Supplementary Table S1 Risk factors for ESUS and stroke recurrent in ESUS

Study	Design	ESUS	Control	Risk factors for ESUS
Risk factors for ESUS				
Grosse 2020[1]	• Prospective cohort of 68 patients with ESUS or paroxysmal AF-related stroke, single center, Germany	• 45 patients with ESUS	• 23 patients with AF-related stroke	• Significantly less presence of nonstenotic carotid plaques, younger age, reduced CHA_2DS_2-VASc score in ESUS
Kamran et al 2020[2]	• Retrospective cohort of 2,536 stroke patients with multiethnic Asian and African ethnicity, single center, Qatar	• 656 patients with ESUS	• 1,348 patients with noncardioembolic stroke 532 patients with cardioembolic stroke	• Multivariate analysis[a]: age, grade 2–3 diastolic dysfunction, LV regional wall motion abnormality, global hypokinesia • Multivariate analysis[b]: age, DM, LA volume, diastolic dysfunction, LV regional wall motion abnormality
Perkins et al 2020[3]	• Retrospective cohort of 2,082 stroke patients in West and South Asian and North African population, Qatar	• 634 patients with ESUS	• 1,439 patients with any other strokes	Multivariate analysis: LV regional wall motion abnormality, global hypokinesia, South Asians, grade 2–3 diastolic dysfunction
Al Khathaami et al 2019[4]	• Retrospective cohort of 147 patients with ESUS, single center, Saudi Arabia	• 39 younger adults (aged ≤50 years 26.5% of the cohort) with ESUS	• 108 older adults with ESUS	• Younger adults with ESUS compared with older adults have fewer vascular risk factors (less Htn, DM, dyslipidemia), although no difference in stroke outcomes, severity of stroke, and the duration of hospital stay.
Gąsiorek et al 2019[5]	• Prospective cohort of 520 patients with stroke, single center, Poland	• 65 patients with ESUS	• 36 matched control with no stroke but similar risk profile	• Multivariate risk factors: arterial stiffness parameter Aix 75, IVRT, LAVI, NT-pro-BNP
Meisel et al 2019[6]	• Prospective cohort of 18 patients with ESUS, single center, United States	• 18 patients with ESUS	• 37 healthy control matched in age, gender, body-surface area	• LA dysfunction and spherical remodeling, and lack of response to maximal exercise in LA function in ESUS patients
Modolo et al 2019[7]	• Retrospective cohort of 550 stroke patients, single center, Brazil	• 51 patients with ESUS	• NA	• Htn (60%), DM (34%), smoking (36%)
Ntaios et al 2015[8]	• Retrospective analysis of 2,731 patients with acute first-onset of stroke, Athens Stroke Registry, Greece	• 275 patients with ESUS	• NA	• Htn (64.7%), dyslipidemia (50.9%), covert AF (10.9%)
Risk factors for recurrence of stroke in patients with ESUS				
Hart et al 2019[9]	• Prospective trial cohort of 7,213 patients with ESUS, international • Randomized into aspirin versus rivaroxaban • Follow-up: 11 mo (median)	• 309 patients with recurrent ischemic stroke	• 6,904 patients with no recurrent ischemic stroke	• Multivariate risk factor for *recurrent ischemic stroke*: age, current smoker, previous stroke/TIA, DM, multiple acute infarcts on neuroimaging, aspirin prior to qualifying stroke, time from qualifying stroke to randomization
Ntaios et al 2017[10]	• Pooled datasets from 11 stroke registries in Europe and Asia • Follow-up: 31 mo (median)	• 1,095 patients with ESUS	• NA	• Multivariate analysis for *recurrent ischemic stroke/TIA or all-cause death*: age (not sex)
de la Riva et al 2017[11]	• Retrospective cohort of 113 patients with ESUS, single center, Spain • Follow-up: 25.6 mo (median)	• 113 patients with ESUS	• NA	• Multivariate analysis for *brain ischemia recurrence*: age, TC/HDL ratio, LDL/HDL ratio
Arauz et al 2016[12]	• Retrospective cohort from stroke registry, Mexico • Follow-up: 19 mo	• 149 patients with ESUS	• 235 patients with cardioembolic stroke	• Multivariate analysis for *stroke recurrence*: antiplatelet therapy • Multivariate analysis for *bad outcomes*: cardioembolic, ischemic cardiomyopathy, oral anticoagulation, antiplatelet therapy

Abbreviations: AF, atrial fibrillation; AIx 75, augmentation index adjusted to a heart rate of 75 beats per minute; DM, diabetes mellitus; EF, ejection fraction; HDL, high-density lipoprotein cholesterol; Htn, hypertension; IVRT, isovolumetric relaxation time; LA, left atrium; LAVI, left atrial volume index; LDL, low-density lipoprotein cholesterol; LV, left ventricle; NA, not applicable; NT-proBNP, N-terminal pro brain natriuretic peptide; TC, total cholesterol.

[a]ESUS compared with noncardioembolic stroke (large vessel and small vessel diseases).

[b]ESUS compared with cardioembolic stroke.

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