¿Qué dicen las guías de la ESO sobre la SVD?



Dr. Francisco Moniche

Hospital Universitario Virgen del Rocío

Instituto de Biomedicina de Sevilla





RICORS - ICTUS



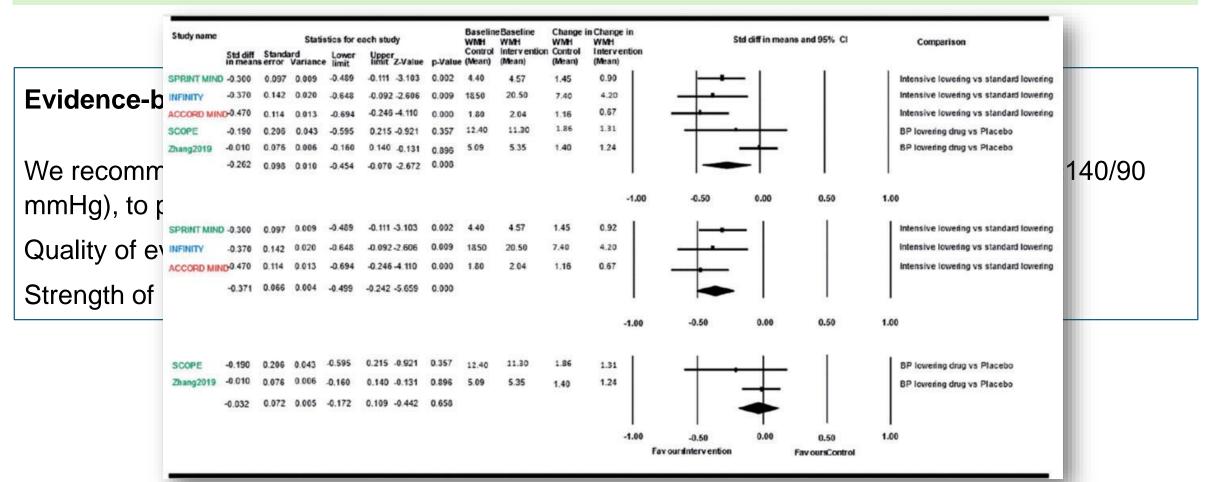
Joanna M Wardlaw¹, Stephanie Debette^{2,3}, Hanna Jokinen⁴, Frank-Erik De Leeuw⁵, Leonardo Pantoni⁶, Hugues Chabriat⁷, Julie Staals⁸, Fergus Doubal^{1,9}, Salvatore Rudilosso¹⁰, Sebastian Eppinger¹¹, Sabrina Schilling², Raffaele Ornello¹², Christian Enzinger¹¹, Charlotte Cordonnier¹³, Martin Taylor-Rowan¹⁴ and Arne G Lindgren¹⁵

European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Joanna M Wardlaw^{1,*}, Hugues Chabriat², Frank-Erik de Leeuw³, Stéphanie Debette⁴, Martin Dichgans⁵, Fergus Doubal⁶, Hanna Jokinen⁷, Aristeidis H Katsanos⁸, Raffaele Ornello⁹, Leonardo Pantoni¹⁰, Marco Pasi¹¹, Aleksandra M Pavlovic¹², Salvatore Rudilosso¹³, Reinhold Schmidt¹⁴, Julie Staals¹⁵, Martin Taylor-Rowan¹⁶, Salman Hussain¹⁷ and Arne G Lindgren^{18*}



Does <u>antihypertensive treatment</u>, reduce ischaemic or haemorrhagic strokes (1.1), cognitive decline or dementia (1.2), dependency (1.3), death (1.4), MACE (1.5), mobility (1.6), or mood disorders (1.7)





Does <u>antiplatelet treatment</u>, reduce ischaemic or haemorrhagic strokes (2.1), cognitive decline or dementia (2.2), dependency (2.3), death (2.4), MACE (2.5), mobility (2.6), or mood disorders (2.7)?

Evidence-based Recommendation

We suggest against antiplatelet treatment in patients with ccSVD as a means to reduce the clinical outcome events of ischaemic or haemorrhagic strokes, cognitive decline or dementia, dependency, death, MACE, mobility, or mood disorders.

Quality of evidence: Very low⊕

Strength of recommendation: Weak against intervention \?

We <u>advise against use of antiplatelet drugs</u> to prevent clinical outcomes in subjects with ccSVD <u>when no other</u> <u>indication for this treatment exists and it may be harmful in older patients</u> (≥70 years of age)



Lipid lowering treatment

Evidence-based Recommendation

We did not find enough evidence of high enough quality on prevention of clinical outcomes in ccSVD to make a definitive recommendation on lipid lowering. However we recognise that lipid lowering is effective in primary prevention in those at high risk of vascular events.

Quality of evidence − Very low ⊕

Strength of recommendation - Weak for intervention ↑?

ESO Guideline on covert cerebral small vessel disease

Lifestyle interventions

Evidence-based Recommendation

In patients with ccSVD, we suggest that physical exercise has beneficial effects on cognition and possibly also on mobility, incidence of cerebrovascular events and all-cause mortality, and therefore, recommend regular physical activity in general. However, we cannot make recommendations on a specific physical intervention based on current evidence.

Quality of evidence: Very Low ⊕

Strength of recommendation: Weak for

intervention ↑?



Do drugs which <u>reduce plasma glucose levels</u> reduce ischaemic or haemorrhagic strokes (2.1), cognitive decline or dementia (2.2), dependency (2.3), death (2.4), MACE (2.5), mobility (2.6), or mood disorders (2.7)?

Evidence-based Recommendation

In patients with diabetes who may also have ccSVD, we recommend the use of current guideline-based glucose lowering therapies, including recommended glucose and HbA1C targets, as appropriate to the management of the individual patient's diabetes. There is no justification for recommending any particular glucose-lowering therapy for this purpose.

We suggest against glucose lowering in patients with ccSVD who do not have any indication for glucose control. Quality of evidence: **Very low** ①

Strength of recommendation: **No recommendation**



European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Does <u>thrombolytic treatment</u> (including at extended time window and wake-up stroke), reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

We suggest that patients with suspected acute lacunar ischaemic stroke should be assessed for and receive treatment with 0.9 mg/kg alteplase according to current guidelines for the treatment of acute ischaemic stroke, since the limited data available suggest that the outcomes for patients with lacunar ischaemic stroke are consistent with the overall results of alteplase trials.

Quality of evidence: Very Low \oplus

Strength of recommendation: Weak for intervention 1?

	Alteplase		Placebo			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
IST-3 2012	100	168	103	164	44.0%	0.87 [0.56, 1.35]	+
NINDS 1995	32	51	12	30	25.2%	2.53 [1.00, 6.37]	-
WAKE-UP 2019	31	55	24	53	30.8%	1.56 [0.73, 3.33]	+-
Total (95% CI)		274		247	100.0%	1.36 [0.73, 2.55]	•
Total events	163		139				
Heterogeneity: Tau ² =	0.18; Chi	2 = 4.9	2, df = 2 (P = 0.0	9); P = 59	%	0.01 0.1 1 10 100
Test for overall effect:	Z = 0.97	(P = 0.3)	33)				0.01 0.1 1 10 100 Favors Placebo Favors Alteplase

1. Twelve of twelve MWG members agreed that in patients with suspected acute lacunar ischaemic stroke, with no contraindication to thrombolytic treatment according to current clinical guidelines for thrombolytic treatment (including wake up stroke), there is no evidence for withholding thrombolytic treatment. Therefore these patients should receive intravenous alteplase at standard dose (0.9 mg/kg) as quickly as possible according to current clinical guidelines.



European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Does acute treatment with antiplatelets (considering single/dual & duration), reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

In patients suspected acute lacunar ischaemic stroke, there is continued uncertainty about a specific combination of antiplatelet therapy over monotherapy.

Quality of evidence: Very low

Strength of recommendation: -



European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Does **immediate antihypertensive treatment**, reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

In hospitalised patients with suspected acute lacunar ischaemic stroke and BP <220/110 mmHg, not treated with intravenous thrombolysis, we suggest against the routine use of blood pressure BP lowering agents in the hyperacute phase, unless this is necessary for a specific comorbid condition.

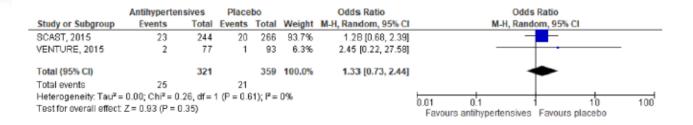
Quality of evidence: Moderate $\oplus \oplus \oplus$

Strength of recommendation: Weak against intervention \downarrow ?

 In patients with suspected acute lacunar ischaemic stroke undergoing intravenous thrombolysis we suggest following the same guideline as in acute ischaemic stroke at large, that is, maintaining BF below 185/110 mmHg before bolus and below 180/105 mmHg after bolus, and for 24 hours after alteplase infusion.

Quality of evidence: Very Low \oplus

Strength of recommendation: Weak for intervention 1?





European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Does **immediate other treatments**, reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

No evidence for acute treatment with:

- ✓ Cilostazol
- ✓ Magnesium
- ✓ Anti-inflammatory age
- ✓ Anticoagulants

 In patients with acute lacunar ischaemic stroke, we recommend against the use of therapeutic LMW heparin/heparinoid to reduce dependency.

Quality of evidence: Moderate $\oplus \oplus \oplus$

Strength of recommendation: Weak against intervention \downarrow ?



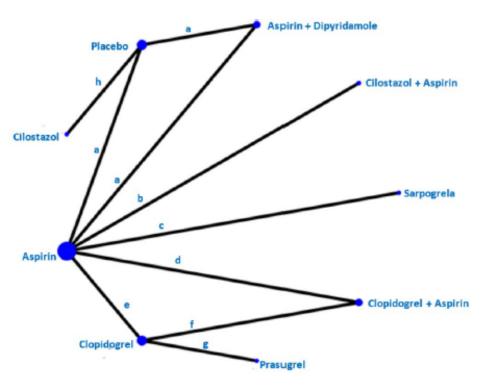
2 a

European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Does **long term antiplatelet treatment**, reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

n

In patie preven single a after st Quality Strengt



In patients with suspected lacunar ischaemic stroke twelve of 12 MWG members recommend against the use of long-term* dual or triple antiplatelet therapy. Instead, single antiplatelet therapy should be used as per the Evidence Based Recommendation, unless other conditions warrant a combination of these medications.

*Defined as more than 2-4 weeks

 In patients with suspected lacunar ischaemic stroke, eleven of 12 MWG members agreed that the current evidence was <u>inadequate</u> to recommend routine use of cilostazol to prevent adverse long term outcomes.



2 a

European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Does **antihypertensive treatment**, reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

In patients with suspected lacunar ischaemic stroke we recommend the use of antihypertensive treatment to prevent recurrent stroke and MACE.

Quality of evidence: Low $\oplus \oplus$

Strength of recommendation: Strong for intervention 11

	<130 mi	mHg	130 -149 mmHg			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
PRESERVE 2021	3	56	3	55	2.4%	0.98 [0.:21, 4.66]	
SPS3 2013	112	1501	131	1519	97.6%	0.87 [0.68, 1.10]	=
Total (95% CI)		1557		1574	100.0%	0.87 [0.68, 1.10]	•
Total events	115		134				
Heterogeneity: Tau ² =	0.00; Chř	= 0.02	df=1 (P=	0.05 0.2 1 5 20			
Test for overall effect	Z = 1.16 (P = 0.25	5)				Decreased recurrent risk Increased recurrent risk

- . Twelve of twelve MWG members suggest that: BP should be appropriately monitored and well controlled, when possible through use of out of office blood pressure measurements. We cannot advise any specific antihypertensive treatment.
- Eleven of twelve MWG members agree that aiming for BP < 130/80 mmHg as generally recommended for patients with previous ischaemic stroke or TIA may be reasonable, but that drastic BP reductions and important BP variability should be avoided, probably targeting SBP between 125 and 130 mmHg and DBP between 70 and 80 mmHg.



2 a

European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

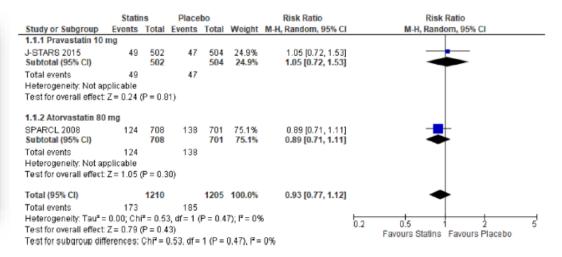
Does **lipid lowering**, reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

There is continued uncertainty regarding the effect of lipid lowering specific to lacunar stroke. However we recognise that lipid lowering is effective in reducing clinically adverse outcomes in patients with undifferentiated ischaemic stroke.

Quality of evidence: Low $\oplus \oplus$

Strength of recommendation: -

 Twelve of 12 MWG members agreed that patients with lacunar ischaemic stroke should receive lipid lowering therapy given there is some evidence of benefit and no clear evidence of harm.





2 a

European stroke organisation (ESO) guideline on cerebral small vessel disease, part 2, lacunar ischaemic stroke

Does **lifestyle interventions**, reduce recurrent ischaemic stroke, dependency, death, cognitive impairment or dementia, haemorrhagic stroke, MACE, mobility or gait disorder, and mood disorders?

In patients with lacunar stroke, there is continued uncertainty to indicate that any specific lifestyle interventions prevent adverse clinical outcomes.

Quality of evidence: Very low \oplus

Strength of recommendation: -

Despite lack of direct evidence, twelve of 12 MWG members suggest that it is advisable to promote healthy lifestyle modifications in patients with lacunar stroke as recommended in secondary prevention for stroke and VCI. These include regular physical exercise, maintaining healthy body weight, avoiding smoking and excess alcohol, and eating a healthy balanced diet with low sodium intake.



"Guidelines

+

0

Covert SVD:

 α α α α

- Lifestyle interventions: No direct evidence of any specific lifestyle interventions prevent clinical outcomes in patients with ccSVD
- Glucose lowering treatments who do not have any indication for glucose control

Acute and prevention SVD:

- Combination of antiplatelet therapy over monotherapy
- Stopping vs continuing BP lowering therapy
- Acute stroke treatments (anticoagulants, antiinflammatory,...)
- Consensus definition for progressive symptoms & no evidence to recommend any particular
- Prevention with: lipid lowering therapies, lifestyle interventions, other therapies (nitrix oxide donors, anticoagulants, cilostazol, phosphodiestersase-5 inh,...)