

## Online Supplementary Materials

Table I. Baseline characteristics of a random sample of 275 patients collected to test the validity and reliability of SPARKLE

<b>Demographic characteristics and laboratory investigations (mean ± SD)</b>		
Age	56.97 ± 16.43	
Sex (males %)	122 (44.4%)	
TIA (n, %)	111 (40%)	
Systolic blood pressure	135.73 ± 18.38	
Diastolic blood pressure	80.47 ± 11.31	
Total Plaque Area	0.74 ± 1.08	
Total Cholesterol	6.62 ± 26.69	
Triglycerides	1.65 ± 0.98	
High-Density Lipoprotein cholesterol	1.39 ± 0.47	
Low-Density Lipoprotein cholesterol	2.8 ± 0.96	
Glucose	5.85 ± 1.73	
International Normalized Ratio	2.52 ± 15.46	
Vitamin B12	335.27 ± 234.61	
Homocysteine	9.61 ± 3.63	
Pack-Years	13.99 ± 21.75	
<b>Medical Conditions related to Stroke/TIA and Laboratory Imaging</b>		
	<b>n</b>	<b>%</b>
Myocardial Infarction	18	6.5
Hypertension	187	68
Diabetes Mellitus	39	14.2
Hyperlipidemia	221	80.7
Atrial Fibrillation	10	3.6
Current Smoking	58	21.1
Follow-up TIA	46	16.7
Follow-up Stroke	12	4.4
Follow-up Death	13	4.7
Transcranial Doppler	199	72.4
Computed Tomography	205	74.5
Magnetic Resonance Imaging	188	68.4
Echocardiography	273	99.3
Holter	102	37.1
<b>Ischemic Stroke/TIA Subtypes</b>		
	<b>n</b>	<b>%</b>
CCS large artery	40	14.5
CCS cardioembolic	138	50.2
CCS small vessel	20	7.3
CCS Other	20	7.3
CCS undetermined	57	20.7
SPARKLE large artery	59	21.5
SPARKLE cardioembolic	160	58.2
SPARKLE small vessel	19	6.9
SPARKLE Other	15	5.5
SPARKLE undetermined	22	8

TIA= Transient Ischemic Attack, CCS=Causative Classification of acute Stroke, SPARKLE= Subtypes of ischemic stroke classification system

**Table II. Cardiac Sources of Cerebrovascular Embolism<sup>1</sup>**

Adapted by permission of Wiley Publishers from: Ay H, Furie KL, Singhal A, Smith WS, Sorensen AG, Koroshetz WJ. An evidence-based causative classification system for acute ischemic stroke. *Ann Neurol* 2005 November ;58(5):688-97.

High Risk Cardiac Sources of Embolism	Left Atrial Thrombus
	Left Ventricular Thrombus
	Atrial Fibrillation (AF)
	Paroxysmal Atrial Fibrillation
	Sustained Atrial Flutter
	Recent Myocardial Infarction (within 1 month)
	Chronic Myocardial Infarction with ejection fraction <28%
	Symptomatic Congestive Heart Failure with ejection fraction <30%
	Ventricular Dyskinesia or Hypokinesia in Echocardiogram
	Rheumatoid Mitral or Aortic Valve Disease
	Bioprosthetic or Mechanical Heart Valve
	Nonbacterial Thrombotic or Infective Endocarditis
	Papillary Fibroelastoma
	Left Atrial Myxoma
Left Ventricular Aneurysm or PFO with clinical clues to paradoxical embolism*	
Low Risk Cardiac Sources of Embolism	Mitral Annular Calcification and/or Aortic Valve Calcification
	Atrial Septal Aneurysm without Shunt
	Left Ventricular Aneurysm without Thrombus or PE or DVT
	Isolated Left Atrial Smokey, without Mitral Stenosis or AF
	Mitral Valve Prolapse
	Complex Atheroma in the Ascending Aorta or Proximal Arch
Clinical clues to paradoxical embolism with negative imaging for shunt*	

PFO: Patent Foramen Ovale

DVT: Deep Venous Thrombosis

PE: Pulmonary Embolism

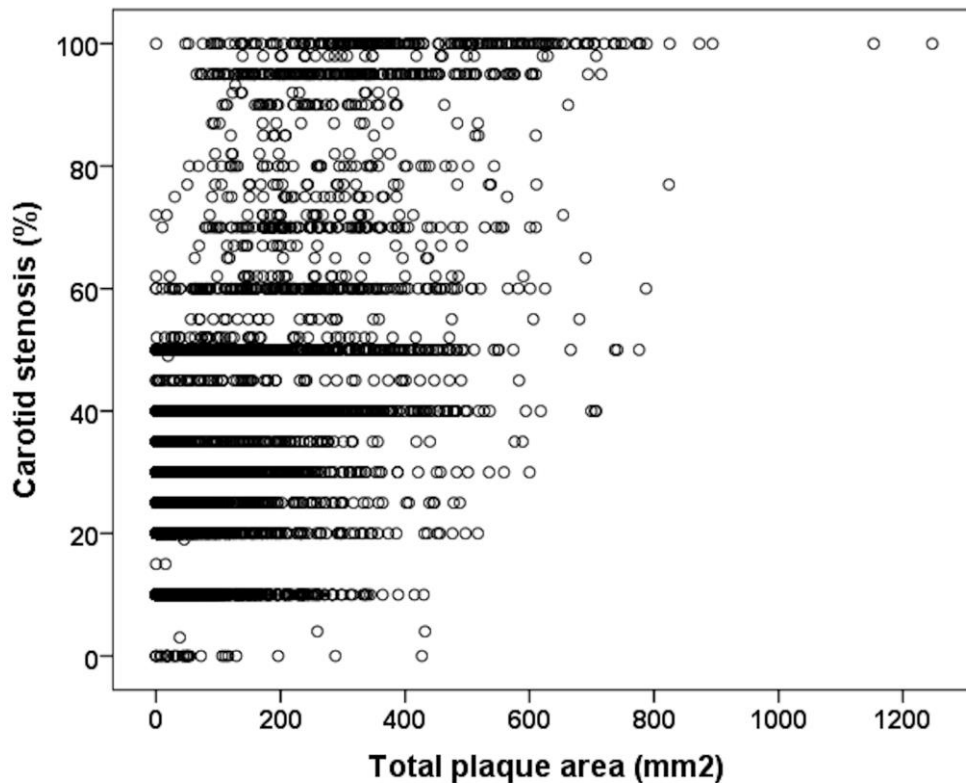
\*Clinical clues to paradoxical embolism: young patient with no other defined cause of stroke, with a history of DVT or PE, Valsalva maneuver at the onset of the cerebrovascular event, recent prolonged travel or sitting or immobilization, waking up with stroke symptoms, sleep apnea, shortness of breath during the cerebrovascular event, loud pulmonary regurgitation murmur (P2), varicose veins, asymmetric swollen legs, DVT or PE in the past.<sup>2</sup>

## Legends for figures

**Figure I. The distribution of carotid total plaque area (TPA) by % stenosis**  
(in the internal carotid artery with more severe stenosis; n = 7,048)

Many patients with no carotid stenosis  $\geq 50\%$  have a high risk from large artery disease, with a TPA  $\geq 119 \text{ mm}^2$  and a 20% 5-year risk of stroke, death or myocardial infarction.<sup>4</sup> Thus, limiting the diagnosis of large artery disease to patients with carotid stenosis  $\geq 50\%$  in one carotid artery misclassifies many cases of ischemic stroke.

Figure I. Distribution of total plaque area by percent carotid stenosis.



## References

- (1) Ay H, Furie KL, Singhal A, Smith WS, Sorensen AG, Koroshetz WJ. An evidence-based causative classification system for acute ischemic stroke. *Ann Neurol* 2005 November;58(5):688-97.
- (2) Ozdemir AO, Tamayo A, Munoz C, Dias B, Spence JD. Cryptogenic stroke and patent foramen ovale: clinical clues to paradoxical embolism. *J Neurol Sci* 2008 December 15;275(1-2):121-7.
- (3) *Harrison's Neurology in Clinical Medicine*. 2 ed. McGraw-Hill Professional; 2010.
- (4) Spence JD, Eliasziw M, DiCicco M, Hackam DG, Galil R, Lohmann T. Carotid plaque area: a tool for targeting and evaluating vascular preventive therapy. *Stroke* 2002 December;33(12):2916-22.