EUROPEAN STROKE ORGANISATION

ESO Guideline on Endarterectomy and Stenting for Carotid Artery Stenosis

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How to generate evidence for the treatment of carotid stenosis – the 2021 carotid guideline of the European Stroke Organization (ESO)

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Disclosures (Presenter)

Intellectual Disclosures:

- Co-Principal Investigator of the SPACE-2 trial
- Member of the Carotid Stenosis Trialist Collaboration (CSTC)
- Local PI of TCAR trials (Roadster 2 and DWI Trial, SILKROAD)

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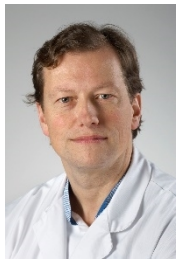

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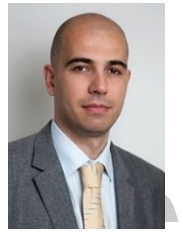

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Methods

	Interventions and Comparators		
Population	**Stenting**	**Endarterectomy**	**Medical therapy**
Asymptomatic carotid stenosis	**Outcomes**		
Symptomatic carotid stenosis			
Patient subgroups • Age • Sex • Severity of stenosis • Time since most recent event			

Peri-procedural outcomes (≤30 days)
- Death
- Stroke
- Myocardial infarction
- Cranial nerve injury

Post-procedural outcomes
- Stroke
- Restenosis

The guidelines were developed using GRADE methodology and the ESO Standard Operating Procedure

→ ***35 PICO questions***

Only RCT data considered for evidence-based recommendations

Asymptomatic carotid stenosis

Asymptomatic carotid stenosis

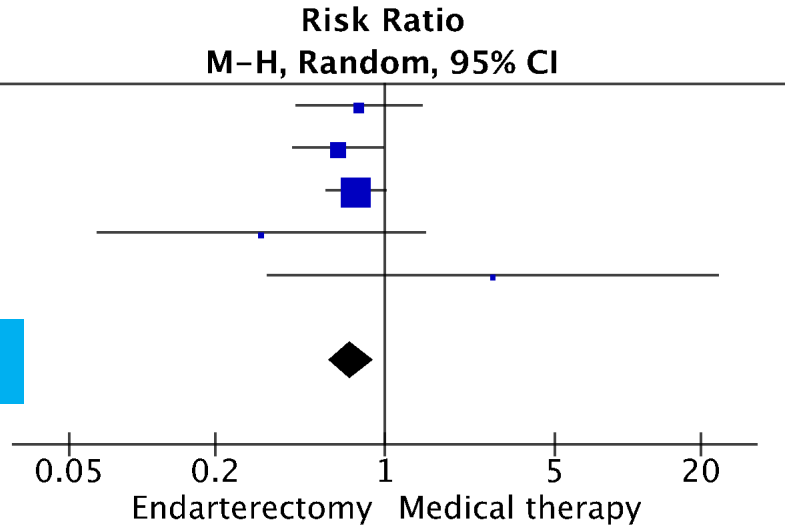
Endarterectomy versus medical therapy

Long-term ipsilateral stroke or peri-procedural stroke or death (PCIO 1.1)

	Endarterectomy		Medical therapy			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
VA 1993	17	211	24	233	13.0%	0.78 [0.43, 1.41]	1993
ACAS 1995	33	825	52	834	25.2%	0.64 [0.42, 0.98]	1995
ACST 1 2010	82	1560	108	1560	58.9%	0.76 [0.57, 1.00]	2010
AMTEC 2015	2	31	5	24	1.9%	0.31 [0.07, 1.46]	2015
SPACE-2 2019	5	203	1	113	1.0%	2.78 [0.33, 23.53]	2020
Total (95% CI)		**2830**		**2764**	**100.0%**	RR 0.73 (0.59-0.90)	
Total events	139		190				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.17$, df = 4 (P = 0.53); $I^2 = 0\%$

Test for overall effect: Z = 2.92 (P = 0.004)



Quality: Moderate ⊕⊕⊕
(Indirectness)

Asymptomatic carotid stenosis

Endarterectomy versus medical therapy

Evidence-based Recommendation

In patients with ≥60% asymptomatic carotid artery stenosis **considered to be at increased risk of stroke** on best medical therapy alone, **we recommend carotid endarterectomy**.
Quality of evidence: Moderate ⊕⊕⊕
Strength of recommendation: **Strong for carotid endarterectomy** ↑↑

This recommendation is independent of sex and stenosis severity.

Supporting information: characteristics associated with increased stroke risk:

- Silent infarction on neuroimaging
- High degree or progression of stenosis
- Echolucent plaque on ultrasound
- Intra-plaque haemorrhage on MRI
- Micro-emboli or reduced cerebrovascular reserve on trans-cranial Doppler

Asymptomatic carotid stenosis

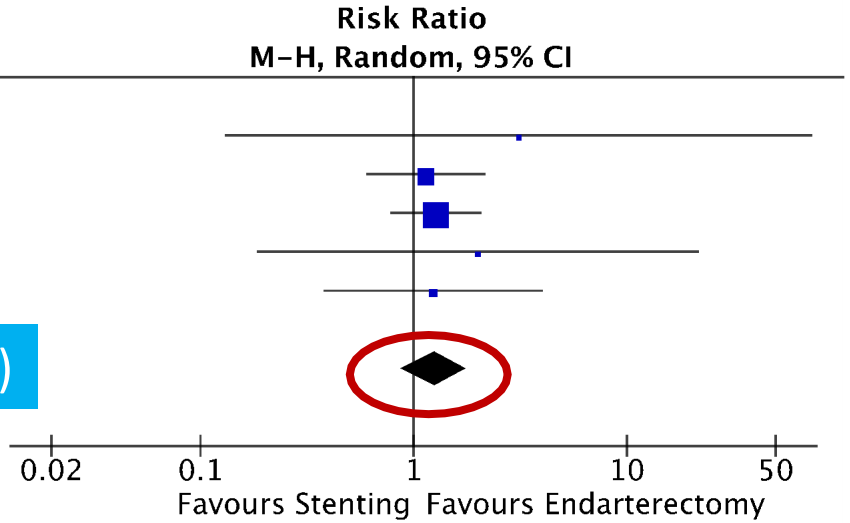
Stenting versus endarterectomy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 3.1)

Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kentucky 2004	0	43	0	42		Not estimable	2004
Houston 2014	1	27	0	28	1.3%	3.11 [0.13, 73.11]	2014
ACT-1 2016	41	1089	12	364	31.9%	1.14 [0.61, 2.15]	2016
CREST 2016	36	594	28	587	55.2%	1.27 [0.79, 2.05]	2016
Carmel Medical Center 2017	2	68	1	68	2.3%	2.00 [0.19, 21.54]	2017
SPACE-2 2019	6	197	5	203	9.3%	1.24 [0.38, 3.99]	2020
Total (95% CI)		**2018**		**1292**	**100.0%**	RR 1.25 (0.88-1.79)	
Total events	86		46				

Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.55, df = 4 (P = 0.97); I^2 = 0%

Test for overall effect: Z = 1.23 (P = 0.22)



Quality: Moderate ⊕⊕⊕

(Imprecision)

Asymptomatic carotid stenosis

Stenting versus endarterectomy

Evidence-based Recommendation

In patients with asymptomatic carotid stenosis in whom revascularisation is considered to be appropriate, **we suggest endarterectomy as the current treatment of choice**.
Quality of evidence: Moderate ⊕⊕⊕
Strength of recommendation: Weak for carotid endarterectomy ↑

Asymptomatic carotid stenosis

Stenting versus endarterectomy

Expert consensus statements

In patients with asymptomatic carotid stenosis in whom revascularisation is considered to be appropriate and **who are less suitable for surgery, stenting may be suggested**. We recommend careful consideration of the risks and benefits at a multi-disciplinary team meeting.

The independently assessed **risk of in-hospital stroke or death** following endarterectomy or stenting for asymptomatic carotid stenosis should be as low as possible, **ideally below 2%**.

Supporting information: The *Asymptomatic Carotid Surgery Trial-2* (ACST-2) has recently completed recruitment of 3.625 patients with asymptomatic carotid stenosis who were randomly assigned to CAS or CEA. First results are expected in late 2021 and will considerably increase the evidence base, which may lead to updates to the above recommendation.

Asymptomatic carotid stenosis

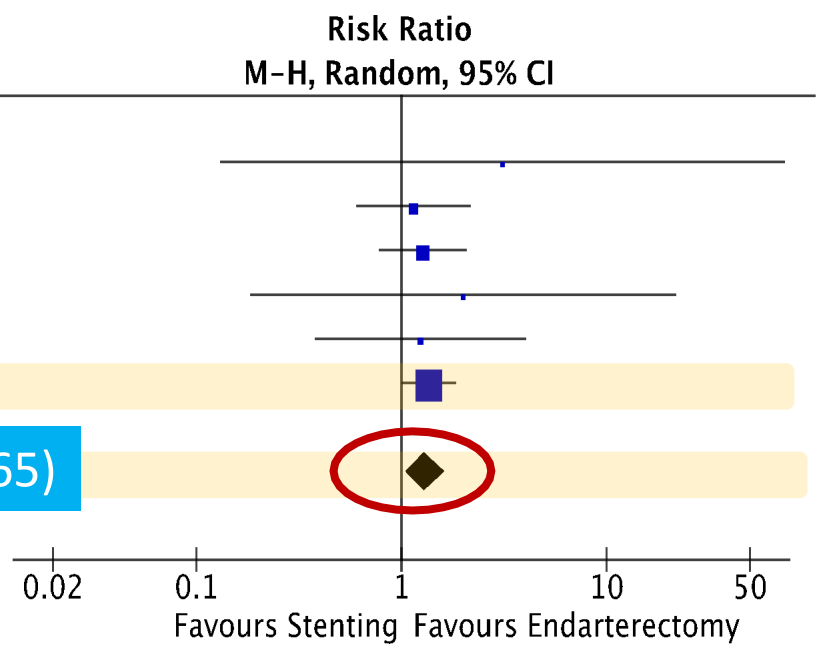
Stenting versus endarterectomy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 3.1)

	Stenting		Endarterectomy			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Kentucky 2004	0	43	0	42		Not estimable	2004
Houston 2014	1	27	0	28	0.5%	3.11 [0.13, 73.11]	2014
ACT-1 2016	41	1089	12	364	13.0%	1.14 [0.61, 2.15]	2016
CREST 2016	36	594	28	587	22.4%	1.27 [0.79, 2.05]	2016
Carmel Medical Center 2017	2	68	1	68	0.9%	2.00 [0.19, 21.54]	2017
SPACE-2 2019	6	197	5	203	3.8%	1.24 [0.38, 3.99]	2020
ACST-2 2021	99	1811	73	1814	59.4%	1.36 [1.01, 1.83]	2021
Total (95% CI)		**3829**		**3106**	**100.0%**	RR 1.31 (1.05-1.65)	
Total events	185		119				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.67$, df = 5 (P = 0.98); $I^2 = 0\%$

Test for overall effect: Z = 2.35 (P = 0.02)



Symptomatic carotid stenosis

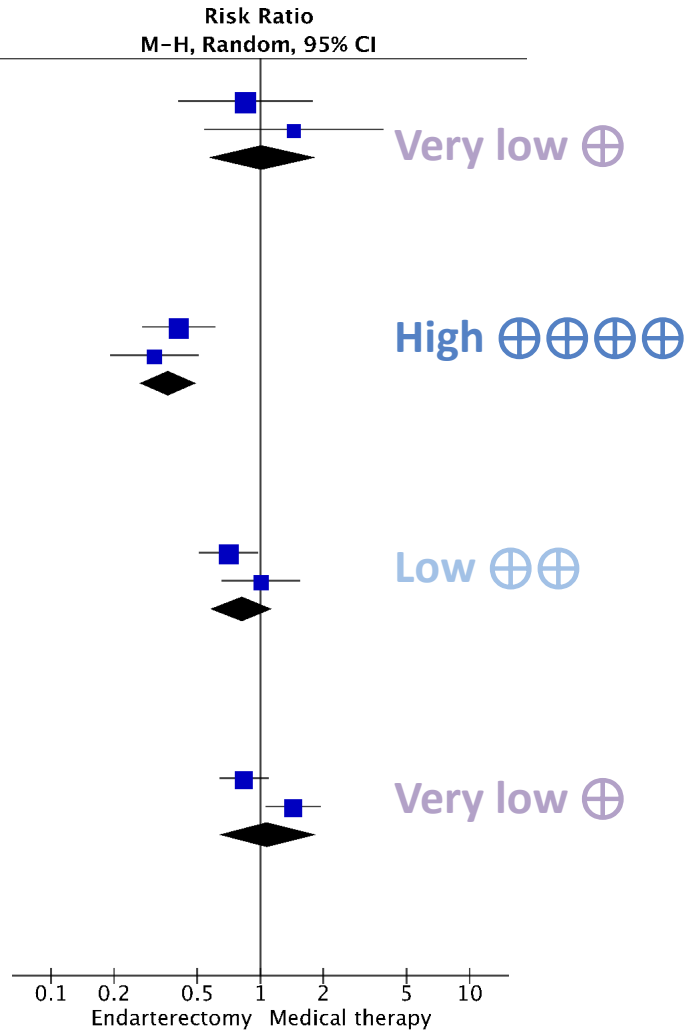
Symptomatic carotid stenosis

Endarterectomy versus medical therapy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 4.1.4)
Subgroup: severity of stenosis

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Medical therapy Events	Medical therapy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Near occlusion							
NASCET 1991	12	79	12	67	64.2%	0.85 [0.41, 1.76]	1991
ECST 1998	12	78	5	47	35.8%	1.45 [0.54, 3.85]	1998
Subtotal (95% CI)		**157**		**114**	**100.0%**	**1.03 [0.57, 1.84]**	
Total events	24		17				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.74$, df = 1 (P = 0.39); $I^2 = 0\%$							
Test for overall effect: Z = 0.09 (P = 0.93)							
Severe stenosis (70-99%)							
NASCET 1991	29	261	72	264	59.6%	0.41 [0.27, 0.61]	1991
ECST 1998	21	257	45	172	40.4%	0.31 [0.19, 0.51]	1998
Subtotal (95% CI)		**518**		**436**	**100.0%**	**0.37 [0.27, 0.50]**	
Total events	50		117				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.70$, df = 1 (P = 0.40); $I^2 = 0\%$							
Test for overall effect: Z = 6.45 (P < 0.00001)							
Moderate stenosis (50-69%)							
NASCET 1991	55	428	78	428	58.0%	0.71 [0.51, 0.97]	1991
ECST 1998	46	380	32	266	42.0%	1.01 [0.66, 1.54]	1998
Subtotal (95% CI)		**808**		**694**	**100.0%**	**0.82 [0.58, 1.15]**	
Total events	101		110				
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 1.73$, df = 1 (P = 0.19); $I^2 = 42\%$							
Test for overall effect: Z = 1.14 (P = 0.25)							
Mild stenosis (<50%)							
NASCET 1991	87	677	106	690	50.8%	0.84 [0.64, 1.09]	1991
ECST 1998	125	1085	58	723	49.2%	1.44 [1.07, 1.93]	1998
Subtotal (95% CI)		**1762**		**1413**	**100.0%**	**1.09 [0.64, 1.85]**	
Total events	212		164				
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 7.15$, df = 1 (P = 0.007); $I^2 = 86\%$							
Test for overall effect: Z = 0.32 (P = 0.75)							

Test for subgroup differences: $Chi^2 = 21.16$, df = 3 (P < 0.0001), $I^2 = 85.8\%$



Symptomatic carotid stenosis

Endarterectomy versus medical therapy

Evidence-based Recommendations

In patients with **severe (70-99%) symptomatic carotid artery stenosis, we recommend carotid endarterectomy**.
Quality of evidence: High ⊕⊕⊕⊕
Strength of recommendation: **Strong for carotid endarterectomy ↑↑**

In patients with **moderate (50-69%) symptomatic carotid artery stenosis, we suggest carotid endarterectomy**.
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak for carotid endarterectomy ↑

Symptomatic carotid stenosis

Endarterectomy versus medical therapy

Evidence-based Recommendations *(continued)*

In patients with **mild (<50%) symptomatic carotid artery stenosis, we recommend against carotid endarterectomy**.

Quality of evidence: Very low ⊕

Strength of recommendation: **Strong against carotid endarterectomy** ↓↓

In patients with 50-99% symptomatic carotid stenosis in whom surgery is considered appropriate, **we recommend early endarterectomy, ideally within two weeks** of the first neurological event.

Quality of evidence: High ⊕⊕⊕⊕

Strength of recommendation: **Strong for carotid endarterectomy** ↑↑

These recommendations are independent of sex and age.

Symptomatic carotid stenosis

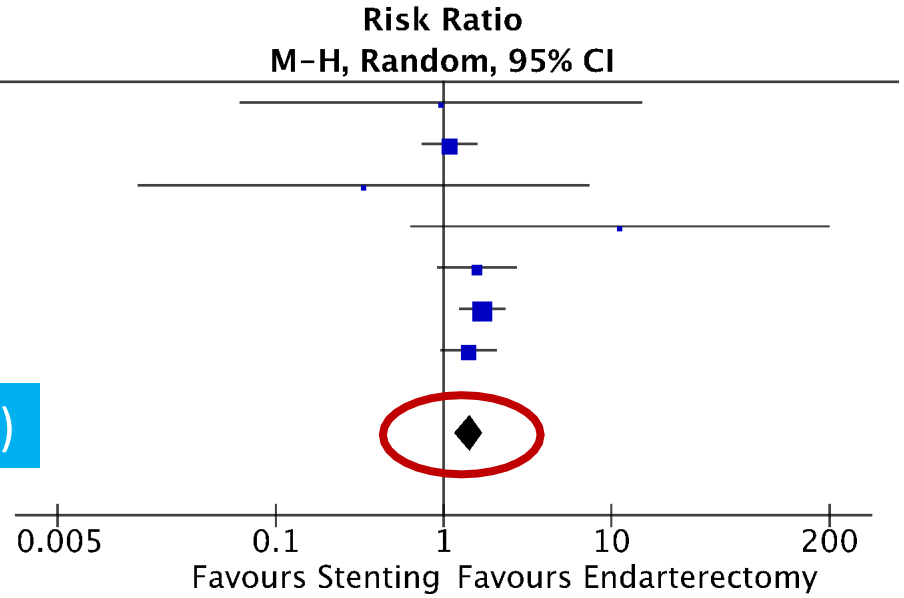
Stenting versus endarterectomy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 6.1)

	Stenting		Endarterectomy			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year
Kentucky 2001	1	53	1	51	0.5%	0.96 [0.06, 14.98]	2001
SPACE 2008	56	607	50	589	25.6%	1.09 [0.76, 1.56]	2008
BACASS 2008	0	10	1	10	0.4%	0.33 [0.02, 7.32]	2008
Regensburg 2008	5	43	0	44	0.5%	11.25 [0.64, 197.44]	2008
EVA-3S 2014	32	265	20	262	13.2%	1.58 [0.93, 2.69]	2014
ICSS 2015	105	853	62	857	35.2%	1.70 [1.26, 2.30]	2015
CREST 2016	62	668	43	653	24.5%	1.41 [0.97, 2.05]	2016
Total (95% CI)		**2499**		**2466**	**100.0%**	RR 1.43 (1.17-1.75)	
Total events	261		177				

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.56$, df = 6 (P = 0.36); $I^2 = 8\%$

Test for overall effect: Z = 3.50 (P = 0.0005)



Quality: Moderate ⊕⊕⊕
(Indirectness)

Symptomatic carotid stenosis

Stenting versus endarterectomy

Evidence-based Recommendation

In patients with symptomatic carotid artery stenosis requiring revascularisation, **we recommend endarterectomy as the treatment of choice**.
Quality of evidence: Moderate ⊕⊕⊕
Strength of recommendation: **Strong for carotid endarterectomy ↑↑**

In patients with symptomatic carotid stenosis **<70 years old** requiring revascularisation, we suggest that **stenting may be considered as an alternative to endarterectomy**.
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak for carotid stenting ↑

Symptomatic carotid stenosis

Stenting versus endarterectomy

Expert consensus statements

The suitability of a patient with symptomatic carotid stenosis for carotid endarterectomy versus stenting should also take into account the **interval** since their last ischaemic cerebrovascular event, as well as **anatomical and morphological features**, including the atherosclerotic burden of the aortic arch.

The independently assessed **risk of in-hospital stroke or death** following endarterectomy or stenting for symptomatic carotid stenosis **should not exceed 4%.**

Conclusions

- ✓ Evidence-based practice guideline for individualised treatment
- ✓ Ongoing trials will provide new evidence for asymptomatic stenosis (ACST-2, CREST-2, ACTRIS)
- ✓ Research needed in:
  - ✓CAS with novel stent designs, protection devices and access routes
  - ✓Selection of patients for treatments (ECST-2)

Thank you very much

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