

A: Causality grades for atherothrombosis

A1 (potentially causal)	Atherothrombotic stroke defined as: <ol style="list-style-type: none">(1) ipsilateral atherosclerotic stenosis between 50 and 99% in an intra- or extracranial artery supplying the ischemic field; <i>or</i>(2) ipsilateral atherosclerotic stenosis <50% in an intra- or extracranial artery with an endoluminal thrombus supplying the ischemic field; <i>or</i>(3) mobile thrombus in the aortic arch; <i>or</i>(4) ipsilateral arterial occlusion in an intra- or extracranial artery with evidence of underlying atherosclerotic plaque supplying the ischemic field
A2 (causal link is uncertain)	<ol style="list-style-type: none">(1) ipsilateral atherosclerotic stenosis 30–50% in an intra- or extracranial artery supplying the ischemic field; <i>or</i>(2) aortic plaque ≥ 4 mm without mobile lesion
A3 (causal link is unlikely, but the disease is present)	<ol style="list-style-type: none">(1) plaque (stenosis <30%) in an intra- or extracranial artery, ipsilateral to the infarct area;(2) aortic plaque <4 mm without mobile thrombus;(3) stenosis (any degree) or occlusion in a cerebral artery not supplying the infarct area (e.g. contralateral side or opposite circulation);(4) history of myocardial infarction, coronary revascularization or peripheral arterial disease;(5) ipsi- or bilateral atherosclerotic stenosis 50–99% with bihemispheric MR-DWI lesion
A0 (atherosclerosis not detected)	Ruling out atherosclerosis: <ol style="list-style-type: none">(1) extracranial arterial stenosis: one or several of the following diagnostic tests are performed and are negative: US-Duplex, CTA, MRA, XRA, or autopsy;(2) intracranial arterial stenosis: one or several of the following diagnostic tests are performed and are negative: US-TCD, MRA, CTA, XRA, or autopsy;(3) aortic arch atheroma: TEE with specific assessment of the aortic arch (when the probe is pulled back at the end of the cardiac examination, turn the probe counter clockwise and take time to watch the aortic arch) or specific aortic arch assessment with CTA
A9 (incomplete workup)	US-Duplex, US-TCD or CTA, or MRA, or XRA or autopsy not performed. [A minimum workup is extra- and intracranial assessment of cerebral arteries – maximum workup also includes transesophageal assessment of the aortic arch (or a default CTA of the aortic arch)]

S: Causality grades for small-vessel disease

S1	(potentially causal)	Combination of: (1) lacunar infarction: small deep infarct <15 mm (in perforator branch territory) on MRI-DWI (or a default CT) in an area corresponding to the symptoms and at least one of the three following criteria: (2) one or several small deep older infarct(s) of lacunar type in other territories, <i>and/or</i> (3) severe (confluent – Fazekas III) leukoaraiosis, or microbleeds, or severe dilatation of perivascular spaces (‘état criblé’); (4) repeated, recent (<1 month), TIAs attributable to the same territory as the index infarct
S2	(causal link is uncertain)	(1) only one, recent, lacunar infarction and no other abnormality on MRI (or CT) <i>or</i> (2) clinical syndrome suggestive of a deep branch artery stroke, without ischemic lesion in the appropriate area seen on MRI or CT (main clinical syndrome suggesting a deep branch artery – lacunar – stroke: pure hemiparesis, pure hemisensory loss, ataxic hemiparesis, dysarthria-clumsy hand syndrome, unilateral sensorimotor deficit, others: hemichorea, hemiballism, pure dysarthria, etc.)
S3	(causal link is unlikely, but the disease is present)	Severe (confluent – Fazekas III) leukoaraiosis visible on MRI and/or CT scan, and/or microbleeds visible on T2*-weighted MRI, and/or severe dilatation of perivascular spaces (visible on T2-weighted MRI), and/or one or several old, small deep infarcts of lacunar type

Grades for cardioembolism (C)

1. Definitely a potential cause of the index stroke	<p>Cardioembolic stroke – demonstration of:</p> <ul style="list-style-type: none">(a) Mitral stenosis;(b) Prosthetic heart valve;(c) Myocardial infarction within the past 4 weeks;(d) Mural thrombus in left cavities;(e) Left ventricular aneurysm;(f) Any documented history or permanent or transient atrial fibrillation or flutter with or without spontaneous echo contrast or left atrial thrombus;(g) Sick sinus syndrome; <hr/> <ul style="list-style-type: none">(h) Dilated cardiomyopathy;(i) Ejection fraction <35%;(j) Endocarditis;(k) Intracardiac mass;(l) PFO plus in situ thrombosis;(m) PFO plus concomitant PE or DVT preceding the brain infarction. <hr/>
2. Causality uncertain	<ul style="list-style-type: none">(a) PFO and ASA;(b) PFO and concomitant DVT or PE (but not preceding the index stroke);(c) Spontaneous echo contrast;(d) Apical akinesia of the left ventricle and impaired ejection fraction (but >35%);(e) Only suggested by history of myocardial infarction or palpitation and multiple repeated brain infarcts on both sides or in both the anterior and posterior circulation;(f) Only suggested by abdominal CT/MRI or autopsy demonstration of the presence of systemic infarction (e.g. kidney, splenic, mesenteric) or lower limb embolism (in addition to the index stroke). <hr/>
3. Unlikely a direct cause of index stroke	<p>One of the following abnormalities: PFO, ASA, valvular strands, mitral annulus calcification, calcified aortic valve, nonapical akinesia of the left ventricle.</p>

Grades for other causes (O)

1. Definitely a potential cause of the index stroke (examples)	<ul style="list-style-type: none"> (a) Arterial dissection by A or B evidence (table 3); (b) Dolichoectasia with complicated aneurysm; (c) Polycythemia vera, thrombocythemia $>800,000/\text{mm}^3$; (d) Lupus erythematosus; (e) Disseminated intravascular coagulation; (f) Criteria for antiphospholipid antibody syndrome; (g) Fabry's disease; (h) Concomitant meningitis; (i) Sickle cell disease; (j) Ruptured cerebral aneurysm with or without demonstration of spasm in the territory of the brain infarct; (k) Homozygote for hyperhomocystinuria.
2. Causality uncertain	<ul style="list-style-type: none"> (a) Arterial dissection diagnosed by level C evidence (see table 3; only suggestive history or clinical syndrome, e.g. isolated acute painful Horner's syndrome, or only history of previous dissection); (b) Fibromuscular dysplasia.
3. Unlikely a direct cause of index stroke (but disease is present)	<ul style="list-style-type: none"> (a) Kinking or dolichoectasia without complicated aneurysm or plicature; (b) Arteriovenous malformation or saccular aneurysm; (c) Thrombocytosis $>450,000$ and $<800,000/\text{mm}^3$; (d) Antiphospholipid antibodies <100 GPL units; (e) Mild hyperhomocysteinemia heterozygote.

TIA = Transient ischemic attack; BI = brain infarction; PFO = patent foramen ovale; PE = pulmonary embolism; ASA = Atrial septal aneurysm; DVT = deep vein thrombosis. In the absence of disease the grade is 0. In case of insufficient work-up and that the patient cannot be graded, the grade is 9.