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

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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). 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. 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).

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-
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 | 0.2567 |
| No | 1,483 (84.1) | 32,024 (92.3) | |
| Yes | 281 (15.9) | 2,675 (7.7) | |
| Diabetes mellitus (n=14,242) | | | |
| New onset diabetes mellitus | 653 | 16,296 | 0.1049 |
| No | 611 (93.6) | 15,629 (95.9) | |
| Yes | 42 (6.4) | 667 (4.1) | |
| Atrial fibrillation (n=4,069) in cardioembolic stroke | | | |
| New onset atrial fibrillation | 102 | 3,967 | |
| 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 | | 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 | | | | |
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 identified 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-

### 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

| Variable                  | Crude analysis | Adjusted analysis |
|---------------------------|----------------|-------------------|
| Age ≤45 years             | 2.607          | 1.707–3.382       | <0.0001 | 2.503 | 1.507–4.155 | 0.0004 |
| Female                    | 0.798          | 0.673–0.946       | 0.0092 | 0.873 | 0.678–1.215 | 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           | Reference      | Reference        |       |       |           |       |
| 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 ratio; CI, confidence interval; TIA, transient ischemic attack.
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.

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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. 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). 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, anti-diabetic, and antidyshlipemic 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. 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. 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 and DM 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 antidyshlipemic medications. However, 34,339 (80.1%) patients were treated with antidyshlipemic 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. 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

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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 |
| Male sex                        |                               |                                            |                             |      |
| 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 (20.9)                  | 483 (23.5)                                 | 6,746 (21.7)               |      |
| 7–9                             | 4,386 (14.8)                  | 402 (21.5)                                 | 3,984 (13.7)               |      |
| 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)                       | 0.1200|
| Age >45                              | 13,740 (96.5)                      | 667 (94.1)                                    | 13,073 (96.6)                   | 0.1200|
| 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)                    | 0.2052|
| SVO                                  | 3,797 (27.1)                       | 149 (21.3)                                    | 3,648 (27.5)                    | 0.2052|
| CE                                   | 1,946 (13.9)                       | 141 (20.1)                                    | 1,805 (13.6)                    | 0.2052|
| Other determined                     | 187 (1.3)                          | 11 (1.6)                                      | 176 (1.3)                       | 0.2052|
| Undetermined                         | 2,442 (17.5)                       | 119 (17.0)                                    | 2,323 (17.5)                    | 0.2052|
| **Education years**                  |                                    |                                               |                                 | 0.0306|
| 0–3                                  | 519 (5.1)                          | 24 (4.9)                                      | 495 (5.1)                       | 0.0306|
| 4–6                                  | 3,014 (29.7)                       | 150 (30.7)                                    | 2,864 (29.6)                    | 0.0306|
| 7–9                                  | 2,027 (20.0)                       | 94 (19.3)                                     | 1,933 (19.9)                    | 0.0306|
| 9–12                                 | 2,927 (28.8)                       | 142 (29.1)                                    | 2,785 (28.8)                    | 0.0306|
| ≥13                                  | 1,670 (16.4)                       | 78 (16.0)                                     | 1,592 (16.4)                    | 0.0306|
| **Reperfusion therapy**              |                                    |                                               |                                 | 0.2427|
| IV thrombolysis only                 | 841 (5.9)                          | 73 (10.3)                                     | 768 (5.7)                       | 0.2427|
| ERT only                             | 202 (1.4)                          | 18 (2.5)                                      | 184 (1.4)                       | 0.2427|
| Combined IV thrombolysis and ERT    | 237 (1.7)                          | 26 (3.7)                                      | 211 (1.6)                       | 0.2427|
| 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.
### 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.