Supplemental Materials

Table I. Demographic and clinical characteristics of included versus excluded participants.

Characteristics	Included (n=12180)	Excluded (n=2986)	P-value
Age, y, median (IQR)	63 (54–70)	62 (53–70)	0.012
Women, n (%)	3818 (31.35%)	984 (32.95%)	0.091
mRS prior to current event, median (IQR)	0 (0–1)	0 (0–0)	<0.001
BMI, median (IQR), kg/m^2	24.49 (22.58–26.57)	24.49 (22.75–26.42)	0.875
Medical history, n (%)			
Ischaemic stroke	2495 (20.48%)	654 (21.90%)	0.087
TIA	257 (2.11%)	159 (5.32%)	<0.001
Myocardial infarction	1213 (9.96%)	395 (13.23%)	<0.001
Known atrial fibrillation or flutter	827 (6.79%)	192 (6.43%)	0.482
Hypertension	7675 (63.01%)	1819 (60.92%)	0.034
Dyslipidaemia	923 (7.58%)	268 (8.98%)	0.011
Diabetes mellitus	2812 (23.09%)	698 (23.38%)	0.737
Current or previous smoker, n (%)	4427 (36.35%)	985 (32.99%)	<0.001
Baseline blood pressure, mmHg			
<140/90	2580 (21.18%)	829 (27.76%)	<0.001

Baseline NIHSS score, median (IQR)	3 (2–6)	2 (0–5)	<0.001
Admitting diagnosis, n (%)			<0.001
Ischaemic stroke	11897 (97.68%)	2085 (69.83%)	
TIA	283 (2.32%)	901 (30.17%)	

IQR, interquartile range; mRS, modified Rankin Scale; BMI, body mass index; NIHSS, NIH Stroke Scale.

Table II. Baseline characteristics of the study population

Characteristics	Study population (n=12180)
Age, y, median (IQR)	63 (54-70)
Women, n (%)	3818 (31.4%)
mRS prior to current event, median (IQR)	0 (0-1)
BMI, median (IQR), kg/m^2	24.5 (22.6-26.6)
Medical history, n (%)	
Ischaemic stroke	2495 (20.5%)
TIA	257 (2.1%)
Myocardial infarction	1213 (10.0%)
Known atrial fibrillation or flutter	827 (6.8%)
Hypertension	7675 (63.0%)
Dyslipidaemia	923 (7.6%)
Diabetes mellitus	2812 (23.1%)
Current or previous smoker, n (%)	3897 (32.0%)
Baseline blood pressure, mmHg	
<140/90	2850 (21.2%)
Baseline NIHSS score, median (IQR)	3 (2–6)
Brain imaging	12180 (100%)
DWI	12180 (100%)
Evaluation of intracranial artery	11586 (95.1%)
MRA	10251 (88.5%)
CTA	1287 (11.1%)

DSA	48 (0.4%)
Evaluation of extracranial artery	11454 (94.0%)
Carotid artery doppler	9360 (81.6%)
CTA	1164 (10.2%)
CE-MRA	860 (7.5%)
DSA	70 (0.6%)
Evaluation of cardiac rhythm	
EKG	11150 (94.3%)
Holter	9884 (83.6%)
Evaluation of cardiac structure	
TTE	11219 (94.7%)
TEE	11 (0.09%)

IQR, interquartile range; mRS, modified Rankin Scale; BMI, body mass index; NIHSS, NIH Stroke Scale; MRA, Magnetic Resonance Angiography; CTA, computed tomography angiography; DSA, digital subtraction angiography; CE-MRA, contrast-enhanced magnetic resonance angiography; TTE, transthoracic echocardiography; TEE, transoesophageal echocardiography.

Table III. Univariate analysis of potential causes of inconsistency between non-centralised and centralised aetiologic sub-classification of the study population.

LAA:

Variable	Consistent LAA (n=2517)	Centrally reassigned LAA (n=4886)	Newly diagnosed LAA (n=735)	P-value
Age, y, median (IQR)	63 (55–70)	63 (55–71)	63 (55–70)	0.452
Women, n (%)	773 (30.7%)	1496 (30.6%)	232 (31.6%)	0.874
mRS prior to current event, median (IQR)	0 (0–1)	0 (0–1)	0 (0–1)	0.239
BMI, median (IQR), kg/m^2	24.49 (22.60–26.57)	24.47 (22.60–26.42)	24.56 (22.58–26.81)	0.248
Medical history, n (%)				
Ischaemic stroke	618 (24.6%)	1037 (21.2%)	150 (20.4%)	0.002
TIA	84 (3.3%)	101 (2.1%)	15 (2.0%)	0.003
Myocardial infarction	290 (11.5%)	486 (1.0%)	64 (8.7%)	0.035
Known atrial fibrillation or flutter	0 (0%)	270 (5.5%)	0 (0%)	<0.001
Hypertension	1661 (66.0%)	3121 (63.9%)	470 (64.0%)	0.186
Dyslipidaemia	225 (9.0%)	360 (7.4%)	53 (7.2%)	0.047
Diabetes mellitus	661(26.2%)	1178(24.1%)	169(23.0%)	0.068

Current or previous smoker, n (%)	932(37.0%)	1779(36.4%)	248(33.8%)	0.263
Baseline blood pressure, mmHg				
<140/90	1990 (79.1%)	3887 (79.6%)	568 (77.3%)	0.359
Baseline NIHSS score, median (IQR)	4 (2–8)	4 (2–6)	3 (1–5)	<0.01
Inpatient department (n, %)				
Stroke unit	527 (20.9%)	1121 (23.0%)	158 (21.5%)	0.129
General neurological ward	1887 (75.0%)	3569 (73.1%)	537 (73.1%)	0.191
Neurosurgical ward	3 (0.1%)	7 (0.1%)	2 (0.3%)	0.632
Neurointerventional ward	0 (0%)	10 (0.2%)	0 (0%)	0.036
Neuro-ICU	53 (2.1%)	104 (2.1%)	17 (2.3%)	0.941
ICU	22 (0.9%)	44 (0.9%)	15 (2.0%)	0.011
General medical ward	43 (1.7%)	95 (1.9%)	10 (1.4%)	0.480
Geological region				<0.001
West	170 (6.8%)	365 (7.5%)	93 (12.7%)	
Middle	943 (37.5%)	1863 (38.1%)	249 (33.9%)	
East	1404 (55.8%)	2658 (54.4%)	393 (53.5%)	
Area				0.001

Rural	545 (21.7%)	990 (20.3%)	192 (26.1%)	
Urban	1972 (78.4%)	3896 (79.7%)	543 (73.9%)	
Hospital type				0.020
Secondary	305 (12.1%)	667 (13.7%)	117 (15.9%)	
Tertiary	2212 (87.9%)	4219 (86.4%)	618 (84.1%)	
Evaluation of intracranial artery				0.003
MRA	2203 (88.1%)	4049 (89.8%)	632 (86.5%)	
CTA	277 (11.1%)	449 (10.0%)	95 (13.0%)	
DSA	20 (0.9%)	13 (0.3%)	4 (0.6%)	
Evaluation of extracranial artery				<0.001
Carotid artery doppler	1898 (78.7%)	3736 (82.0%)	546 (78.7%)	
CTA	282 (11.7%)	380 (8.3%)	102 (14.7%)	
CE-MRA	199 (8.3%)	419 (9.2%)	40 (5.8%)	
DSA	28 (1.2%)	18 (0.4%)	5 (0.7%)	
Evaluation of cardiac rhythm				
EKG	2300 (94.9%)	4461 (94.2%)	685 (94.9%)	0.499

Holter	2018 (83.3%)	3899 (82.3%)	622 (85.9%)	0.051
Evaluation of cardiac structure				
TTE	2297 (94.8%)	4450 (93.8%)	692 (95.7%)	0.051
TEE	0 (0%)	0 (0%)	0 (0%)	NE

CE:

Variables	Consistent CE (n=284)	Centrally reassigned CE (n=266)	Newly diagnosed CE (n=449)	P value
Age, y, median (IQR)	71.0 (62.0–77.0)	66.5 (57.0–76.0)	70.0 (63.0–77.0)	0.001
Women, n (%)	99 (34.9%)	119 (44.7%)	171 (38.1%)	0.053
mRS prior to current event, median (IQR)	0 (0–0)	0 (0–1)	0 (0–1)	0.081
BMI, median (IQR), kg/m^2	24.0 (21.5–26.1)	24.0 (21.8–26.1)	24.2 (22.5–26.1)	0.238
Medical history, n (%)				
Ischaemic stroke	60 (21.1%)	51 (19.2%)	97 (21.6%)	0.733
TIA	2 (0.7%)	3 (1.1%)	4 (0.9%)	0.871
Myocardial infarction	50 (17.6%)	60 (22.6%)	84 (18.7%)	0.300
Known atrial fibrillation or flutter	261 (91.9%)	160 (60.2%)	234 (52.1%)	<0.001
Hypertension	149 (52.5%)	143 (53.8%)	286 (63.7%)	0.003
Dyslipidaemia	9 (3.2%)	14 (5.3%)	30 (6.7%)	0.118
Diabetes mellitus	40 (14.1%)	46 (17.3%)	103 (23.0%)	0.009
Current or previous smoker, n (%)	74 (26.1%)	80 (30.1%)	125 (27.8%)	0.575
Baseline blood pressure, mmHg				

<140/90	210 (73.9%)	191 (71.8%)	345 (76.8%)	0.309
Baseline NIHSS score, median (IQR)	4 (2–8)	5 (2–10)	4 (2–7)	<0.001
Inpatient department (n, %)				
Stroke unit	82 (29.0%)	64 (24.1%)	114 (25.4%)	0.402
General neurological ward	178 (62.7%)	178 (67.0%)	314 (69.9%)	0.125
Neurosurgical ward	1 (0.4%)	0 (0%)	0 (0%)	0.284
Neurointerventional ward	0 (0%)	1 (0.4%)	1 (0.2%)	0.609
Neuro-ICU	21 (7.4%)	14 (5.3%)	10 (2.2%)	0.004
ICU	4 (1.4%)	9 (3.4%)	9 (2.0%)	0.268
General medical ward	5 (1.8%)	3 (1.1%)	6 (1.3%)	0.809
Geological region				0.010
West	41 (14.4%)	41 (15.4%)	45 (10.2%)	
Middle	75 (26.4%)	94 (35.3%)	128 (28.5%)	
East	168 (59.2%)	131 (49.3%)	276 (61.5%)	
Area				0.736
Rural	50 (17.6%)	42 (15.8%)	81 (18.0%)	
Urban	234 (82.4%)	224 (84.2%)	368 (82.0%)	

Hospital type				0.047
Secondary	20 (7.1%)	17 (6.4%)	50 (11.1%)	
Tertiary	264 (93.0%)	249 (93.6%)	399 (88.9%)	
Evaluation of intracranial artery				0.035
MRA	225 (86.5%)	217 (83.1%)	367 (90.8%)	
CTA	34 (13.1%)	44 (16.9%)	36 (8.9%)	
DSA	1 (0.4%)	0 (0%)	1 (0.3%)	
Evaluation of extracranial artery				0.004
Carotid artery doppler	211 (79.0%)	185 (74.0%)	346 (84.4%)	
CTA	29 (10.9%)	40 (16.0%)	25 (6.1%)	
CE-MRA	23 (8.6%)	23 (9.2%)	37 (9.0%)	
DSA	4 (1.5%)	2 (0.8%)	2 (0.5%)	
Evaluation of cardiac rhythm				
EKG	268 (96.4%)	243 (93.1%)	419 (96.8%)	0.056
Holter	245 (87.8%)	229 (87.7%)	358 (82.1%)	0.046
Evaluation of cardiac structure				
TTE	271 (97.1%)	246 (93.9%)	416 (95.4%)	0.191

TEE	0 (0%)	0 (0%)	0 (0%)	NE

SVO:

Variables	Consistent SVO (n=1193)	Centrally reassigned SVO (n=2003)	Newly diagnosed SVO (n=1749)	P value
Age, y, median (IQR)	61 (53–68)	62 (54–69)	62 (54–69)	<0.001
Women, n (%)	362 (30.3%)	659 (33.0%)	472 (27.0%)	<0.001
mRS prior to current event, median (IQR)	0 (0–0)	0 (0–0)	0 (0–1)	<0.001
BMI, median (IQR), kg/m^2	24.8 (23.0–26.9)	24.6 (22.6–26.7)	24.5 (22.9–26.4)	0.099
Medical history, n (%)				
Ischaemic stroke	220 (18.4%)	346 (17.3%)	363 (20.8%)	0.023
TIA	16 (1.3%)	37 (1.9%)	26 (1.5%)	0.489
Myocardial infarction	87 (7.3%)	163 (8.1%)	124 (7.1%)	0.442
Known atrial fibrillation or flutter	0 (0%)	65 (3.3%)	0 (0%)	<0.001
Hypertension	762 (63.9%)	1244 (62.1%)	1156 (66.1%)	0.040
Dyslipidaemia	103 (8.6%)	138 (6.9%)	118 (6.8%)	0.109
Diabetes mellitus	249 (20.9%)	431 (21.5%)	460 (26.3%)	<0.001
Current or previous smoker, n (%)	490 (41.1%)	707 (35.3%)	672 (38.4%)	0.004
Baseline blood pressure, mmHg				

<140/90	970 (81.3%)	1582 (79.0%)	1421 (81.3%)	0.138
Baseline NIHSS score, median (IQR)	2 (1–4)	3 (1–5)	3 (1–5)	<0.001
Inpatient department (n, %)				
Stroke unit	250 (21.0%)	421 (21.0%)	390 (22.3%)	0.565
General neurological ward	922 (77.3%)	1524 (76.1%)	1292 (73.9%)	0.085
Neurosurgical ward	1 (0.1%)	6 (0.3%)	1 (0.1%)	0.136
Neurointerventional ward	0 (0%)	1 (0.1%)	3 (0.2%)	0.225
Neuro-ICU	13 (1.1%)	28 (1.4%)	32 (1.8%)	0.245
ICU	3 (0.3%)	22 (1.1%)	16 (0.9%)	0.034
General medical ward	9 (0.8%)	22 (1.1%)	35 (2.0%)	0.007
Geological region				0.006
West	104 (8.7%)	142 (7.1%)	157 (9.0%)	
Middle	424 (35.5%)	714 (35.7%)	688 (39.3%)	
East	665 (55.7%)	1147 (57.3%)	904 (51.7%)	
Area				<0.001
Rural	410 (34.4%)	679 (33.9%)	338 (19.3%)	
Urban	783 (65.6%)	1324 (66.1%)	1411 (80.7%)	

Hospital type				<0.001
Secondary	220 (18.4%)	400 (20.0%)	236 (13.5%)	
Tertiary	973 (81.6%)	1603 (80.0%)	1513 (86.5%)	
Evaluation of intracranial artery				0.13
MRA	1050 (91.1%)	1704 (88.7%)	1479 (90.4%)	
CTA	101 (8.8%)	213 (11.1%)	151 (9.2%)	
DSA	2 (0.2%)	5 (0.3%)	7 (0.4%)	
Evaluation of extracranial artery				<0.001
Carotid artery doppler	1009 (88.1%)	1586 (83.9%)	1376 (82.8%)	
CTA	92 (8.0%)	192 (10.2%)	142 (8.5%)	
CE-MRA	42 (3.7%)	105 (5.6%)	134 (8.1%)	
DSA	2 (0.2%)	8 (0.4%)	10 (0.6%)	
Evaluation of cardiac rhythm				
EKG	1098 (94.7%)	1870 (95.8%)	1614 (94.7%)	0.234
Holter	1004 (86.6%)	1695 (86.7%)	1400 (82.2%)	<0.001
Evaluation of cardiac structure				
TTE	1140 (97.9%)	1885 (96.3%)	1607 (94.1%)	<0.001

TEE	0 (0%)	0 (0%)	0 (0%)	NE

OE:

Variables	Consistent OE (n=20)	Centrally reassigned OE (n=451)	Newly diagnosed OE (n=144)	P value
Age, y, median (IQR)	54.5 (41.0–63.5)	62.0 (53.0–70.0)	61.0 (50.5–68.0)	0.033
Women, n (%)	10 (50%)	126 (27.9%)	65 (45.1%)	<0.001
mRS prior to current event, median (IQR)	0 (0–0)	0 (0–1)	0 (0–1)	0.350
BMI, median (IQR), kg/m^2	21.8(20.1–26.2)	24.2(22.5–26.3)	24.2(22.5–26.4)	0.070
Medical history, n (%)				
Ischaemic stroke	4 (20%)	69 (15.3%)	25 (17.4%)	0.740
TIA	1 (5%)	7 (1.6%)	6 (4.2%)	0.132
Myocardial infarction	1 (5%)	34 (7.5%)	10 (6.9%)	0.896
Known atrial fibrillation or flutter	0 (0%)	29 (6.4%)	0 (0%)	0.004
Hypertension	12 (60.0%)	282 (62.5%)	85 (59.0%)	0.745
Dyslipidaemia	1 (5%)	33 (7.3%)	7 (4.9%)	0.563
Diabetes mellitus	3 (15%)	110 (24.4%)	29 (20.1%)	0.392
Current or previous smoker, n (%)	4 (20%)	153 (33.9%)	47 (32.6%)	0.428
Baseline blood pressure, mmHg				

<140/90	13 (65%)	341 (75.6%)	102 (70.8%)	0.333
Baseline NIHSS score, median (IQR)	3.5 (1.5–10.0)	3.0 (1.0–5.0)	3.0 (2.0–6.0)	0.078
Inpatient department (n, %)				
Stroke unit	7 (35.0%)	135 (30.0%)	27 (18.6%)	0.024
General neurological ward	13 (65%)	288 (63.9%)	114 (79.2%)	0.003
Neurosurgical ward	0 (0%)	0 (0%)	1 (0.7%)	0.20
Neurointerventional ward	0 (0%)	0 (0%)	0 (0%)	NA
Neuro-ICU	0 (0%)	15 (3.3%)	3 (2.1%)	0.544
ICU	0 (0%)	12 (2.7%)	1 (0.7%)	0.289
General medical ward	0 (0%)	6 (1.3%)	1 (0.7%)	0.73
Geological region				0.016
West	1 (5%)	95 (21.1%)	15 (10.4%)	
Middle	7 (35%)	97 (21.5%)	40 (27.8%)	
East	12 (60%)	259 (57.4%)	89 (61.8%)	
Area				0.32
Rural	3 (15.0%)	44 (9.8%)	20 (13.9%)	
Urban	17 (85.0%)	407 (90.2%)	124 (86.1%)	

Hospital type				0.42
Secondary	1 (5%)	36 (8.0%)	7 (4.9%)	
Tertiary	19 (95%)	415 (92.0%)	137 (95.1%)	
Evaluation of intracranial artery				0.229
MRA	12 (60.0%)	333 (79.3%)	105 (79.6%)	
CTA	8 (40.0%)	81 (19.3%)	26 (19.7%)	
DSA	0 (0%)	6 (1.4%)	1 (0.8%)	
Evaluation of extracranial artery				0.284
Carotid artery doppler	12 (66.7%)	311 (76.2%)	98 (72.1%)	
CTA	6 (33.3%)	72 (17.7%)	24 (17.7%)	
CE-MRA	0 (0%)	18 (4.4%)	13 (9.6%)	
DSA	0 (0%)	6 (1.5%)	1 (0.7%)	
Evaluation of cardiac rhythm				
EKG	16 (80.0%)	387 (87.8%)	131 (96.3%)	0.007
Holter	13 (65.0%)	325 (73.4%)	110 (80.9%)	0.124
Evaluation of cardiac structure				

TTE	19 (95.0%)	400 (90.1%)	129 (94.9%)	0.189
TEE	0 (0%)	0 (0%)	0 (0%)	NE

LAA, large artery atherosclerosis; CE, cardiac embolism; SAO, small vessel occlusion; OE, other determined cause; UE, undetermined cause; Neuro-ICU, neurological intensive care unit; ICU, intensive care unit; West includes Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia, and Xinjiang; Middle includes Shanxi, Anhui, Jiangxi, Henan, Hubei, and Hunan; East include Beijing, Tianjin, Hebei, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, Hainan, Liaoning, Jilin, and Heilongjiang; IQR, interquartile range; mRS, modified Rankin Scale; BMI, body mass index; NIHSS, NIH Stroke Scale; MRA, Magnetic Resonance Angiography; CTA, Computed Tomography Angiography; DSA, Digital Subtraction Angiography; CE-MRA, Contrast-Enhanced Magnetic Resonance Angiography; TTE, transthoracic echocardiography and TEE, transoesophageal echocardiography.

Table IV. Medication of patients categorised based on the consistency of centralised and discharge subtype in the subgroup with complete information

Treatment	Consistent LAA (n/N, %)	Centrally reassigned LAA (n/N, %)	Newly diagnosed LAA (n/N, %)	P-value
Discharge treatment				
Antiplatelet	2070/2254, 91.8%	3708/4011, 92.5%	627/664, 94.4%	0.085
Oral anticoagulation	4/2254, 0.2%	57/4011, 1.4%	6/664, 0.9%	<0.0001
Oral anticoagulation with indications*	0/1, 0%	47/284, 16.6%	0/0, 0%	
Lipid-lowering in patients with dyslipidaemia	189/208, 90.9%	288/298, 96.6%	46/48, 95.8%	
Antidiabetic in patients with diabetes	464/587, 79.0%	752/946, 79.5%	119/150, 79.3%	
Antihypertensive in patients with hypertension	894/1500, 59.6%	1682/2547, 66.0%	287/428, 67.1%	
Treatment	**Consistent CE (n/N, %)**	**Centrally reassigned CE (n/N, %)**	**Newly diagnosed CE (n/N, %)**	**P-value**
Discharge treatment				
Antiplatelet	99/236, 42.0%	136/230, 59.1%	295/360, 81.9%	<0.0001
Antiplatelet with indication within cardioembolic stroke†	2/7, 28.6%	2/4, 50.0%	4/5, 80.0%	

Oral anticoagulation	126/236, 53.4%	62/230, 27.0%	35/360, 9.7%	<0.0001
Oral anticoagulation with indications*	122/227, 53.7%	54/141, 38.3%	34/234, 14.5%	<0.0001
Lipid-lowering in patients with dyslipidaemia	8/8, 100.0%	12/12, 100.0%	23/25, 92.0%	
Antidiabetic in patients with diabetes	24/32, 75.0%	32/42, 76.2%	64/84, 76.2%	
Antihypertensive in patients with hypertension	83/123, 67.5%	63/122, 51.6%	153/229, 66.8%	
Treatment	**Consistent SVO (n/N, %)**	**Centrally reassigned SVO (n/N, %)**	**Newly diagnosed SVO (n/N, %)**	**P-value**
Discharge treatment				
Antiplatelet	1063/1085, 98.0%	1706/1782, 95.7%	1381/1469, 94.0%	<0.0001
Oral anticoagulation	0/1085, 0%	13/1782, 0.7%	4/1469, 0.3%	0.007
Oral anticoagulation with indications*	0/0, 0%	8/72, 11.1%	0/0, 0%	
Lipid-lowering in patients with dyslipidaemia	93/95, 97.9%	121/124, 97.6%	96/99, 97.0%	
Antidiabetic in patients with diabetes	189/228, 82.9%	322/379, 85.0%	301/367, 82.0%	
Antihypertensive in patients with hypertension	529/689, 76.8%	770/1116, 69.0%	674/976, 69.1%	

Treatment	Consistent OE (n/N, %)	Centrally reassigned, OE (n/N, %)	Newly diagnosed OE (n/N, %)	P-value
Discharge treatment				
Antiplatelet	14/16, 87.5%	313/339, 92.3%	100/118, 84.8%	0.053
Oral anticoagulation	1/16, 6.3%	4/339, 1.2%	2/118, 1.7%	0.254
Oral anticoagulation with indications*	0/0, 0%	1/22, 4.6%	0/0, 0%	
Lipid-lowering in patients with dyslipidaemia	2/16, 12.5%	88/339, 26.0%	25/118, 21.2%	
Antidiabetic in patients with diabetes	4/16, 25.0%	183/339, 54.0%	40/118, 33.9%	
Antihypertensive in patients with hypertension	1/1, 100.0%	28/29, 96.6%	7/7, 100.0%	

*: Indications of oral anticoagulation treatment included mechanical prosthetic valve, mitral stenosis with atrial fibrillation, atrial fibrillation, left atrial/atrial appendage thrombus, left ventricular thrombus, and atrial flutter.

†: Indications of antiplatelet treatment within aetiologies of cardioembolic stroke included mitral valve prolapse without atrial fibrillation and mitral annulus calcification without atrial fibrillation.

LAA, large artery atherosclerosis; CE, cardiac embolism; SVO, small vessel occlusion; OE, another determined cause.

Table V. Oral anticoagulant treatment of cardioembolic stroke patients received with unchanged and reassigned subtype in the subgroup with complete information.

Treatment	Consistent CE* (n=235)			Centrally reassigned CE† (n=262)			Newly diagnosed CE‡ (n=447)		
	With indication** n=225	Without indication n=10	P value	With indication** n=161	Without indication n=101	P value	With indication** n=300	Without indication n=147	P-value
In-hospital anticoagulant	132 (58.7%)	4 (40.0%)	0.329	75 (53.2%)	18 (20.0%)	<0.0001	57 (24.5%)	8 (6.3%)	<0.0001
Warfarin	78/132 59.1%	3/4, 75.0%	0.647	39/75, 52.0%	5/90, 27.8%	0.073	19/57, 33.3%	1/8, 12.5%	0.417
LWHP	70/132 53.0%	1/4, 25.0%	0.348	45/75, 60.0%	9/18, 50.0%	0.596	34/57, 59.7%	5/8, 62.5%	1.000
Heparin	1/132 0.8%	0/4, 0%	1.000	0/75, 0%	4/18, 22.2%	0.001	1/57, 1.8%	0/8, 0%	1.000
Rivaroxaban	6/132 4.6%	0/4, 0%	1.000	2/75, 2.7%	0/18, 0%	1.000	2/57, 3.5%	0/8, 0%	1.000
Dabigatran	20/132 15.2%	1/4, 25.0%	0.493	4/75, 5.3%	1/18, 5.6%	1.000	3/57, 5.3%	0/8, 0%	1.000
Apixaban	0/132 0%	0/4, 0%	NE	0/75, 0%	0/18, 0%	NE	0/57, 0%	0/8, 0%	NE
Others	3/132 2.3%	0/4, 0%	1.000	2/75, 2.7%	1/18, 5.6%	0.480	1/57, 0%	2/8, 25.0%	0.038
Treatment	**Consistent CE§ (n=283)**			**Centrally reassigned CE || (n=261)**			**Newly diagnosed CE # (n=448)**		
	With indication n=271**	**Without indication n=12**	**P value**	**With indication** n=157**	**Without indication n=104**	**P value**	**With indication** n=300**	**Without indication n=148**	**P-value**

Discharge anticoagulant	57 (24.5%)	8 (6.3%)	<0.0001	56/139, 40.3%	8/91, 8.8%	<0.0001	36 (15.5%)	1 (0.8%)	<0.0001
Warfarin	19/57, 33.3%	1/8, 12.5%	0.417	46/56, 82.1%	7/8, 87.5%	1.000	26/36, 72.2%	1/1, 100.0%	1.000
LWHP	34/57, 59.7%	5/8, 62.5%	1.000	2/56, 3.6%	1/8, 12.5%	0.335	2/36, 5.6%	0/1, 0%	1.000
Heparin	1/57, 1.8%	0/8, 0%	1.000	0/56, 0%	0/8, 0%	NE	0/36, 0%	0/1, 0%	NE
Rivaroxaban	2/57, 3.5%	0/8, 0%	1.000	3/56, 5.4%	1/8, 12.5%	0.422	4/36, 11.1%	0/1, 0%	1.000
Dabigatran	3/57, 5.3%	0/8, 0%	1.000	5/56, 8.9%	0/8, 0%	1.000	4/36, 11.1%	0/1, 0%	1.000
Apixaban	0/57, 0%	0/8, 0%	NE	0/56, 0%	0/8, 0%	NE	0/36, 0%	0/1, 0%	NE
Others	1/57, 0%	2/8, 25.0%	0.038	0/56, 0%	0/8, 0%	NE	0/36, 0%	0/1, 0%	NE

*: missing data of two patients; †: missing data of two patients; ‡: missing data of one patient; §: missing data of one patient; | |: missing data of three patients; #: missing data of one patient; * *: Indications of oral anticoagulation treatment included mechanical prosthetic valve, mitral stenosis with atrial fibrillation, atrial fibrillation, left atrial/atrial appendage thrombus, left ventricular thrombus, and atrial flutter; CE, cardiac embolism; LWHP, low molecular weight heparin; NE, not estimable.

Supplementary Methods

Ischaemic stroke was defined as "brain, spinal cord, or retinal cell death attributable to ischaemia, based on neuropathological, neuroimaging, or clinical evidence of permanent injury" with overt symptoms.

Data collection and standard aetiologic examinations

During hospitalisation at the baseline interview, all patients without contradictions to MRI examinations were recommended for a complete aetiologic evaluation, according to the study protocol. All patients were recommended to undergo complete aetiologic evaluation during hospitalisation, including brain magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI; 3.0T or 1.5T), intracranial artery imaging (CT/MR angiography or digital subtraction angiography), extracranial artery imaging (carotid ultrasound, CT/MR angiography or digital subtraction angiography), cardiac rhythm examination (12-lead electrocardiograph or 24-hour electrocardiograph), and cardiac structure imaging (transthoracic or transoesophageal echocardiography). The MRI test could be 3.0T or 1.5T according to the available MRI machine at each individual investigation site.

Site investigators gathered the demographic information (age, sex, living condition, etc.) and medical history (history of hypertension, diabetes, myocardial infarction, ischaemic stroke, etc.) of patients at baseline face-to-face interview and performed a standardised physical examination to record vital signs (blood pressure, etc.) and other parameters (such as National Institutes of Health Stroke Scale [NIHSS]). An interactive electronic data capture (EDC) system was developed for data collection.

Except for complete entry of typing-in data elements, including demographic characteristics, physical examination results, and medical history after a face-to-face interview when admitted to participating centres, all laboratory results, auxiliary test results, and medical records were uploaded to the EDC system after the removal of private information.

Image data, including brain MRI and vascular assessment for intracranial arteries (MRA, CTA, and DSA) or extracranial arteries (CTA and CE-MRA) were saved in DICOM format on discs which were then delivered to the centralised review centre.

Aetiologic diagnosis

Non-centralised aetiologic diagnosis at participating centres

Site investigators and raters were trained by committee-assigned stroke specialists before the initiation of patient enrolment. The investigators and raters of each study site received a manual and a videotape that included a detailed description of the Trial of Org 10172 in Acute Stroke Treatment (TOAST) subtyping system and operation guidelines to determine aetiologic subtype.

Following a standard diagnostic process, the trained investigators or raters reviewed the patients' clinical, imaging, and laboratory features and categorised patients into different causative subtypes according to the TOAST system. Raters at each study site received case-based training using abstracted data from medical records. Because most of the study sites have very large neurology departments, there were many neurologists involved in patient enrolment and aetiologic diagnosis at discharge. Site raters strove to reach excellent intrarater and interrater reliability ($\kappa > 0.80$) before aetiologic diagnosis. Intrarater and interrater reliabilities were assessed and controlled by the site investigator. However, detailed information (κ) of the intrarater and interrater reliabilities were not reported to the study committee.

Centralised aetiologic diagnosis

Standardised screening report forms were generated from the EDC (See Supplementary Methods, Supplementary Materials-Screening Report Form). According to the definition used by the TOAST system, we defined the phenotypic elements of each subtype as follows.

Large-artery atherosclerosis (LAA) was determined by the presence of symptomatic intracranial/extracranial artery atherosclerotic stenosis. Symptomatic stenosis was defined as severe (50%–99%) stenosis or occlusion of clinically relevant intracranial and extracranial arteries. The relevance of intracranial artery stenosis (ICAS) and the index stroke was determined by raters. ICAS judgement was based on the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial criteria. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria were adopted to adjust the stenosis of extracranial artery stenosis (ECAS).

Cardio-embolism (CE) was determined using cardio-embolic sources. Patients were screened for high-risk and medium-risk embolic sources according to the TOAST classification system.

Small-vessel occlusion (SVO) was determined by the presence of a single relevant brain stem or subcortical hemispheric lesion which was less than 1.5 cm in diameter at the widest sectional on axial diffusion-weighted imaging (DWI).

We defined the other determined aetiology (OE) subtype based on potential causative disorders. This category included rare causes, including an intrinsic disorder with arterial wall abnormality (moyamoya disease, nonatherosclerotic vasculopathy or dissection), an iatrogenic injury to a clinically relevant artery wall (such as an injury caused by endovascular treatment), and disorders of blood composition (such as disorders of the haemostatic system).

All elements competed in a hierarchical algorithm in the first gradation of comparison (See Supplementary Materials-Decision Algorithm). When there was an evident artery wall abnormality in the absence of a high-risk CE element, the causative subtype was assigned as OE. If there was a co-existing apparent artery wall abnormality and a high-risk CE element, the subtype was considered to be undetermined aetiology (UE).

In the second gradation of comparison among patients without artery wall abnormalities, if there was only one element of LAA, high-risk CE, or disorders of blood composition (indicating OE), the subtype was classified as LAA, CE, or OE, respectively. If there were multiple elements mentioned above, the subtype was classified as UE.

In patients without elements mentioned in previous gradations, when there was only one element among the medium-risk elements of CE, the elements of SVO, or the blood composition disorder element of OE, the cause was designated as CE, SVO, or OE, respectively. When none or multiple elements mentioned above existed, the subtype of the patient was designated as UE.

Senior neurologists designed standardised online screening report forms of imaging and other auxiliary test results, which allowed a double-blind double-entry mode and senior adjudication with a blind-paired comparison mode. Raters were blinded to each other's input information. Each senior adjudicator was blinded to the raters' names. By comparing the double-entry results on the report forms, a senior adjudicator would resolve the discrepancies and finalise the entry.

During two months from Oct 2018 to Nov 2018, a total of 32 neurologists and radiologists were recruited and centrally trained to analyse all brain MRI and vascular assessment data. By reviewing imaging data, they distinguished the characteristics necessary for aetiologic classification, such as infarction pattern, location, blood supply, and stenosis of arteries, and entered the relevant information into online screening report forms. Using anonymous imaging data from 120 patients, we evaluated the interrater reproducibility for multiple raters. After a systematic comparison of entry fields within the screening report forms, we assessed the agreement and scheduled any necessary retraining. Daily feedback of difficult situations from all image analysers was received and answered by the senior analyser in a timely manner. Imaging interpretation started after excellent interrater reproducibility was achieved. From January 2019 to May 2019, a total of 10 senior radiologists from the previous 32 raters re-examined all imaging data and corrected inaccurate information within the relevant online forms for quality control. Another senior radiologist resolved any discrepancies between the senior analysers.

Fifty-seven neurologists, each with more than 5 years of clinical experience, were recruited to review auxiliary test results and to enter specific relevant parameters into the online screening report form. During data entry, the senior analyser for the group resolved disagreements among the entry fields.

Another sixteen neurologists with more than 5 years of clinical experience reviewed discharge summary screenings for any supplementary information that was essential for subtyping, such as diagnosis of a specific disease as the direct cause of ischaemic stroke, and entered these onto the online screening report form. The senior analyser for the group resolved disagreements among the entry fields.

Finally, the complete data within the screening report forms were automatically compared by the online system, and discrepancies between the two forms were resolved by a third senior analyser.

Supplementary Materials-Screening Report Form (separate file)

Supplementary Materials-Decision Algorithm (separate file)