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A critical review of ESVS/ESC 2017 guidelines

Silent infarction and impaired cerebrovascular reactivity

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Disclosures

Peter A. Ringleb, MD

- Professor of Vascular Neurology and head of the Stroke service at the University hospital Heidelberg (GER)
- Lecture-fees and travel-expenses from Bayer, Boehringer Ingelheim, Daiichi Sankyo, Pfizer
- Member of the WSO, ESO, DGN, DSG, DGNI, DEGUM
- Secretary of the German Stroke Society (DSG) and the Working-Group Stroke Unit BW (ASBW)
- Clinical Coordinator of SPACE, Member of the Steering-Committee of SPACE-2, ECASS4, PRESTIGE-AF, PRECISE

Asymptomatic Carotid Artery Stenosis

Guideline recommendation 2017 (ESC)

2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS)

Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries

Recommendations	Class	Level
In 'average surgical risk' patients with an asymptomatic 60–99% stenosis, <u>CEA</u> should be considered in the presence of clinical and/or more imaging characteristics that may be associated with an increased risk of late ipsilateral stroke , provided documented perioperative stroke/death rates are <3% and the patient's life expectancy is > 5 years	IIa	B
In asymptomatic patients who have been deemed 'high risk for CEA' and who have an asymptomatic 60–99% stenosis in the presence of clinical and/or imaging characteristics that may be associated with an increased risk of late ipsilateral stroke , <u>CAS</u> should be considered, provided documented perioperative stroke/death rates are <3% and the patient's life expectancy is > 5 years	IIa	B

Asymptomatic Carotid Artery Stenosis

Guideline recommendation 2017 (ESC)

Recommendations

In 'average surgical risk' patients, CAS should be considered in the presence of any of the following features. CAS may be associated with an increased risk of perioperative stroke. Life expectancy is > 5 years

In asymptomatic patients who have any of the following characteristics that may be associated with an increased risk of stroke, CAS should be considered. Life expectancy is > 5 years

Table 4 Features associated with increased risk of stroke in patients with asymptomatic carotid stenosis treated medically (for details see Web Table 5)

Clinical^a	<ul style="list-style-type: none"> • Contralateral TIA/stroke¹²¹
Cerebral imaging	<ul style="list-style-type: none"> • Ipsilateral silent infarction¹²²
Ultrasound imaging	<ul style="list-style-type: none"> • Stenosis progression (> 20%)¹²³ • Spontaneous embolization on transcranial Doppler (HITS)¹²⁴ • Impaired cerebral vascular reserve¹²⁵ • Large plaques^{b,126} • Echolucent plaques⁹⁶ • Increased juxta-luminal black (hypoechoogenic) area¹²⁷
MRA	<ul style="list-style-type: none"> • Intraplaque haemorrhage¹²⁸ • Lipid-rich necrotic core

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HITS = high intensity transient signal; MRA = magnetic resonance angiography; TIA = transient ischaemic attack.

^aAge is not a predictor of poorer outcome.

^bMore than 40 mm² on digital analysis.

Class

Level

Ila

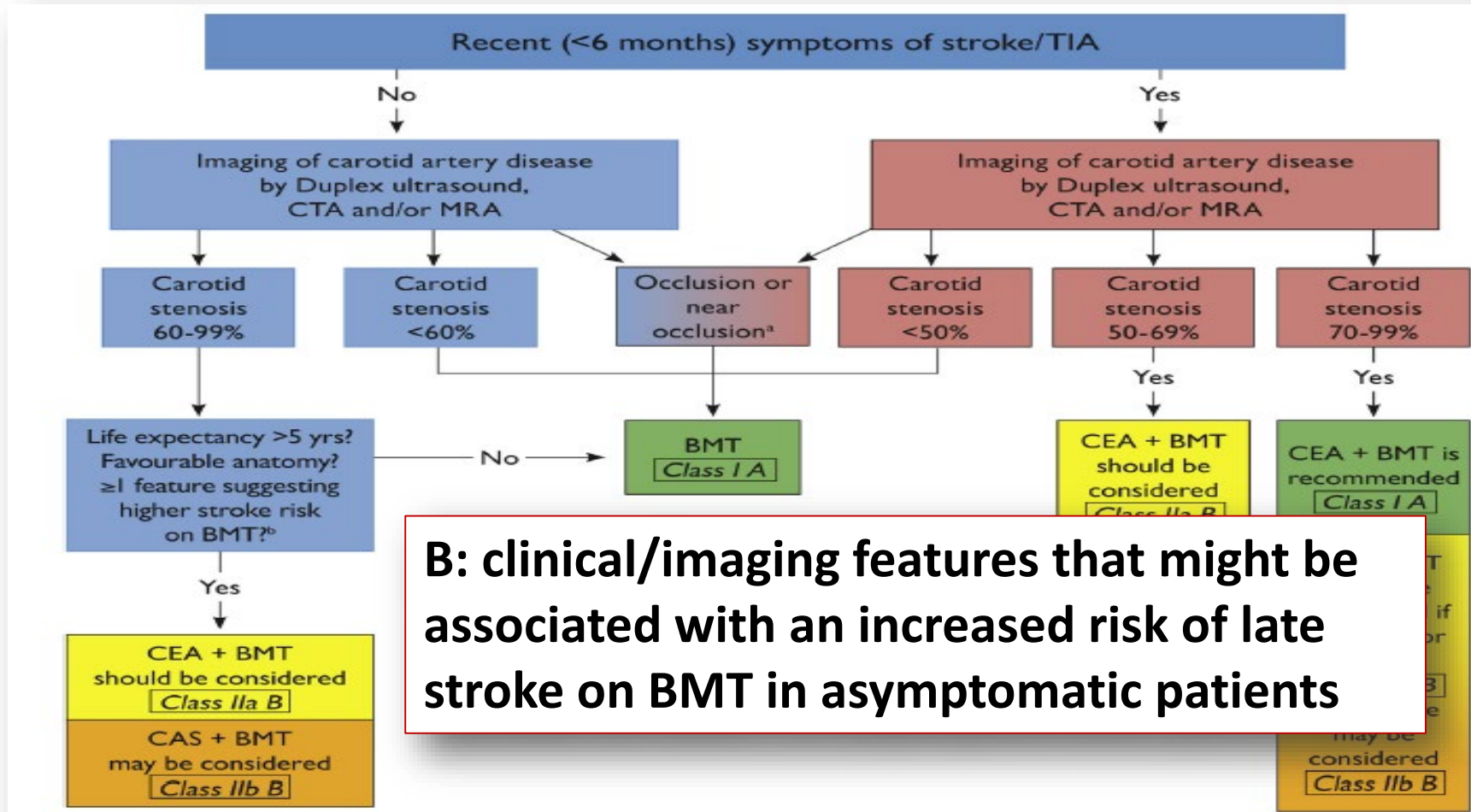
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B

Asymptomatic Carotid Artery Stenosis

Guideline recommendation 2017 (ESVS)



Asymptomatic Carotid Artery Stenosis

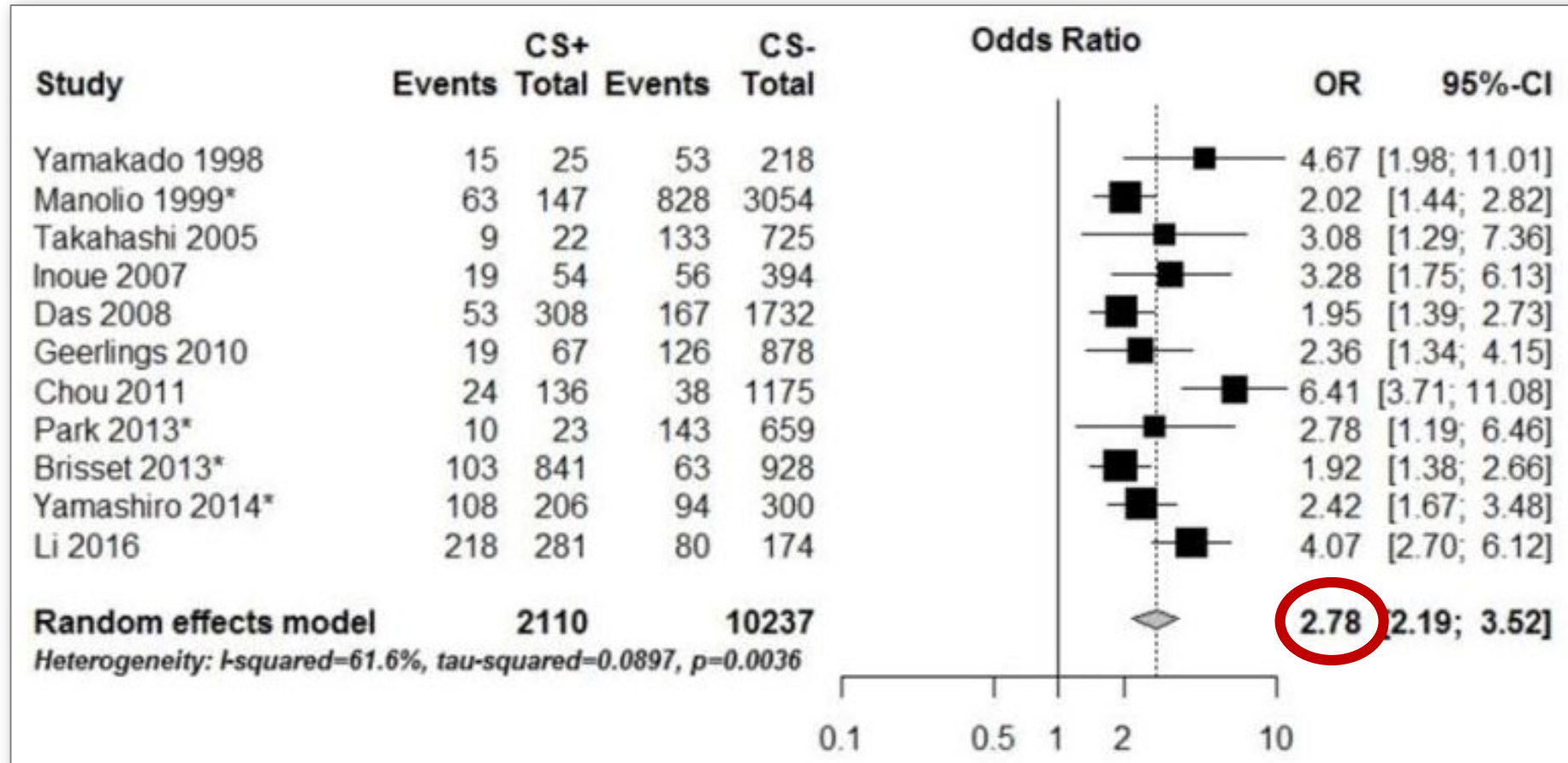
Guideline recommendations ESVS 2017 (excerpt)

Criteria		Source	OR/HR (95% CI)	P-value
Silent infarction on CT MRI	3.6 % vs 1.0%	OBS	3.0 (1.46 - 6.29)	0.002
Impaired cerebral vascular reserve	Yes vs. No	MA	3.7 (1.27 – 29.5)	0.02

MA: Meta-analysis; **OBS:** observational

Silent infarctions in patients with aCS

Correlation between aCS and SI



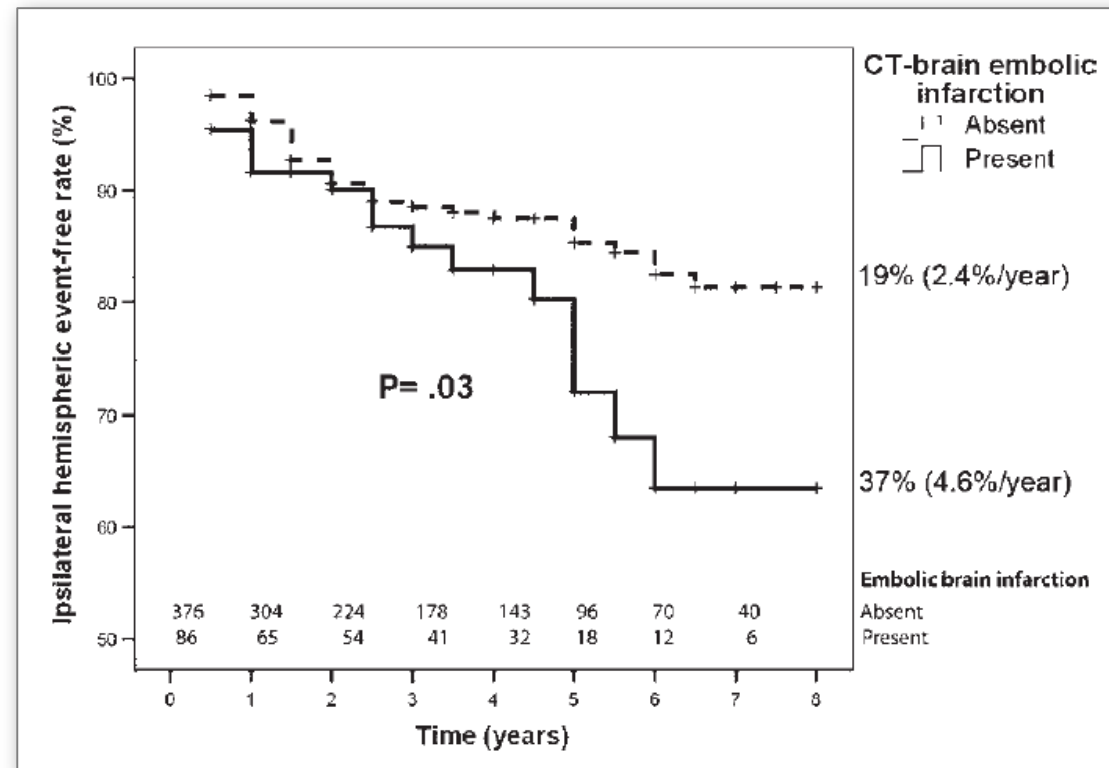
Silent infarctions in patients with aCS

ACSRS analysis

- Prospective, multicenter natural history study
- 821 patients with aCS who had CT brain scans were monitored every 6 months for a up to 8 years

Silent embolic infarcts on computed tomography brain scans and risk of ipsilateral hemispheric events in patients with asymptomatic internal carotid artery stenosis

Stavros K. Kakkos, MD, MSc, PhD, RVT,^a Michael Sabetai, MD, FRCS,^a Thomas Tegos, MD, PhD,^a John Stevens, MB, BS,^b Dafydd Thomas, MA, MD, FRCP,^c Maura Griffin, MSc, PhD,^{a,d} George Geroulakos, FRCS, PhD,^a and Andrew N. Nicolaides, MS, FRCS, PhD (Hon),^{a,d} for the Asymptomatic Carotid Stenosis and Risk of Stroke (ACSRS) Study Group,^a London, United Kingdom



Silent infarctions in patients with aCS

ACST post hoc analysis

- 2333 patients with baseline imaging from ACST (787 patients excluded because of missing imaging)
- **Group 1 (n=1331):**
history of ischemic stroke or TIA
>6 months before randomization or positive CT
- **Group 2 (n=1002):**
normal imaging and no cerebrovascular event

Ten-year risk of stroke in patients with previous cerebral infarction and the impact of carotid surgery in the Asymptomatic Carotid Surgery Trial

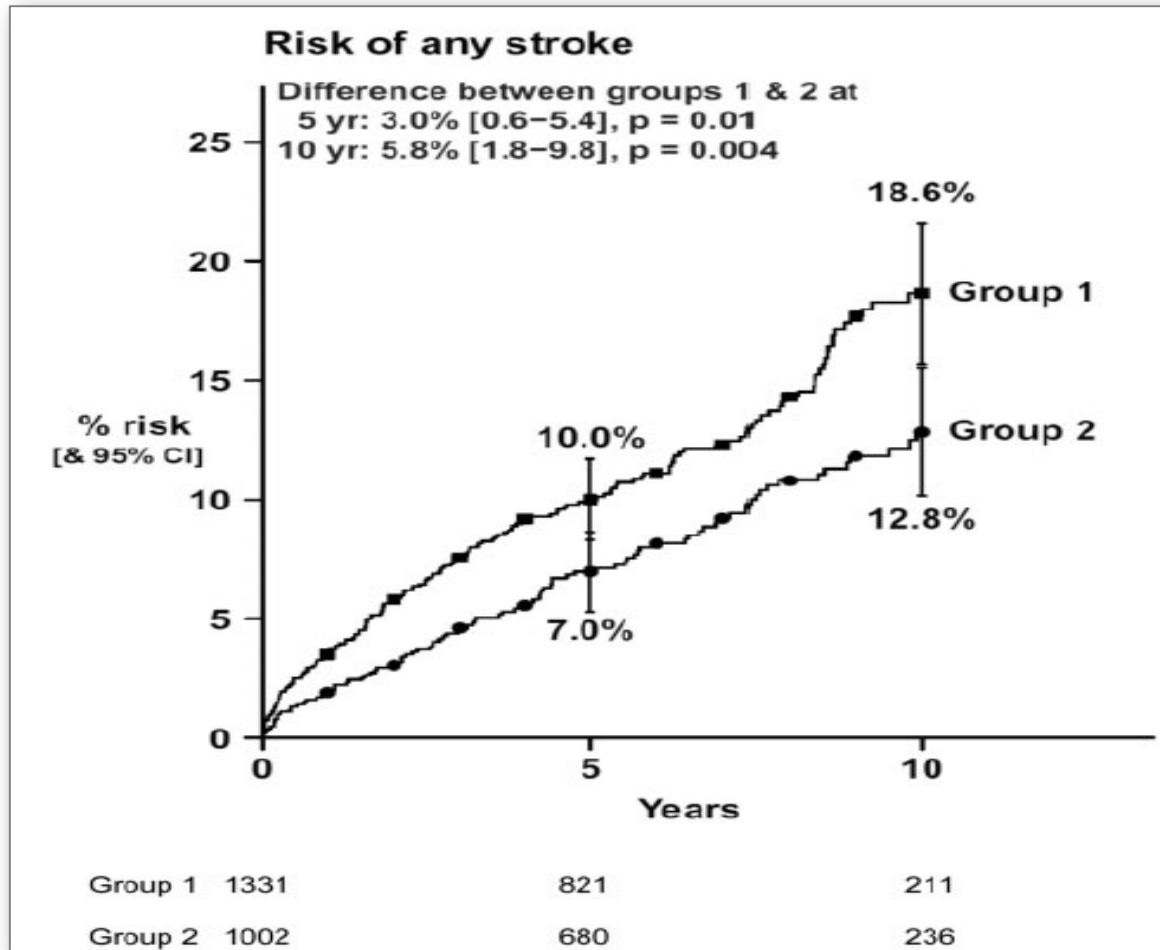
Jonathan Y Streifler¹, Anne G den Hartog², Samuel Pan³, Hongchao Pan³, Richard Bulbulia³, Dafydd J Thomas⁴, Martin M Brown⁵ and Alison Halliday⁶; on behalf of the ACST-1 trial collaborators

Table 1. Symptoms in group 1 (clinical or radiological evidence of cerebral infarction)

	N = 1331 n (%)
Ipsilateral	
Silent brain infarct	898 (67.47)
Amaurosis fugax	67 (5.03)
Cortical TIA	131 (9.84)
Stroke	121 (9.09)
Other/unknown symptoms	114 (8.56)
Contralateral	
Silent brain infarct	466 (35.01)
Amaurosis fugax	164 (12.32)
Cortical TIA	348 (26.15)
Stroke	331 (24.87)
Other/unknown symptoms	22 (1.65)

Silent infarctions in patients with aCS

ACST post hoc analysis



- 10 years benefits from immediate CEA vs. deferred CEA:
- **Group 1:** 6.7% vs. 14.7%;
HR 0.47 (0.34–0.65), p=0.003
- **Group 2:** 6.0% vs. 9.9%;
HR 0.61 (0.39–0.94), p=0.005

Does Impaired Cerebrovascular Reactivity Predict Stroke Risk in Asymptomatic Carotid Stenosis?

A Prospective Substudy of the Asymptomatic Carotid Emboli Study

Alice King, BSc (Hons); Joaquin Serena, MD, PhD; Natan M. Bornstein, MD; Hugh S. Markus, FRCP;
ACES Investigators

Asymptomatic Carotid Artery Stenosis

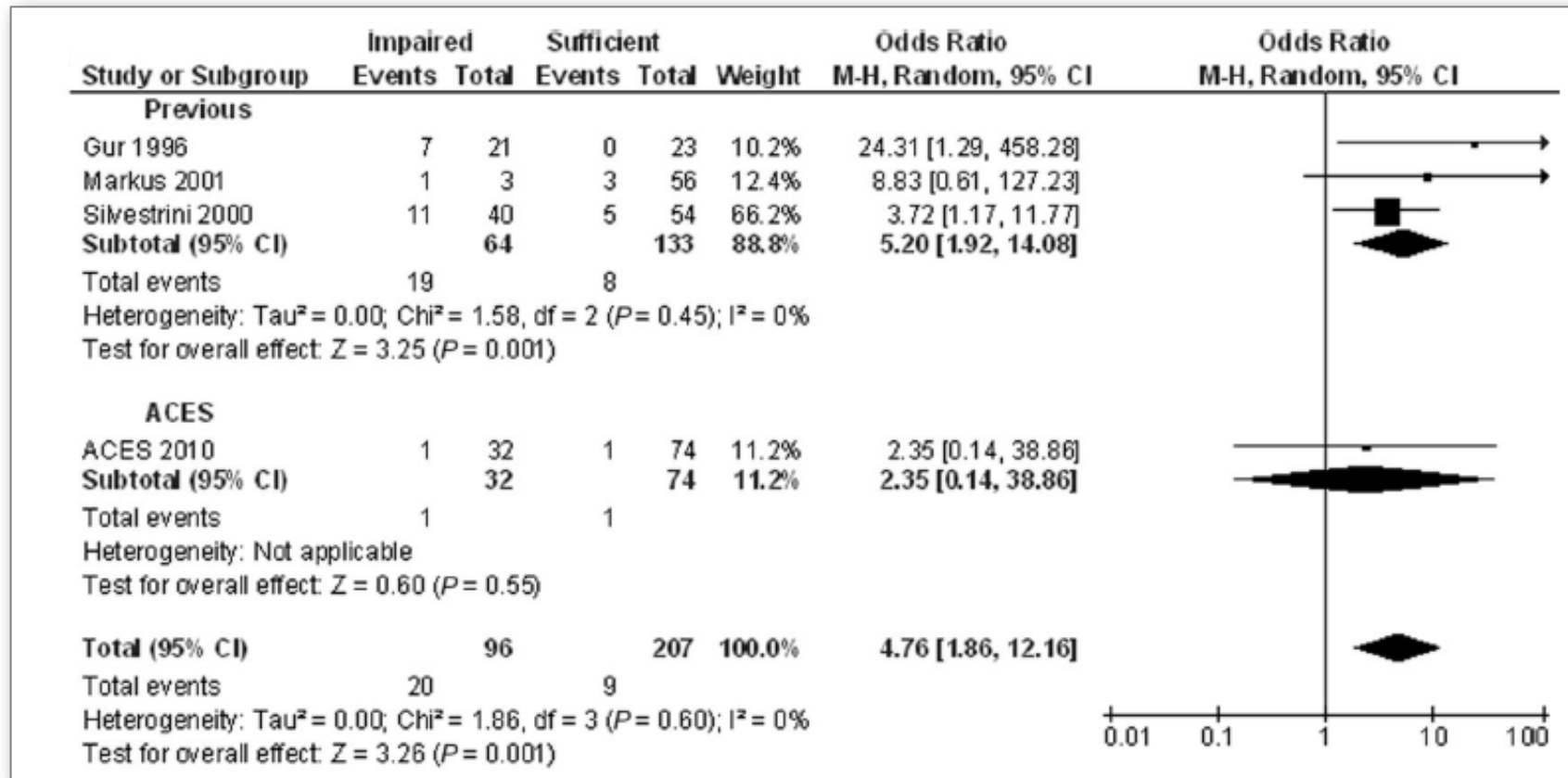
Impaired Cerebral Vascular Reactivity (CVR)

- Preplanned substudy of the Asymptomatic Carotid Emboli Study
- 106 patients with $\geq 70\%$ aCS
- TCD used to measure CVR with a vasodilatory response of CO₂ or acetazolamide
- 32 (30.2%) had severely impaired CVR ipsilateral to the study artery
- Mean follow-up 680 days:
 - no (!) ipsilateral strokes
 - Non-significant 'trend' to more stroke/TIA in patients with severely impaired CVR (9.4% vs 2.7%; HR 2.54; 95% CI 0.61-21.74; P=0.158)

Asymptomatic Carotid Artery Stenosis

Impaired Cerebrovascular Reactivity (CVR)

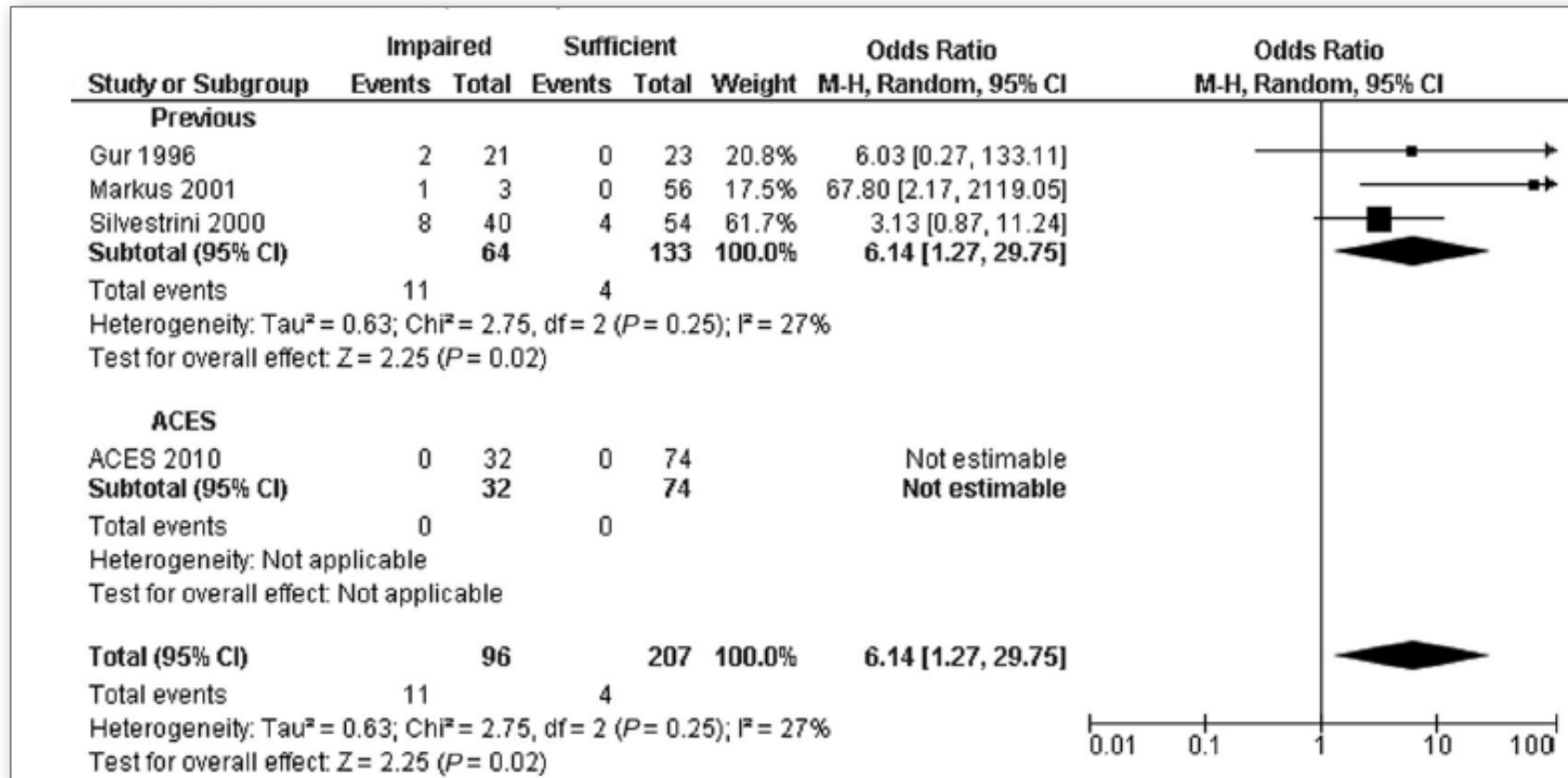
Endpoint: ipsilateral stroke or TIA



Asymptomatic Carotid Artery Stenosis

Impaired Cerebrovascular Reactivity (CVR)

Endpoint: ipsilateral stroke



Asymptomatic Carotid Artery Stenosis

Guideline recommendations regarding SI | iCVS

Criteria		Source	OR/HR (95% CI)	P-value
Silent infarction on CT	3.6 % vs 1.0%	OBS	3.0 (1.46 - 6.29)	0.002
Impaired cerebral vascular reserve	Yes vs. No	MA	3.7 (1.27 – 29.5)	0.02

- The evidence for the relevance of SI is based on several, independent registries, studies and an increased effect of CEA has been shown
- The evidence for impaired CVS comes from a metaanalysis, the underlying studies are very small, the effect limited and a beneficial effect of CEA | CAS has not been proven in the situation



THANK YOU

FOR

your

ATTENTION!

ANY QUESTIONS?