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Letter to the Editor

A Retrospective Study on the Status of Risk Factor Management in Patients with Ischemic Stroke Based on a Large Linked Dataset of Stroke Patients in Korea

Tae Jung Kim,[a,b,*] Ji Sung Lee,[c,*] Jae Sun Yoon,[a] Soo-Hyun Park,[d] Mi Sun Oh,[e] Keun-Hwa Jung,[a] Kyung-Ho Yu,[e] Byung-Chul Lee,[e] Sang-Bae Ko,[a,b] Byung-Woo Yoon[f]

[a]Department of Neurology, Seoul National University Hospital, Seoul, Korea
[b]Department of Critical Care Medicine, Seoul National University Hospital, Seoul, Korea
[c]Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[d]Department of Critical Care Medicine, Inha University Hospital, Incheon, Korea
[e]Department of Neurology, Hallym University Sacred Heart Hospital, Anyang, Korea
[f]Department of Neurology, Uijeongbu Eulji Medical Center, Eulji University, Uijeongbu, Korea

*These authors contributed equally to the manuscript as first author.

Dear Sir:

Stroke is the second leading cause of death and disability worldwide. The incidence and recurrence of stroke are strongly associated with the management of modifiable vascular risk factors, including hypertension (HT), diabetes mellitus (DM), dyslipidemia, and atrial fibrillation (AF).[1,2] Although modifiable risk factors are important to reduce the risk of stroke, awareness of risk factors and the control rate of risk factors in many patients with stroke remain low, especially in young adults.[1,2] Given that there is little information on the clinical factors related to uncontrolled risk factors for stroke, we aimed to investigate the proportion of new diagnoses of major risk factors for ischemic stroke and identify the factors associated with the poor control rate using a linked dataset of stroke in Korea.

The study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital (IRB No. H-1608-078-785), those of other 34 participating hospitals, and the Health Insurance Review and Assessment Service (HIRA). The need for informed consent was waived by the IRBs.

We included data for 42,879 patients with acute ischemic stroke within 7 days after symptom onset from the linked Clinical Research Center for Stroke Registry and the HIRA between January 2008 and December 2014. We evaluated the proportion of patients with newly identified conventional risk factors (HT, DM, and AF) after index ischemic stroke and assessed factors related to poor control of risk factors. Detailed methodological descriptions and statistical analyses are provided in Supplementary methods. Among the total patients included (n=42,879; 59.5%, male [n=25,529]; mean±standard deviation age, 65.7±12.5 years), 78.0% (n=33,462) were hypertensive, 33.2% (n=14,242) were diabetic, and 9.5% (n=4,069) had AF with cardioembolic stroke. Among patients with HT, 8.8% (2,956/33,462) were newly diagnosed with HT. Similarly, 5.0% of the patients (n=709) were newly diagnosed with diabetes, and 15.9% of the patients (n=648) were newly diagnosed with AF after stroke (Supplementary Tables 1-3). The detailed baseline characteristics are discussed in the Supplementary Results. Young-age patients (≤45 years) were more likely to have newly identified vascular risk factors after index stroke (Table 1). After adjusting for confounding variables, younger age (≤45 years) was independently associated with a higher proportion of newly identified risk factors (odds ratio [OR], 1.865; 95% confidence interval [CI], 1.579 to 2.203; P<0.0001 in HT, OR, 1.726; 95% CI, 1.163 to 2.562; P=0.0067 in DM, and OR, 2.503; 95% CI, 1.507 to 4.155; P=0.0004 in AF) (Table 2). Furthermore, fac-

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Table 1. Newly identified risk factors according to age

Variable	Age ≤45 years	Age >45 years	ASD*
Hypertension (n=33,462)			
New onset hypertension	1,764	34,699	
No	1,483 (84.1)	32,024 (92.3)	0.2567
Yes	281 (15.9)	2,675 (7.7)	
Diabetes mellitus (n=14,242)	653	16,296	
New onset diabetes mellitus			
No	611 (93.6)	15,629 (95.9)	0.1049
Yes	42 (6.4)	667 (4.1)	
Atrial fibrillation (n=4,069) in cardioembolic stroke	102	3,967	
New onset atrial fibrillation			
No	69 (67.6)	3,352 (84.5)	0.4029
Yes	33 (32.4)	615 (15.5)	

Values are presented as number (%).
ASD, absolute standardized difference.
*ASD >0.1, considered meaningful imbalances.

Table 2. Multivariable analyses of the relationship between clinical factors and newly identified risk factors in patients with ischemic stroke

Variable	Crude analysis			Adjusted analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Hypertension						
Age ≤45 years	2.673	2.333–3.063	<0.0001	1.865	1.579–2.203	<0.0001
Female	0.673	0.621–0.729	<0.0001	0.930	0.818–1.056	0.2628
Diabetes mellitus	0.533	0.489–0.581	<0.0001	0.572	0.514–0.636	<0.0001
Dyslipidemia	0.679	0.623–0.740	<0.0001	0.741	0.666–0.824	<0.0001
Atrial fibrillation	0.549	0.487–0.618	<0.0001	0.480	0.386–0.595	<0.0001
Coronary artery disease	0.319	0.259–0.393	<0.0001	0.399	0.311–0.512	<0.0001
Previous stroke/TIA	0.391	0.342–0.447	<0.0001	0.448	0.378–0.532	<0.0001
Smoking	1.660	1.539–1.790	<0.0001	1.336	1.191–1.497	<0.0001
Education years						
0–3	0.553	0.430–0.712	<0.0001	0.745	0.571–0.970	0.0289
4–6	0.626	0.545–0.720	<0.0001	0.813	0.697–0.949	0.0085
7–9	0.882	0.763–1.021	0.0931	1.078	0.923–1.258	0.3444
9–12	1.042	0.915–1.186	0.5394	1.128	0.985–1.292	0.0807
≥13	Reference			Reference		
Diabetes mellitus						
Age ≤45 years	1.790	1.293–2.478	0.0005	1.726	1.163–2.562	0.0067
Female	1.018	0.873–1.187	0.8231	0.965	0.757–1.229	0.7707
Hypertension	0.625	0.527–0.741	<0.0001	0.558	0.451–0.689	<0.0001
Dyslipidemia	0.775	0.660–0.910	0.0018	0.855	0.703–1.041	0.1184
Atrial fibrillation	1.552	1.283–1.878	<0.0001	1.398	0.962–2.031	0.0789
Coronary artery disease	0.890	0.680–1.164	0.3935	0.795	0.562–1.124	0.1935
Previous stroke/TIA	0.816	0.667–0.997	0.0466	0.914	0.705–1.186	0.4994
Smoking	0.983	0.843–1.147	0.8310	0.938	0.749–1.173	0.5738
Education years						
0–3	0.990	0.619–1.581	0.9651	1.001	0.614–1.633	0.9954
4–6	1.062	0.802–1.406	0.6752	1.128	0.830–1.533	0.4426

Table 2. Continued

Variable	Crude analysis			Adjusted analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
7–9	0.993	0.730–1.350	0.9619	1.058	0.769–1.455	0.7308
9–12	1.041	0.784–1.381	0.7825	1.091	0.817–1.457	0.5537
≥13	Reference			Reference		
Atrial fibrillation						
Age ≤45 years	2.607	1.707–3.982	<0.0001	2.503	1.507–4.155	0.0004
Female	0.798	0.673–0.946	0.0092	0.873	0.678–1.125	0.2951
Hypertension	0.934	0.769–1.134	0.4893	1.010	0.794–1.285	0.9331
Diabetes mellitus	1.023	0.849–1.232	0.8114	1.120	0.894–1.404	0.3242
Dyslipidemia	1.003	0.835–1.205	0.9740	1.013	0.812–1.265	0.9066
Coronary artery disease	0.840	0.656–1.077	0.1688	0.924	0.693–1.231	0.5874
Previous stroke/TIA	0.981	0.785–1.224	0.8622	0.954	0.795–1.384	0.7344
Smoking	1.233	1.031–1.475	0.0220	1.049	0.971–1.563	0.0862
Education years						
0–3	0.660	0.422–1.033	0.0688	0.782	0.490–1.248	0.3029
4–6	0.810	0.608–1.080	0.1510	0.957	0.701–1.307	0.7824
7–9	0.927	0.673–1.277	0.6426	1.034	0.743–1.438	0.8430
9–12	0.931	0.695–1.248	0.6338	0.969	0.720–1.305	0.8365
≥13	Reference			Reference		

Adjusted for age, sex, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, coronary artery disease, previous stroke/TIA, history of smoking, initial National Institutes of Health Stroke Scale, pre-stroke modified Rankin Scale, stroke mechanisms, education years, and reperfusion therapy.
OR, odds rtio; CI, confidence interval; TIA, transient ischemic attack.

tors related to newly diagnosed HT were smoking (OR, 1.336; 95% CI, 1.191 to 1.497; *P*<0.0001) and other comorbidities were negatively associated with newly diagnosed HT. Among patients with DM, only the presence of HT was negatively associated with newly diagnosed DM, while other factors were not significant. In addition, no factors other than young age were identified for newly diagnosed AF (Table 2).

Using the linked dataset, we found that age ≤45 years was an independent factor associated with newly diagnosed major stroke risk factors after index stroke. Furthermore, patients with other comorbidities were less likely to have a new diagnosis of risk factors after index stroke. Traditional vascular risk factors account for up to 90% of the attributable risk of stroke development. Therefore, the most effective way to reduce the incidence of stroke is to control modifiable risk factors.[3,4] However, <50% of the public possesses knowledge of stroke, its risk factors, and warning signs.[2,3] According to public surveys, lower socioeconomic status, lower education, and younger age are associated with a lack of knowledge of stroke risk factors.[1,3] Consistent with previous reports, our findings revealed that age ≤45 years was an independent risk factor for newly identified major stroke in patients with index ischemic stroke.[1,2] Young people do not usually seek medical attention to identify vascular risk factors. Otherwise, they become aware of having risk factors during medical examinations for other purposes.[2,3] This partly explains why patients with comorbidities have a lower probability of a new diagnosis of vascular risk factors. Based on these results, regular check-ups during clinic visits could be an important and effective strategy for stroke prevention by identifying and controlling vascular risk factors.

Our study has several limitations. First, there could be a certain degree of unmeasured bias due to the retrospective design using a linked dataset. Second, the linked dataset did not contain data related to knowledge of risk factors in laboratory information and lifestyle aspects of patients, such as healthcare check-up results and socioeconomic status information. Third, we did not investigate risk factor awareness using a questionnaire during hospitalization. However, the status of risk factor management prior to index stroke was evaluated using the linked data. Fourth, we excluded 8.8% of the patients (n=4,578) with inaccurate information due to censored claims data after index stroke. Therefore, these factors may have affected our results.

In conclusion, this study showed that the proportion of patients with uncontrolled risk factors before index ischemic stroke was higher in younger patients (≤45 years). Public edu-

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cation about regular check-ups may contribute to an improvement in the control rate of risk factors to reduce stroke risk. Further large-scale studies are needed to confirm the relationship between clinical factors and control of risk factors among patients with ischemic stroke.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2021.03741.

References

1. Hong KS, Bang OY, Kim JS, Heo JH, Yu KH, Bae HJ, et al. Stroke statistics in Korea: Part II stroke awareness and acute stroke care, a report from the Korean Stroke Society and Clinical Research Center For Stroke. *J Stroke* 2013;15:67-77.
2. Park TH, Ko Y, Lee SJ, Lee KB, Lee J, Han MK, et al. Identifying target risk factors using population attributable risks of ischemic stroke by age and sex. *J Stroke* 2015;17:302-311.
3. Bucholz EM, Gooding HC, de Ferranti SD. Awareness of cardiovascular risk factors in U.S. young adults aged 18-39 years. *Am J Prev Med* 2018;54:e67-e77.
4. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet* 2010;376:112-123.

Correspondence: Sang-Bae Ko
Department of Neurology and Critical Care Medicine, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea
Tel: +82-2-2072-2278
Fax: +82-2-3672-7553
E-mail: sangbai1378@gmail.com
https://orcid.org/0000-0002-9429-9597

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The datasets generated and/or analyzed during the current study are not publicly available due to the data as imposed by ethical approval. Please contact the corresponding author (Sang-Bae Ko), to obtain access to the study data.

The authors have no financial conflicts of interest.

Supplementary Methods

Study population

We initially screened 52,213 patients with ischemic stroke from a large dataset by linking the Clinical Research Center for Stroke (CRCS) registry and the Health Insurance Review and Assessment Service administrative claims database with clinical data collected from patients with acute ischemic stroke within 7 days following the onset of stroke symptoms from 2007 to 2014.[1-3] The exclusion criteria for evaluating risk factors and medication information before index stroke using the linked dataset were as follows: (1) patients who were registered before January 2008 (n=4,756); (2) those with inaccurate claim data on prescribed drug information and those with inaccurate vascular risk factors according to the International Classification of Disease, Tenth Revision (ICD-10) due to censored claim data after index stroke (n=4,578).[1-4] Finally, we included 42,879 patients to evaluate clinical factors associated with uncontrolled risk factors.

Baseline characteristics and clinical information

We collected details on baseline characteristics, including demographic data (age and sex) and vascular risk factors such as hypertension (HT), diabetes mellitus (DM), dyslipidemia, coronary artery disease (CAD), atrial fibrillation (AF), history of smoking, and history of stroke/transient ischemic stroke from the linked data. The history of risk factors, such as HT, DM, and dyslipidemia, was defined as the use of antihypertensive, antidiabetic, and antidyslipidemic medications, respectively, with associated ICD-10 codes assigned within 1 year before ischemic stroke, according to the linked claims data. The history of risk factors, AF and CAD, was determined using ICD-10 codes in claims data within 1 year before the ischemic stroke. The following clinical information on ischemic stroke: severity, mechanism, prestroke functional status, history of smoking, education years, and reperfusion therapy, including intravenous thrombolysis and endovascular recanalization therapy, were obtained from the CRCS registry of linked data. Stroke mechanisms were classified into five categories according to the Trial of Org 10172 in Acute Stroke Treatment criteria as follows: (1) large artery atherosclerosis, (2) small vessel occlusion, (3) cardioembolism, (4) other determined etiology, and (5) undetermined etiology, as previously described.[5] Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) at admission and discharge. The included patients were divided into the following two age groups: (1) 45 years or younger (≤45 years) and (2) over 45 years (>45 years) for further comparison of risk factors according to age.[6,7] Patients newly diagnosed with HT or DM were defined as the use of antihypertensive or antidiabetic medications according to the ICD-10 codes of HT[8] and DM[9] after index ischemic stroke. For an accurate comparison, we defined the "non-hypertensive group" or "non-diabetic group" as patients with ICD-10 codes of HT or DM without prior claim records under these codes or prescription records of antihypertensives or antidiabetic medications before index ischemic stroke (1,605 [3.7%] patients with ICD-10 codes of HT without prescription of antihypertensives before index stroke among patients with HT; 1,076 [2.5%] patients with ICD-10 codes of DM without prescription of antidiabetic medications among those with DM). Furthermore, newly diagnosed AF was defined as patients with ICD codes of AF after index ischemic stroke. We also defined the "non-AF group" as patients whose diagnoses using ICD codes of AF were confirmed only before stroke (427 [1.0%] patients with ICD-10 codes of AF before index ischemic stroke). We evaluated the proportion of patients with newly identified major vascular risk factors, such as HT, DM in all stroke subtypes, and AF in cardioembolic stroke after index stroke and assessed clinical factors that influence uncontrolled vascular risk factors. We defined uncontrolled vascular risk factors based on the presence or absence of prescription information on risk factors at the time of the index stroke. We did not analyze the percentage of patients with dyslipidemia. The presence of dyslipidemia was defined as the use of antidyslipidemic medications. However, 34,339 (80.1%) patients were treated with antidyslipidemic drugs after index stroke, regardless of total cholesterol or low-density lipoprotein. We believed that this working definition of dyslipidemia could overestimate the true prevalence of dyslipidemia and chose not to include dyslipidemia in the analysis.

Statistical analysis

Baseline characteristics are presented as numbers (%). Continuous variables with normal distributions are presented as mean±standard deviation, and other variables that were not normally distributed are presented as medians (interquartile range). We used absolute standardized differences (ASDs) to compare baseline characteristics. ASD analysis was performed because it is expected to be more informative than *P*-values for large linked datasets. For all variables, ASDs less than 0.1 represent small standardized differences.[10,11] We performed multiple logistic regression to evaluate the relationship between clinical factors and newly diagnosed risk factors for ischemic stroke among patients using all statistically significant covariates and important clinical covariates associated with risk factors. In multivariable analyses, a two-tailed *P*-val-

ue of less than 0.05 was considered statistically significant. All statistical analyses were conducted by professional medical statisticians (J.S. Lee and J.S. Yoon) using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Supplementary Results

When comparing baseline characteristics between patients with known risk factors and those with newly identified risk factors after index stroke, those with newly diagnosed risk factors were significantly younger (Supplementary Tables 1-3). Patients with newly identified HT and DM were less likely to have other vascular risk factors (Supplementary Tables 1 and 2). Furthermore, the proportion of patients with good functional status before stroke was significantly higher among patients with newly identified HT (Supplementary Table 1). Patients with newly identified HT and AF were more likely to have higher educational levels than those with known HT or AF (Supplementary Tables 1 and 2). However, there were no differences in educational levels between patients with and without known DM (Supplementary Table 2). Among diabetic patients, newly diagnosed patients were more likely to be treated with reperfusion therapy than those previously diagnosed (Supplementary Table 2). However, newly diagnosed diabetic patients had significantly higher initial and discharge NIHSS scores (Supplementary Table 2), while stroke severity was similar between hypertensive and AF patients (Supplementary Table 3).

Supplementary References

1. Kim TJ, Lee JS, Kim JW, Oh MS, Mo H, Lee CH, et al. Building linked big data for stroke in Korea: Linkage of Stroke Registry and National Health Insurance Claims Data. *J Korean Med Sci* 2018;33:e343.
2. Kim TJ, Lee JS, Yoon JS, Oh MS, Kim JW, Jung KH, et al. Impact of the dedicated neurointensivists on the outcome in patients with ischemic stroke based on the linked big data for stroke in Korea. *J Korean Med Sci* 2020;35:e135.
3. Kim TJ, Lee JS, Oh MS, Kim JW, Yoon JS, Lim JS, et al. Predicting functional outcome based on linked data after acute ischemic stroke: S-SMART Score. *Transl Stroke Res* 2020;11:1296-1305.
4. Shin JY, Choi NK, Jung SY, Lee J, Kwon JS, Park BJ. Risk of ischemic stroke with the use of risperidone, quetiapine and olanzapine in elderly patients: a population-based, case-crossover study. *J Psychopharmacol* 2013;27:638-644.
5. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993;24:35-41.
6. Park TH, Ko Y, Lee SJ, Lee KB, Lee J, Han MK, et al. Identifying target risk factors using population attributable risks of ischemic stroke by age and sex. *J Stroke* 2015;17:302-311.
7. Goldstein LB, Adams R, Becker K, Furberg CD, Gorelick PB, Hademenos G, et al. Primary prevention of ischemic stroke: a statement for healthcare professionals from the Stroke Council of the American Heart Association. *Stroke* 2001;32:280-299.
8. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J* 2018;39:3021-3104.
9. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2019. *Diabetes Care* 2019;42(Suppl 1):S13-S28.
10. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009;28:3083-3107.
11. Kim L, Kim JA, Kim S. A guide for the utilization of Health Insurance Review and Assessment Service national patient samples. *Epidemiol Health* 2014;36:e2014008.

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Supplementary Table 1. Baseline characteristics of patients with hypertension

Characteristic	Total hypertension (n=33,462)	Newly diagnosed with hypertension (n=2,956)	Known hypertension (n=30,506)	ASD*
Age (yr)	67.0±11.5	61.8±12.4	67.5±11.3	0.4864
Age (yr)				0.2313
Age ≤45	1,435 (4.3)	281 (9.5)	1,154 (3.8)	
Age >45	32,027 (95.7)	2,675 (90.5)	29,352 (96.2)	
Male sex	19,377 (57.9)	1,963 (66.4)	17,414 (57.1)	0.1927
Diabetes mellitus	12,558 (37.5)	745 (25.2)	11,813 (38.7)	0.2930
Dyslipidemia	10,919 (32.6)	749 (25.3)	10,170 (33.3)	0.1764
Atrial fibrillation	5,932 (17.7)	325 (11.0)	5,607 (18.4)	0.2098
Coronary artery disease	2,970 (8.9)	95 (3.2)	2,875 (9.4)	0.2574
Previous stroke/TIA	6,058 (18.1)	249 (8.4)	5,809 (19.0)	0.3122
Smoking	13,108 (18.1)	1,493 (50.5)	11,615 (38.1)	0.2523
Pre-stroke mRS=0	25,378 (76.0)	2,388 (80.9)	22,990 (75.6)	0.1299
Initial NIHSS	3.0 (1.0–6.0)	3.0 (1.0–5.0)	3.0 (1.0–6.0)	0.0760
Stroke mechanisms				0.1842
LAA	11,853 (36.1)	973 (33.6)	10,880 (36.4)	
SVO	8,622 (26.3)	925 (32.0)	7,697 (25.7)	
CE	5,724 (17.5)	380 (13.1)	5,344 (17.9)	
Other determined	583 (1.8)	74 (2.6)	509 (1.7)	
Undetermined	6,008 (18.3)	541 (18.7)	5,467 (18.3)	
Education years				0.2281
0-3	1,294 (5.5)	77 (3.7)	1,217 (5.7)	
4-6	7,229 (30.9)	483 (23.5)	6,746 (31.7)	
7-9	4,386 (18.8)	402 (19.5)	3,984 (18.7)	
9-12	6,587 (28.2)	701 (34.0)	5,886 (27.6)	
≥13	3,869 (16.6)	397 (19.3)	3,472 (16.3)	
Reperfusion therapy				0.0248
IV thrombolysis only	2,519 (7.5)	237 (8.0)	2,282 (7.5)	
ERT only	541 (1.6)	43 (1.5)	498 (1.6)	
Combined IV thrombolysis and ERT	717 (2.1)	65 (2.2)	652 (2.1)	
Discharge NIHSS	2.0 (0.0–4.0)	2.0 (0.0–4.0)	2.0 (1.0–4.0)	0.0577

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
ASD, absolute standardized difference; TIA, transient ischemic attack; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; LAA, large artery atherosclerosis; SVO, small vessel occlusion; CE, cardioembolism; IV, intravenous, ERT, endovascular recanalization therapy.
*ASD >0.1, considered meaningful imbalances.

Supplementary Table 2. Baseline characteristics of patients with diabetes mellitus

Characteristic	Total diabetes mellitus (n=14,242)	Newly diagnosed with diabetes mellitus (n=709)	Known diabetes mellitus (n=13,533)	ASD*
Age (yr)	66.3±10.7	66.4±12.0	66.3±10.6	0.0092
Age (yr)				0.1200
Age ≤45	502 (3.5)	42 (5.9)	460 (3.4)	
Age >45	13,740 (96.5)	667 (94.1)	13,073 (96.6)	
Male sex	8,554 (60.1)	423 (59.7)	8,131 (60.1)	0.0086
Hypertension	11,469 (80.5)	515 (72.6)	10,954 (80.9)	0.1977
Dyslipidemia	5,472 (38.4)	233 (32.9)	5,239 (38.7)	0.1223
Atrial fibrillation	2,022 (14.2)	142 (20.0)	1,880 (13.9)	0.1641
Coronary artery disease	1,356 (9.5)	61 (8.6)	1,295 (9.6)	0.0336
Previous stroke/TIA	2,825 (19.8)	120 (16.9)	2,705 (20.0)	0.0790
Smoking	5,840 (41.0)	288 (40.6)	5,552 (41.0)	0.0082
Pre-stroke mRS=0	10,567 (74.3)	530 (75.0)	10,037 (74.3)	0.0158
Initial NIHSS	3.0 (1.0–6.0)	4.0 (2.0–8.0)	3.0 (1.0–6.0)	0.2735
Stroke mechanisms				0.2052
LAA	5,615 (40.1)	281 (40.1)	5,334 (40.1)	
SVO	3,797 (27.1)	149 (21.3)	3,648 (27.5)	
CE	1,946 (13.9)	141 (20.1)	1,805 (13.6)	
Other determined	187 (1.3)	11 (1.6)	176 (1.3)	
Undetermined	2,442 (17.5)	119 (17.0)	2,323 (17.5)	
Education years				0.0306
0–3	519 (5.1)	24 (4.9)	495 (5.12)	
4–6	3,014 (29.7)	150 (30.7)	2,864 (29.62)	
7–9	2,027 (20.0)	94 (19.3)	1,933 (19.99)	
9–12	2,927 (28.8)	142 (29.1)	2,785 (28.80)	
≥13	1,670 (16.4)	78 (16.0)	1,592 (16.46)	
Reperfusion therapy				0.2427
IV thrombolysis only	841 (5.9)	73 (10.3)	768 (5.7)	
ERT only	202 (1.4)	18 (2.5)	184 (1.4)	
Combined IV thrombolysis and ERT	237 (1.7)	26 (3.7)	211 (1.6)	
Discharge NIHSS	2.0 (1.0–4.0)	2.0 (1.0–6.0)	2.0 (1.0–4.0)	0.2658

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
ASD, absolute standardized difference; TIA, transient ischemic attack; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; LAA, large artery atherosclerosis; SVO, small vessel occlusion; CE, cardioembolism; IV, intravenous; ERT, endovascular recanalization therapy.
*ASD >0.1, considered meaningful imbalances.

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Supplementary Table 3. Baseline characteristics of patients with atrial fibrillation in cardioembolic stroke

Characteristic	Total atrial fibrillation (n=4,069)	Newly diagnosed with atrial fibrillation (n=648)	Known atrial fibrillation (n=3,421)	ASD*
Age (yr)	69.8±10.8	68.3±12.1	70.1±10.5	0.1626
Age (yr)				0.1667
Age ≤45	102 (2.5)	33 (5.1)	69 (2.0)	
Age >45	3,967 (97.5)	615 (94.9)	3,352 (98.0)	
Male sex	2,164 (53.2)	375 (57.9)	1,789 (52.3)	0.1123
Hypertension	3,095 (76.1)	486 (75.0)	2,609 (76.3)	0.0295
Diabetes mellitus	1,146 (28.2)	185 (28.5)	961 (28.1)	0.0102
Dyslipidemia	1,216 (29.9)	194 (29.9)	1,022 (29.9)	0.0014
Coronary artery disease	599 (14.7)	84 (13.0)	515 (15.1)	0.0603
Previous stroke/TIA	713 (17.5)	112 (17.3)	601 (17.6)	0.0075
Smoking	1,203 (29.6)	216 (33.3)	987 (28.9)	0.0969
Pre-stroke mRS=0	3,097 (76.1)	506 (78.1)	2,591 (75.7)	0.0557
Initial NIHSS	5.0 (2.0–13.0)	5.0 (2.0–13.0)	5.0 (2.0–12.0)	0.0438
Education years				0.1112
0–3	243 (8.0)	29 (6.2)	214 (8.3)	
4–6	940 (30.8)	134 (28.6)	806 (31.2)	
7–9	538 (17.6)	86 (18.4)	452 (17.5)	
9–12	779 (25.5)	125 (26.7)	654 (25.3)	
≥13	552 (18.1)	94 (20.1)	458 (17.7)	
Reperfusion therapy				0.0276
IV thrombolysis only	610 (15.0)	102 (15.7)	508 (14.8)	
ERT only	179 (4.4)	28 (4.3)	151 (4.4)	
Combined IV thrombolysis and ERT	362 (8.9)	59 (9.1)	303 (8.9)	
Discharge NIHSS	2.0 (0.0–6.0)	2.0 (0.0–6.0)	2.0 (0.0–6.0)	0.0509

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
ASD, absolute standardized difference; TIA, transient ischemic attack; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; IV, intravenous; ERT, endovascular recanalization therapy.
*ASD >0.1, considered meaningful imbalances.