

Young ESUS

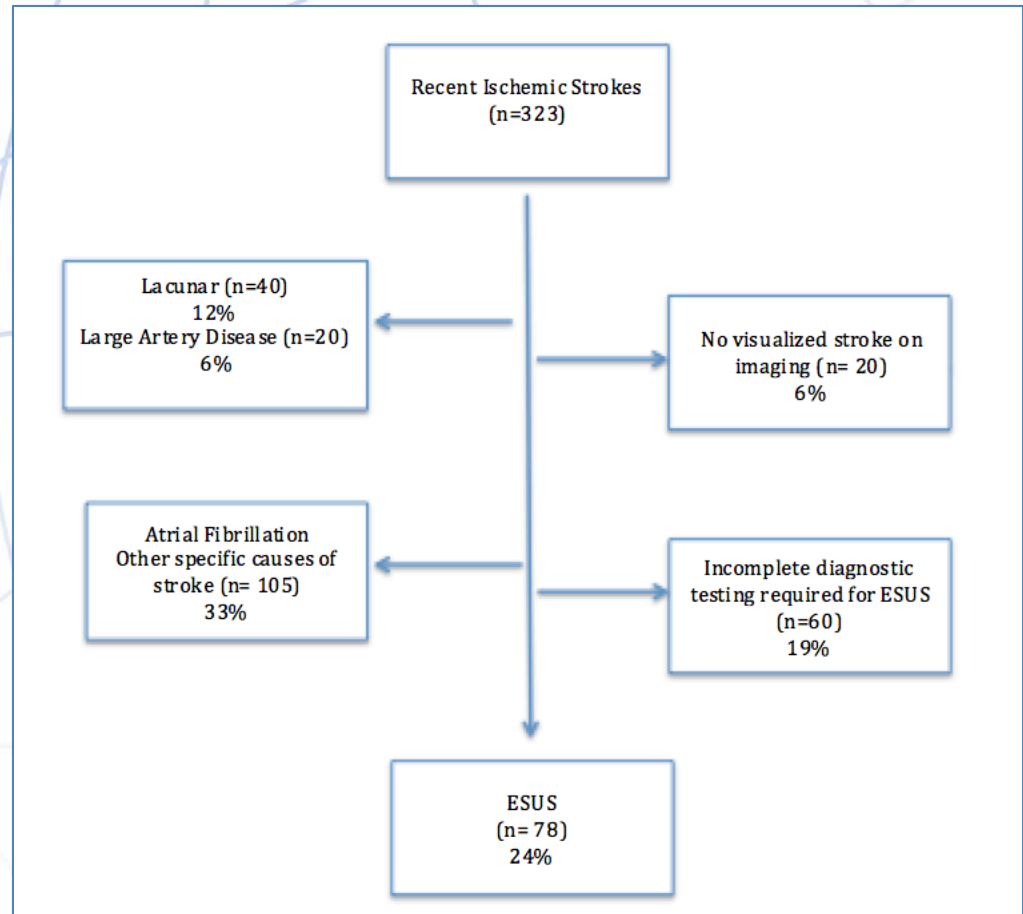
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Rationale for the Study

- Following completion of the NAVIGATE ESUS and other ESUS-related trials, clinical interest in the ESUS construct will increase exponentially
- There will be intense interest to know whether the results of these trials are generalizable to young adults with ESUS:
 - clinical characteristics
 - embolic sources
 - stroke recurrence rates
- Currently there is limited data on clinical characteristics of young ESUS patients
- The Y-ESUS Longitudinal Cohort Study will provide unique insights that would likely influence clinical practice and even guidelines

ESUS Global Registry Results

- Among 2144 patients with recent ischemic stroke from 19 stroke research centers in 19 countries, 323 (15.1%, 95%CI: 13.6-16.7%) were ≤ 50 years-old
- Of the 323 patients aged ≤ 50 years, 78 (24%, 95%CI 20%-29%) met ESUS criteria



Features of ESUS patients < 50years vs > 50years

	ESUS patients				
	Age <=50 years (N=78)		Age >50 years (N=273)		P-value**
	N ^	% or Mean	N ^	% or Mean	
Mean age (years)	78	40(9)	273	68(10)	<0.0001
Men (%)	78	67%	272	54%	0.0688
Diabetes (%)	78	21%	273	26%	0.3755
Hypertension (%)	78	36%	270	73%	<0.0001
Current Tobacco use (%)	78	28%	273	21%	0.1707
Coronary artery disease (%)	74	7%	258	11%	0.3812
History of stroke or TIA prior to index stroke (%)	78	5%	270	21%	0.0006
Heart failure (%)	73	0%	258	2%	0.3452
Hyperlipidemia (%)	72	28%	254	43%	0.0285
Peripheral vascular disease (%)	71	0%	236	4%	0.1240
Antiplatelet therapy at the time of index stroke (%)	76	11%	270	36%	<0.0001
Anticoagulant therapy at the time of index stroke (%)	72	3%	255	1%	0.2117
Median NIHSS score near admission (IQR)	58	3 (1, 7)	228	4 (2, 9)	0.0553
IV TPA for index stroke (%)	78	9%	269	19%	0.0551
Death within 30 days (%)	67	1%	208	2%	>0.90
Antithrombotic therapy at discharge					
- ASA (%)	78	59%	263	53%	0.3669
- Clopidogrel (%)	78	18%	263	19%	>0.90
- Warfarin/vitamin K antagonist only (%)	78	8%	263	3%	0.0980
- Rivaroxaban, Dabigatran or Apixaban only (%)	78	1%	263	2%	>0.90
- None only (%)	78	0%	263	2%	0.5776

ESUS – embolic strokes of undetermined source; ASA = Aspirin;

** P-values for categorical comparison - Fisher's exact test; P-values for continuous comparison - Wilcoxon rank-sum test;



Frequency of potential minor risk embolic sources among ESUS

Minor risk potential embolic sources	Age≤50 N (%)	Age>50 N (%)	P-value**
Carotid artery non-stenotic plaques*	37 (69%)	171 (82%)	0.0393
Mitral Annular calcification and thickening with myxomatous changes [#]	0 (0%)	17 (7%)	0.0296
Aortic valve stenosis and calcification [#]	1 (1%)	23 (9%)	0.0367
Hypokinetic/ Akinetic left ventricle [#]	3 (4%)	10 (4%)	>0.90
Moderate-to-severely dilated left atrium [#]	6 (8%)	13 (5%)	0.3894
Aortic arch atherosclerotic plaques [^]	1 (3%)	34 (40%)	<0.0001
Patent Foramen Ovale [#]	7 (10%)	12 (5%)	0.1487
Patent Foramen Ovale [^]	12 (32%)	19 (22%)	0.2605
Any minor risk potential embolic sources	49 (63%)	209 (77%)	0.0197
≥2 minor-risk embolic sources	11 (14%)	72 (26%)	0.0240

* In all ESUS patients excluding POCS either on CTA, MRA or carotid ultrasonography.

ESUS patients who had TTE

^ ESUS patients who had TEE.

** P-values for categorical comparison - Fisher's exact test;



Study Design

- Investigator-Initiated Study
- Study Sponsor: Population Health Research Institute (PHRI)
- 1000 ESUS patients ≤ 50 years at 85-100 sites in 13 countries
- Followed up prospectively for 18 months via telephone

Study Objectives

- Describe clinical, and imaging characteristics of ESUS patients ≤ 50 years, including antithrombotic therapy used for secondary prevention
- Explore clinical, and imaging predictors of recurrent ischemic stroke and/or death in a cohort of young ESUS patients
- Determine the rates of recurrent ischemic stroke and/or death in a well defined cohort of young ESUS patients
- Determine the rates of new onset atrial fibrillation in a well defined cohort of young ESUS patients

Inclusion/Exclusion

- Similar to NAVIGATE ESUS
- Inclusion:
 - Age ≥ 21 to ≤ 50 years
 - Index ESUS with in 60 days
 - Patients will be eligible to participate in the study even if they have additional tests/ procedures planned, e.g. implantable loop recorder, PFO closure
- Exclusion:
 - Enrollment in an investigational study on ESUS
 - If imaging of intracranial arteries are performed by CT or MR angiography, digital subtraction angiography or transcranial Doppler: $>50\%$ luminal stenosis or occlusion in arteries supplying the area of ischemia (unless deemed embolic)