	47.6	217	27.5	196	24.9	
Education								< 0.001
< High school	1,046	408	39.0	311	29.7	327	31.3	
≥ High school	1,419	744	52.4	385	27.1	290	20.4	
Unknown	384	128	33.3	111	28.9	145	37.8	
Health behavior								
Exercise	547	275	50.3	158	28.9	114	20.8	0.001
Current smoker	752	361	48.0	205	27.3	186	24.7	0.048
Ex-smoker	174	62	35.6	60	34.5	52	29.9	
Alcohol	982	491	50.0	269	27.4	222	22.6	< 0.001
Past medical history								
DM	220	79	35.9	60	27.3	81	36.8	0.001
Hypertension	1,105	462	41.8	317	28.7	326	29.5	0.011
Dyslipidemia	83	41	49.4	22	26.5	20	24.1	0.703
Chronic kidney disease	84	28	33.3	27	32.1	29	34.5	0.082
Heart disease	113	35	31.0	29	25.7	49	43.4	< 0.001
Stroke	173	70	40.5	38	22.0	65	37.6	0.003
Treatment								< 0.001
Coiling	591	358	60.6	157	26.6	76	12.9	

EMS, emergency medical service; ED, emergency department; DM, diabetes mellitus.

shows the demographic findings of the propensity score matched dataset by interhospital transfer. No statistically significant differences were identified. In the multivariate regression analysis, mortality was higher in patients who utilized EMS in both the original and propensity score matched datasets. This result was identified regardless of the patient's interhospital transfer status. In terms of disability, patients who did not use EMS nor underwent interhospital transfer had lower odds of disability (Table 4). Finally, we performed another multivariate regression analysis including an interaction model to identify the effect of interhospital transfer on morbidity and mortality. In this analysis, the presence of interhospital transfer had no effect on disability but mortality was higher especially in the patients who did not use EMS (Table 5).

DISCUSSION

SAH is a critical illness with detrimental outcomes and requires careful, specialized treatment and close neurologic monitoring. Thus, ensuring patients with SAHs are treated at the most appropriate hospital, including the need for interhospital transfer, is regarded as an important factor in the course of treatment for SAH patients. The impact of EMS utilization and interhospital transfer on patient outcomes, however, has not been fully explored.

In terms of patient transfer to more specialized hospitals with larger patient volumes, Bardach et al. (14) studied the cost-effectiveness of interhospital transfer of patients with aneurysmal SAH to large-volume hospitals. They reported a 1.6 times increase in quality-adjusted life year when patients with SAHs were transferred. While this study appeared to recommend interhos-

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Table 3. Demographics of propensity score matched dataset by interhospital transfer

Parameters	Total		Direct		Transfer		*P* value
	No.	%	No.	%	No.	%	
Total	1,510		755		755		
Gender							0.92
Male	606	40.1	304	40.3	302	40.0	
Female	904	59.9	451	59.7	453	60.0	
Age							0.98
≤ 40	220	14.6	111	14.7	109	14.4	
41-60	816	54.0	406	53.8	410	54.3	
61-	474	31.4	238	31.5	236	31.3	
Median (IQR)	53 (45-63)		53 (45-63)		53 (45-63)		0.06
ED visit time							0.38
6PM-6AM	667	44.2	342	45.3	325	43.0	
6AM-6PM	843	55.8	413	54.7	430	57.0	
Week							0.73
Weekday	1,074	71.1	534	70.7	540	71.5	
Weekend	436	28.9	221	29.3	215	28.5	
Education							0.91
< High school	564	37.4	282	37.4	282	37.4	
≥ High school	793	52.5	394	52.2	399	52.8	
Unknown	153	10.1	79	10.5	74	9.8	
Health behavior							
Exercise	280	18.5	137	18.1	143	18.9	0.69
Current smoker	386	25.6	193	25.6	193	25.6	0.90
Ex-smoker	86	5.7	41	5.4	45	6.0	
Alcohol	504	33.4	249	33.0	255	33.8	0.74
Past medical history							
DM	135	8.9	69	9.1	66	8.7	0.79
Hypertension	612	40.5	305	40.4	307	40.7	0.92
Dyslipidemia	36	2.4	16	2.1	20	2.6	0.50
Chronic kidney disease	48	3.2	28	3.7	20	2.6	0.24
Heart disease	62	4.1	30	4.0	32	4.2	0.80
Stroke	96	6.4	47	6.2	49	6.5	0.83
Treatment							0.42
Coiling	331	21.9	159	21.1	172	22.8	
Post-stroke status							0.02
No disability	722	47.8	381	50.5	341	45.2	
Disability	411	27.2	208	27.5	203	26.9	
Death	377	25.0	166	22.0	211	27.9	

EMS, emergency medical service; ED, emergency department.

Table 4. Logistic regression analysis on outcomes by EMS utilization and interhospital transfer in original and propensity score matched dataset

Outcomes	Total	Outcome		Crude				Adjusted*			
	No.	n	%	OR	95% CI		*P* value	OR	95% CI		*P* value
Original dataset											
Outcome: death (n = 2,849)											
EMS and direct	795	304	38.2	1.00				1.00			
EMS and transfer	286	122	42.7	1.20	0.91	1.58	0.163	1.23	0.92	1.64	0.190
Non-EMS and direct	473	65	13.7	0.26	0.19	0.35	< 0.001	0.24	0.18	0.33	< 0.001
Non-EMS and transfer	1,295	271	20.9	0.43	0.35	0.52	< 0.001	0.39	0.32	0.49	< 0.001
Outcome: disability (n = 2,087)											
EMS and direct	491	210	42.8	1.00				1.00			
EMS and transfer	164	58	35.4	0.73	0.51	1.06	0.096	0.72	0.49	1.04	0.082
Non-EMS and direct	408	133	32.6	0.65	0.49	0.85	0.002	0.62	0.47	0.82	< 0.001
Non-EMS and transfer	1,024	406	39.6	0.88	0.71	1.09	0.247	0.83	0.66	1.04	0.223
Propensity score matched dataset											
Outcome: death (n = 1,510)											
EMS and direct	287	103	35.9	1.00				1.00			
EMS and transfer	286	122	42.7	1.33	0.95	1.86	0.097	1.41	0.99	2.02	0.058
Non-EMS and direct	468	63	13.5	0.28	0.19	0.40	< 0.001	0.26	0.18	0.38	< 0.001
Non-EMS and transfer	469	89	19.0	0.42	0.30	0.58	< 0.001	0.41	0.29	0.58	< 0.001
Outcome: disability† (n = 1,133)											
EMS and direct	184	77	41.8	1.00				1.00			
EMS and transfer	164	58	35.4	0.76	0.49	1.17	0.216	0.76	0.49	1.20	0.236
Non-EMS and direct	405	131	32.3	0.66	0.46	0.95	0.026	0.65	0.45	0.95	0.024
Non-EMS and transfer	380	145	38.2	0.86	0.60	1.23	0.401	0.88	0.60	1.27	0.489

*Adjusted for age, sex, ED visit time, weekday, education level, health behavior (exercise, smoking, and alcohol), and past medical history (DM, hypertension, dyslipidemia, chronic kidney disease, heart disease, and stroke); †For disability, the ORs were calculated for alive patients.

Table 5. Interaction model to test transfer effect on outcomes for each EMS use group

Outcomes	Outcome: Death				Outcome: Disability†			
	AOR*	95% CI		*P* value	AOR*	95% CI		*P* value
Original dataset								
EMS use								
Direct	1.00				1.00			
Transfer	1.23	0.92	1.64	0.163	0.72	0.49	1.04	0.082
No EMS use								
Direct	1.00				1.00			
Transfer	1.65	1.22	2.24	0.001	1.34	1.05	1.73	0.020
Propensity score matched dataset								
EMS use								
Direct	1.00				1.00			
Transfer	1.41	0.99	2.02	0.058	0.76	0.49	1.19	0.236
No EMS use								
Direct	1.00				1.00			
Transfer	1.57	1.09	2.26	0.016	1.35	1.00	1.83	0.054

*Adjusted for age, sex, ED visit time, weekday, education level, health behavior (exercise, smoking, and alcohol), and past medical history (DM, hypertension, dyslipidemia, chronic kidney disease, heart disease, and stroke); †For disability, the ORs were calculated for alive patients.

pital transfer of SAH patients to large-volume hospitals, other studies question this practice as transferred patients required more resources, had a worse prognosis than patients who visited hospitals directly, had delayed boarding time, and had extended treatment period in intensive care units. Therefore, the benefits and decisions to transfer patients to large-volume hospitals require careful consideration (15-19).

Recent studies have addressed the effects of interhospital transfer of patients with myocardial infarction (20,21), and one study reported no significant effects of interhospital transfer in these populations (22). In a previous study of patients with SAHs, interhospital transfer improved clinical outcomes for patients treated at high-volume hospitals, but no analysis on the cost and risk of interhospital transfer have been reported (21).

The current study demonstrates that mortality is higher in patients initially transported to the emergency department via EMS. Initial symptoms in patients with SAHs are highly variable and the utilization of EMS likely increases in patients with severe symptoms. Unfortunately, CAVAS data are not only for SAH but also for whole acute severe cardiovascular diseases, we cannot use the variables like initial symptom or Hunt Hess classification. So, after propensity score matched, this tendency which the higher mortality in EMS used patients is maintained. It means we cannot successfully reach the even distribution containing initial severity by propensity score matching.

When evaluating the effect of interhospital transfer on clinical outcomes the effect is greatest in patients not transported by EMS as mortality was highest in the group. This finding may be due to several reasons. First, the initial hospital may not have the capabilities to treat patients with SAHs. The patient may select a closer hospital, not be aware of the severity of their illness or lack education about the possibility of EMS transport. Second, a resource problem may exist. Smaller emergency departments may not be able to manage patients with SAH after the diagnosis is made. Availability of specialists to treat patients with SAHs in rural and suburban areas especially on the weekend or at night is limited. Finally, the transfer process itself can lead to problems and additional morbidity or mortality. Transfer of patients with SAH should be both swift and safe to minimize possible complications such as rebleeding, but this is not always possible. Further study is required to determine the relationship of EMS use and interhospital transfer on morbidity and mortality in patients with SAH.

This study has certain limitations. It is a retrospective analysis of an existing database and subject to the inherent biases in such a study. The database did not have initial GCS score at the time of emergency department presentation or results of the initial emergency department cranial CT scan. Consequentially, there is insufficiency in severity adjustment.

In conclusion, patients with SAH who use the EMS system have worse clinical outcomes than those who do not. Patients who undergo interhospital transfer without initial EMS transport have higher mortality.

DISCLOSURE

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Conception and design: Song KJ, Lee SH. Performing the experiments: Song KJ, Shin SD. Analysis of data: Ro YS. Writing: Lee SH, Song KJ. English editing: Kim MJ, Holmes JF. Agreeing with manuscript results and conclusions: all authors

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