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PS-10

Risk Factor Identification of Early Stroke Recurrence in Ischemic Stroke Patients in Korea

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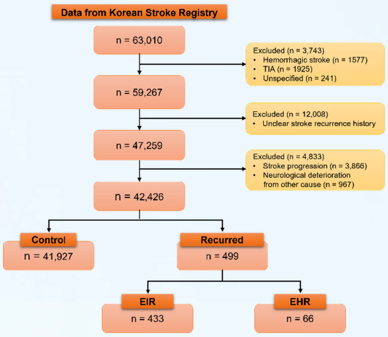
I. INTRODUCTION

Identifying risk factors for early stroke recurrence in ischemic stroke patients is critical in the clinical setting because it allows for timely intervention and personalized management strategies to prevent subsequent strokes. Early stroke recurrence is associated with increased morbidity, mortality and healthcare costs. Identification of these risk factors allows clinicians to optimize secondary prevention measures and improve patient outcomes. However, it is difficult to predict stroke recurrence based on the inference that detects risk factors. Here, we aim to detect the incidence of early stroke recurrence and the characteristic risk factors based on Korean big data analysis.

II. METHODS

1. Subject

- Study groups
  - **Control group:** no early recurrence within 12 weeks or stroke progression/deterioration, 98.82% (n=41,927)
  - **EIS group:** Early recurrence within 12 weeks of ischemic stroke, 1.02% (n=433)
  - **EHS group:** Early recurrence within 12 weeks of hemorrhagic stroke, 0.16% (n=66)



2. Analyzed parameters

- 31 parameters were selected from Korean Stroke Registry database (**Red words**)

3. Statistics

- Chi-square test, Independent T-test: to compare clinical parameters between the control and EIS group, and the control and EHS group
- Logistic regression analysis: for accuracy & area under curve (AUC), sensitivity, specificity in the EIS and EHS of ischemic stroke patients
- Statistical significance: p-value < 0.05

List of parameters in Korean Stroke Registry database

Initial	Pre-hospital	TOAST/RISK	Management	Discharge	Early Neurological Deterioration/Outcome
Gender	Via another hospital	Ischemia / Hemorrhage	**Antiplatelet in acute treatment**	Date of discharge	Early neurological deterioration (END) during admission
Age	Arrival time to another hospital	**TOAST (large artery atherosclerosis / small vessel occlusion / cardio-aortic embolism / other determined)**	**Anticoagulation in acute treatment**	**Total hospital days**	**MI during admission**
Clear / Unclear onset	Visit route to another hospital (OPD / ER / in-hospital)	Intracerebral hemorrhage (ICH)	**Initial SBP**	**Stroke unit**	Date of MI onset
Last known normal time	Number of hospitals visited	Intraventricular hemorrhage (IVH)	**Initial DBP**	**Hospital days of stroke unit**	END1/2
First observed abnormal time	1st/2nd/3rd hospital visit	Subarachnoid hemorrhage (SAH)	Time of first brain imaging	**NIHSS at discharge**	Type of END1/2 (stroke recurrence / stroke progression / symptomatic hemorrhagic transformation / others)
Arrival time	Name of the 1st/2nd/3rd hospital	Subdural hemorrhage (SDH)	Reason for not imaging within 1 hour of visit	**mRS at discharge**	Stroke recurrence subtype (ischemic / hemorrhagic / unknown)
Stroke type (Ischemic / Hemorrhagic / TIA)	Extraction of the 1st/2nd/3rd hospital's database	Epidural hemorrhage (EDH)	Test for LDL	**Antiplatelet medication on discharge**	Date of END1/2 onset
Height	Mode of arrival to other hospital	transient ischemic attack (TIA)	Date of test for LDL	**Anticoagulation medication on discharge**	Reporting time of END1/2
Weight	Brain imaging in other hospital	Imaging study	Screening test of dysphagia	**Statin on discharge**	NIHSS before END1/2
Initial NIHSS	Name of the hospital where the brain imaging was done	**History of TIA**	Date of screening test of dysphagia	Discharge state	NIHSS after END1/2
Previous mRS	Type of household at the time of outbreak	**History of stroke**	Reasons for not performing the screening test of dysphagia	Expired cause of death	Follow up loss after 3 months/1year
Visit route (OPD / ER / in-hospital)	Household – other housemates	**Coronary heart disease**	Onset of oral feeding	Transfer to other department	Date of examination for 3 months/1year follow up (f/u)
Via another hospital	Household – family/spouse	Evidence of slient MI or myocardial ischemia	Oral feeding	Transfer to department of rehabilitation medicine from another department	Medical adherence_3 months/1year f/u
Arrival time to another hospital	Household – family/parents	History of coronary angioplaasty or surgery	Request for rehabilitation	Date of discharge (based on hospital administration department)	Have you ever forgotten to take your medication?_3 months/1 year f/u
Visit route to another hospital (OPD / ER / in-hospital)	Household – family/children	History of acute myocardial infarction (AMI)	Date of request for rehabilitation	After discharge (to home / referred to other hospital / expired)	Have you ever failed to take your medication on time?_3 months/1 year f/u
The time of decision to visit the hospital after the onset of first symptoms	Household – family/relatives	**Diabetes mellitus (DM)**	Transfer to department of rehabilitation medicine	Refer to other hospital	Have you ever forgotten to get your prescription medication on time?_3 months/1 year f/u
Recognition of stroke before first hospital visit	Household – family/others	**Hyperlipidemia (HL)**		Primary caregiver after discharge	Have you ever skipped your medication when you felt good?_3 months/1 year f/u
Mode of arrival (ambulance / own car / taxi / public transport / etc)		**Hypertension (HTN)**		**Stroke education**	Have you ever skipped your medication when you felt not good?_3 months/1 year f/u
Type of ambulance (119 / private / hospital)		**Subtypes of smoking (current smoker / quit ≥5ys / <5ys)**			Do you know what your doctor says about the long-term benefits of taking medication?_3 months/1 year f/u
First aid log		History of atrial fibrillation			Amount of drug taken in the past month (%)
Reception time of 119					Reasons for stopping the drug
Arrival time of 119					Smoking_3 months/1 year f/u
Whether paramedics recognized stroke					Clinical event until 3 months/1 year
Notice before the paramedic visit the ER room					Clinical event 1/2/3_3 months/1 year f/u
Attending physician/staff					Type of clinical event1/2/3__3 months/1 year f/u (stroke recurrence / cardiovascular event / other death)
Admission in stroke unit					Survival at 3 months/1year in patients with stroke recurrence1/2/3
Admission date in stroke unit					Date of death due to stroke recurrence
Thrombolysis					Subtype of cardiovascular event1/2/3
Type of thrombolysis (IV / IA / IV + IA)					Survival at 3 months/1 year in patients with cardiovascular event1/2/3
Thrombolysis starting time					Date of death due to cardiovascular event
Thrombolysis in another hospital					Date of clinical event1/2/3_3 months/1 year f/u
IA/IV thrombolysis starting time					
IV-rTPA					
Dose of IV thrombolysis tPA					

III. RESULTS

Featured parameters in EIS and EHS groups

- **EIS group**: Hx. of transient ischemic attack, coronary heart disease, hypertension, dyslipidemia, and atrial fibrillation, current smoker No., initial SBP and DBP, hospital days
- **EHS group**: age (older), weight (heavier)
- **Both EIS and EHS groups**: scores of mRS at previous and discharge state, NIHSS at admission and discharge, incidence of large artery atherosclerosis and cardio-aortic embolism, myocardial infarction during hospitalization

Parameters		Control group (n=41,927)	EIS group (n=433)	p value	EHS group (n=66)	p value
Demographics	Gender (male)	24903 (59.4%)	248 (57.3%)	0.371	39 (59.1%)	0.960
	Age	68.78±13.153	69.75±13.992	0.126	71.92±11.179	0.026*
	Height	185.49±136.348	188.58±148.736	0.640	249.53±260.481	0.050
	Weight	86.81±146.416	91.14±160.395	0.541	164.49±289.943	0.033*
Smoking	Current smoker	10444 (66.6%)	86 (55.8%)	0.007*	17 (77.3%)	0.317
	Quit ≥5yrs	3903 (24.9%)	46 (29.9%)		5 (22.7%)	
	Quit <5ys	1342 (8.6%)	22 (14.3%)		0 (0.0%)	
Past medical history	Transient ischemic attack	528 (1.3%)	15 (3.5%)	0.000*	1 (1.5%)	0.852
	Coronary heart disease	3511 (8.4%)	50 (11.5%)	0.018*	6 (9.1%)	0.310
	Hypertension	25389 (60.6%)	283 (65.4%)	0.042*	44 (66.7%)	0.310
	Diabetes mellitus	12542 (29.9%)	138 (31.9%)	0.376	22 (33.3%)	0.544
	Dyslipidemia	12156 (29.0%)	145 (33.5%)	0.040*	26 (39.4%)	0.063
	Atrial fibrillation	8221 (19.6%)	127 (29.3%)	0.000*	25 (37.9%)	0.000*
Premorbid state	previous mRS	0.48±1.061	0.64±1.239	0.006*	1.02±1.631	0.009*
Ischemic type	Large artery atherosclerosis	13742 (32.8%)	161 (37.2%)	0.000*	27 (40.9%)	0.000*
	Small artery occlusion	9672 (23.1%)	25 (5.8%)		3 (4.5%)	
	Cardio-aortic embolism	8636 (20.6%)	135 (31.2%)		23 (34.8%)	
	Other determined	9873 (23.6%)	112 (25.9%)		13 (19.7%)	
Initial state	initial SBP	152.21±31.048	158.29±49.736	0.011*	146.83±24.432	0.160
	initial DBP	86.62±21.531	89.31±46.627	0.0232*	84.62±14.047	0.450
	Initial NIHSS	5.41±5.911	6.69±6.389	0.000*	12.26±6.931	0.000*
Hospitalization	Total hospital days	9.36±12.590	15.22±17.645	0.000*	14.12±11.327	0.001*
	Stroke Unit	31774 (75.8%)	386 (89.1%)	0.000*	54 (81.8%)	0.253
	Hospital days of Stroke Unit	2.99±20.741	6.03±11.982	0.000*	5.31±5.419	0.370
Other complication	Myocardial infarction	82 (0.2%)	17 (3.9%)	0.000*	2 (3.0%)	0.000*
Discharge state	Discharge NIHSS	3.97±6.291	11.81±12.530	0.000*	20.21±14.404	0.000*
	Discharge mRS	2.09±1.657	3.55±1.736	0.000*	4.27±1.574	0.000*
Acute treatment	Thrombolysis	7868 (18.8%)	134 (30.9%)	0.000*	45 (68.2%)	0.000*
	IA thrombolysis	3394 (43.1%)	48 (35.8%)	0.226	16 (35.6%)	0.377
	IV thrombolysis	2529 (32.1%)	50 (37.3%)		14 (31.1%)	
	IA+IV thrombolysis	1945 (24.7%)	36 (26.9%)		15 (33.3%)	
	IV tPA dose = 0.6mg/kg	1470 (27.7%)	31 (37.3%)	0.050	1 (3.2%)	0.002*
	IV tPA dose = 0.9mg/kg	3846 (72.3%)	52 (62.7%)		30 (96.8%)	
	Antiplatelet	36391 (86.8%)	353 (81.5%)	0.001*	36 (54.5%)	0.000*
	Anticoagulation	5525 (13.2%)	78 (18.0%)	0.003*	7 (10.6%)	0.003*
Discharge treatment	Antiplatelet	32753 (78.1%)	246 (56.8%)	0.000*	21 (31.8%)	0.000*
	Anticoagulation	8761 (20.9%)	143 (33.0%)	0.000*	11 (16.7%)	0.398
	Statin	37618 (89.8%)	330 (76.2%)	0.000*	30 (45.5%)	0.000*
	Stroke education	38047 (90.8%)	356 (82.2%)	0.000*	46 (69.7%)	0.000*

Summary

- **We found 24 parameters in EIS group, and 17 parameters in EHS group were significantly different from control group, and these parameters might be candidates for risk factors to prevent early stroke recurrence.**
- **Logistic regression analysis showed excellent AUC (0.825, 0.898) and accuracy (99%, 99%) in EIS and EHS groups, respectively.**
- **Low incidence of early stroke recurrence (<2%) in Korean Stroke Registry presents potential problems with data imbalance and model generalizability.**

Logistic regression analysis

- EIS group: 11 from 13 featured parameter were significant
- EHS group: 6 from 8 featured parameters were significant

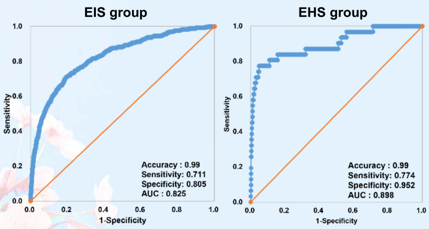
EIS group

Parameters	B	S.E	Wals	p value	Exp(B)
Stroke unit	-.924	.316	8.535	.003*	.397
Acute treatment_thrombolysis	-1.017	.201	25.501	.000*	.362
Large artery atherosclerosis	.175	.220	.630	.427	1.191
Small artery occlusion	-.922	.355	6.750	.009*	.398
Cardio-aortic embolism	-.147	.275	.286	.593	.863
History of transient ischemic attack	-1.176	.453	6.746	.009*	.309
Acute treatment_antiplatelet	-.709	.283	6.280	.012*	.492
Discharge treatment_coagulation	-1.215	.247	24.286	.000*	.297
Myocardial infarction	-1.886	.634	8.864	.003*	.152
Initial NIHSS	-.200	.023	77.851	.000*	.818
Initial SBP	.005	.002	7.133	.008*	1.005
Discharge NIHSS	.073	.013	33.276	.000*	1.076
Discharge mRS	.531	.079	45.228	.000*	1.701

EHS group

Parameters	B	S.E	Wals	p value	Exp(B)
IV tPA dose	-3.086	1.071	8.301	.004*	.046
Atrial fibrillation	1.148	.541	4.510	.034	3.153
Acute treatment_antiplatelet	1.618	.453	12.761	.000*	5.042
Acute treatment_anticoagulation	15.960	1121.635	.000	.989	8536812.299
Stroke education	-1.693	.603	7.889	.005*	.184
Weight	.002	.001	8.427	.004*	1.002
Initial NIHSS	-.075	.038	4.000	.045*	.927
Discharge NIHSS	.137	.019	51.978	.000*	1.147

Receiver operating characteristics (ROC) curve



IV. CONCLUSION

This study identified significant differences in several clinical characteristics between first-ever ischemic stroke patients with early recurrence and those without early recurrence by analyzing data from the Korean Stroke Registry. Results indicate that these parameters have a significant role to prevent early stroke recurrence. However, future research efforts are needed to address potential problems and develop predictive models by improving these aspects.

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