Supplementary

Table S1 Search strategy for trials comparing CAS to CEA

Carotid stenosis OR Carotid artery stenosis OR Carotid disease OR Carotid artery disease
AND
CAS OR Carotid artery stenting OR Carotid angioplasty OR Carotid stenting
AND
CEA OR Carotid endarterectomy OR Endarterectomy OR Carotid surgery OR Carotid revascularization
AND
Symptomatic or Asymptomatic
AND
Randomized controlled trial OR trial OR Randomized OR Groups OR Randomly OR Controlled clinical trial NOT Animals

CEA, carotid endarterectomy; CAS, carotid artery stenting.

Table S2 Definitions of major stroke, minor stroke, disabling stroke, nondisabling stroke, ipsilateral stroke, and fatal stroke in the involved trials

Trials and year	Stroke outcome definitions	
ACT I 2016	The stroke was divided into minor and major stroke. The major stroke must contain one or more of the listed items: (1) The score of National Institute of Health stroke scale (NIHSS) improved by at least 4 points than before stroke. (2) The score of modified Rankin scale (MRS) improved by at least 2 points than before the stroke. (3) The score of MRS was 5 or more caused by the stroke. The score must last 30 minutes.	Minor stroke: a new stroke occurred for more than 24 hours; however, it did not meet the requirements of the major stroke.
CREST 2010 and 2016	The stroke was divided into minor and major stroke. Major stroke: the score of NIHSS was 9 or more within 3 months.	The minor stroke also named nondisabling stroke. Minor stroke: The patients suffered an infarction due to the intracranial arterial occlusion with a neurological deficit. It must last at least 24 h, and all patients was not disability (the MRS score was 2 or less).
EVA-3S 2006	The symptoms of stroke lasted at least 7 days. It was divided into disabling stroke, nondisabling stroke.	The MRS was used to define the disabling stroke, it was at least 3 for 30 days or more, with an increase of at least 2 points than before the stroke. And the higher the MRS score, the more severe the disability.
ICSS 2010 and 2015	The stroke was divided into the disabling, nondisabling and stroke fatal stroke. Fatal stroke: A patient suffered a rapidly developing syndrome, which caused by focal disturbance of cerebral function lasting at least 24 hours. Or, the patient died within 30 days of the stroke, and no other cause of vascular stroke was found to be accidental.	Disabling stroke: MRS was used to define the disabling stroke, it was at least 3 for 30 days or more. Meanwhile, the remaining nonfatal strokes was defined as nondisabling.
SPACE 2006	The stroke was divided into the ipsilateral stroke and disabling ipsilateral stroke. Ipsilateral stroke: A patient suffered an ipsilateral stroke or intracerebral bleeding or both, and the symptom lasted at least 24 h.	Disabling stroke: MRS was used to define the disabling stroke, it was at least 3.
CAVATAS-CEA 2009	The strokes were divided into disabling, non-disabling, fatal stroke and TIA. Disabling stroke: A patient suffered a rapidly developing syndrome, which caused by focal disturbance of cerebral function lasting at least 24 hours. And the patient needed help from others for at least one month due to the stroke. Fatal stroke: patient had rapidly developing syndrome, which caused by focal disturbance of cerebral function lasting at least 24 hours. Or, the patient died within 30 days of the stroke, and no other cause of vascular stroke was found to be accidental.	Non-disabling stroke: the patient had acute syndrome caused by focal disturbance of cerebral function lasting more than 24 hours, except fatal and disabling stroke. TIA: patient had rapidly developing syndrome, which caused by focal disturbance of cerebral function lasting at least 24 hours due to cerebrovascular disease.
Eckstein *et al.* 2008	The stroke was divided into the ipsilateral stroke and any ipsilateral stroke. Ipsilateral stroke: the cerebral infarction and/or cerebral bleeding.	Any ipsilateral stroke: the cerebral infarction and/or cerebral bleeding combined with persistent impairment of brain function (the MRS score was 3 or more).
Kentucky 2001	Not Available.	
Wallstent 2001	Not Available.	
Mannheim *et al.* 2016	Not Available.	

CEA, carotid endarterectomy; CAS, carotid artery stenting; NIHSS, National Institute of Health stroke scale; MRS, modified Rankin scale; CREST, carotid revascularization endarterectomy versus stenting trial; SPACE, Stent-Protected Angioplasty versus Carotid Endarterectomy; EVA-3S, Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis; ACT I, Asymptomatic Carotid Trial I; ICSS, International Carotid Stenting Study; CAVATAS-CEA, Carotid And Vertebral Artery Transluminal Angioplasty Study-carotid endarterectomy, TIA, transient ischemic attacks.

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Table S3 Overview of included studies

Trial	Country	Years	Type of Study	Participants (n)		Use of EPDs	Carotid stenosis
				CAS	CEA		
CREST	USA	2010, 2011	RCT	1262	1240	97.9%	Symptomatic and asymptomatic
ACT I	USA	2016	RCT	1089	364	97.6%	Asymptomatic
Mannheim *et al.*	Israel	2016	RCT	68	68	95.9%	Asymptomatic
SPACE	Germany	2006, 2008	RCT	599	584	27%	Symptomatic
CAVATAS-CEA	UK	2009	RCT	251	253	NA	Symptomatic
EVA 3S	USA	2006, 2011	RCT	261	259	91.9%	Symptomatic
Kentucky	USA	2001	RCT	53	51	None	Symptomatic
Wallstent	NA	2001	RCT	107	112	None	Symptomatic
ICSS	UK	2010, 2015	RCT	853	857	70.7%	Symptomatic
Eckstein *et al.*	Germany	2008	RCT	607	589	NA	Symptomatic

CEA, carotid endarterectomy; CAS, carotid artery stenting; EPDs, embolic-protection devices; NA, not available; CREST, carotid revascularization endarterectomy versus stenting trial; SPACE, Stent-Protected Angioplasty versus Carotid Endarterectomy; EVA-3S,Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis; ACT I, Asymptomatic Carotid Trial I; ICSS, International Carotid Stenting Study; CAVATAS-CEA, Carotid And Vertebral Artery Transluminal Angioplasty Study-carotid endarterectomy.

Table S4 Cochrane Collaboration's tool for quality assessment in trials comparing CAS to CEA

Trials	Sequence generation	Allocation concealment	Blinding of outcome assessors	Incomplete outcome data	Selective outcome reporting	Others
CREST	Low	Unclear	Low	Low	Low	Low
ACT I	Low	Unclear	Low	Low	Low	Unclear
Mannheim et al	Low	Unclear	Low	Low	Low	Low
SPACE	Low	Low	Low	Low	Low	Low
CAVATAS-CEA	Low	Unclear	Low	Low	Low	Low
EVA 3S	Low	Low	Low	Low	Low	Low
Kentucky	Low	Unclear	Low	High	Low	Low
Wallstent	Unclear	Unclear	Unclear	High	Low	Unclear
ICSS	Low	Low	Low	Low	Low	Low
Eckstein *et al.*	Low	Low	Low	Low	Low	Low

CEA, carotid endarterectomy; CAS, carotid artery stenting; CREST, carotid revascularization endarterectomy versus stenting trial; SPACE, Stent-Protected Angioplasty versus Carotid Endarterectomy; EVA-3S, Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis; ACT I, Asymptomatic Carotid Trial I; ICSS, International Carotid Stenting Study; CAVATAS-CEA, Carotid And Vertebral Artery Transluminal Angioplasty Study-carotid endarterectomy.

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Table S5 Procedural characteristics and intervention of antiplatelet therapy

Trials	Procedural characteristics		Antiplatelet therapy	
	Carotid endarterectomy	Carotid artery stenting	Carotid endarterectomy	Carotid artery stenting
Wallstent 2001	Not discussed	Not discussed	Not discussed	Not discussed
Kentucky 2001	Conventional surgical techniques	Placing a 0.014-in Sport wire (Guidant-ACS, Inc.) in the petrous field of the internal carotid artery. The 4.0 20 mm Symmetry balloon was used to inflated the stenosis artery to 8 atms for 5 s. Then a 10-20 mm Wallstent. Postdilation was used	325 mg aspirin combined with 75 mg clopidogrel were used before procedure	325 mg aspirin combined with 75 mg clopidogrel were used before procedure
EVA-3S 2006	Not discussed	The stents and protection devices approved by the accreditation committee was used	Not discussed	100 to 300 mg aspirin combined with 75 mg clopidogrel or 500 mg ticlopidine for 3 days before operation and 30 days after operation
SPACE 2006	Shunting was optional (not available clearly)	The surgeons decided how to select protection devices, predilation, and balloon size were. All devices were approved to use by surgical standards committee	100 mg aspirin or more was taken before, during, and after surgery	100 mg aspirin combined with 75 mg clopidogrel daily was used for 3 days before surgery and 30 days after operation
Eckstein *et al.* 2008	Shunting was optional (not available clearly)	Not discussed	100 mg aspirin was taken during the operation	The aspirin combined with clopidogrel was used for 3 days before surgery and 30 days after operation
CAVATAS-CEA 2009	Not discussed	Not discussed	Antiplatelet and Warfarin were used for duration of follow-up and randomization	Antiplatelet and Warfarin were used for duration of follow-up and randomization
CREST 2010	Not discussed	The RX Acculink stent and the RX Accunet embolic-protection device were used	325 mg aspirin daily was used for 2 days before surgery and more than one year after the surgery. 250 mg ticlopidine bid; 75 mg clopidogrel daily, 81 mg aspirin daily, or Aggrenox® bid was used for intolerant at aspirin dose patients	325 mg aspirin bid for 2 days before the surgery and after surgery. Or, 75 mg clopidogrel bid for 2 days before the procedure and 75 mg clopidogrel or 250 mg ticlopidine daily for 30 days after surgery. Alternatively, 325 mg aspirin and 75 mg clopidogrel taken more than four hours before surgery
ICSS 2010	39.5% patients used a shunt. 22.1% patients used “standard” primary closure. 55.9% patients used patch closure. 6.0% patients conducted an eversion endarterectomy	Less than 10% of patients used following stents: Exponent, Acculink, Xact, Cristallo Ideale, Smart, Next Stent. Protection devices were used in 593 of 828 patients	Not discussed	Of 821 patients, 726 cases used an antiplatelet agent before surgery, 247 cases taken dual antiplatelet therapy
Mannheim *et al.* 2016	The surgeons decided how to select shunting, primary closure, patch or eversion	The distal protection, angioguard™ or spiderfX™, was used for all patients	Not discussed	75 mg Clopidogrel for the day before surgery and for 45 days after surgery
ACT I 2016	The surgeons decided how to select the protection devices, type of anesthetic, patches or shunts	Closed-cell, nitinol stents with a tapering diameter were used in conjunction with distal embolic protection	325 mg aspirin was used for 3 days before the surgery and indefinitely after surgery	aspirin (325 mg) for 3 days before the surgery and indefinitely after surgery. Or, clopidogrel daily for 3 days before surgery and for 30 days after surgery

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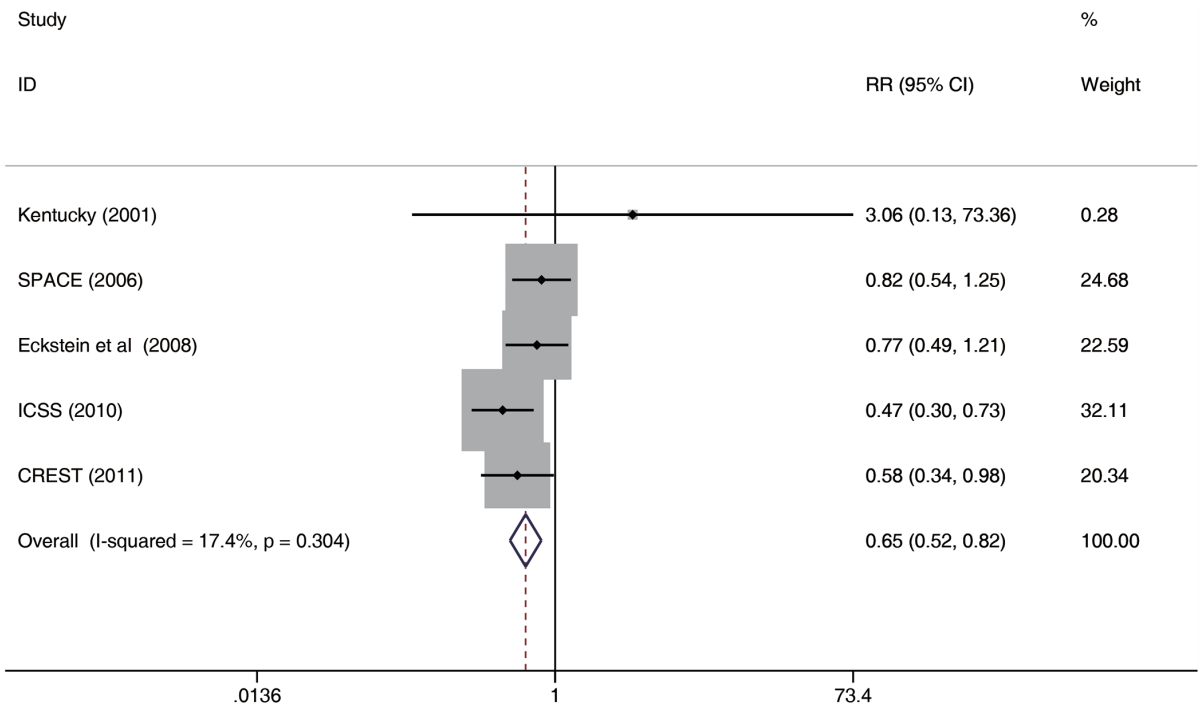

Figure S1 Forest plot of risk ratios (RR) of any stroke with carotid endarterectomy (CEA) *vs.* carotid artery stenting (CAS; control) for patients with symptomatic carotid stenosis.

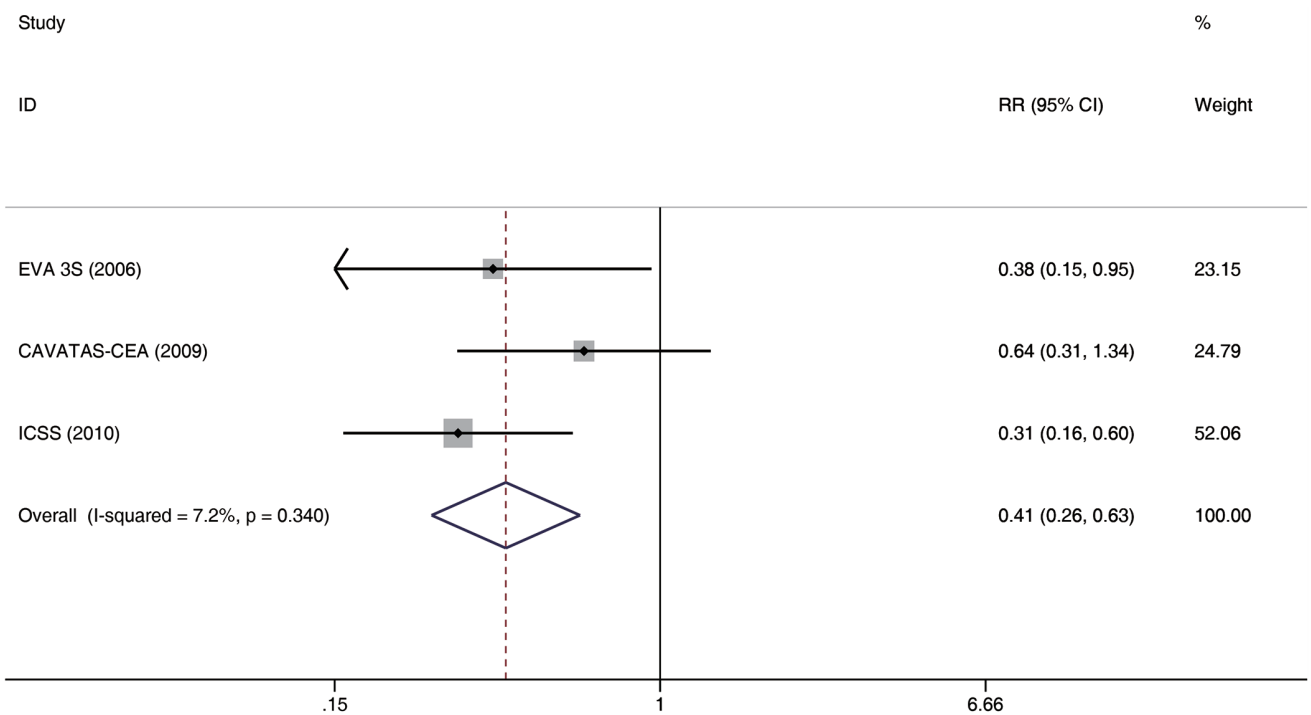

Figure S2 Forest plot of risk ratios (RR) of periprocedural non-disabling stroke with carotid endarterectomy (CEA) *vs.* carotid artery stenting (CAS; control) for patients with symptomatic carotid stenosis.

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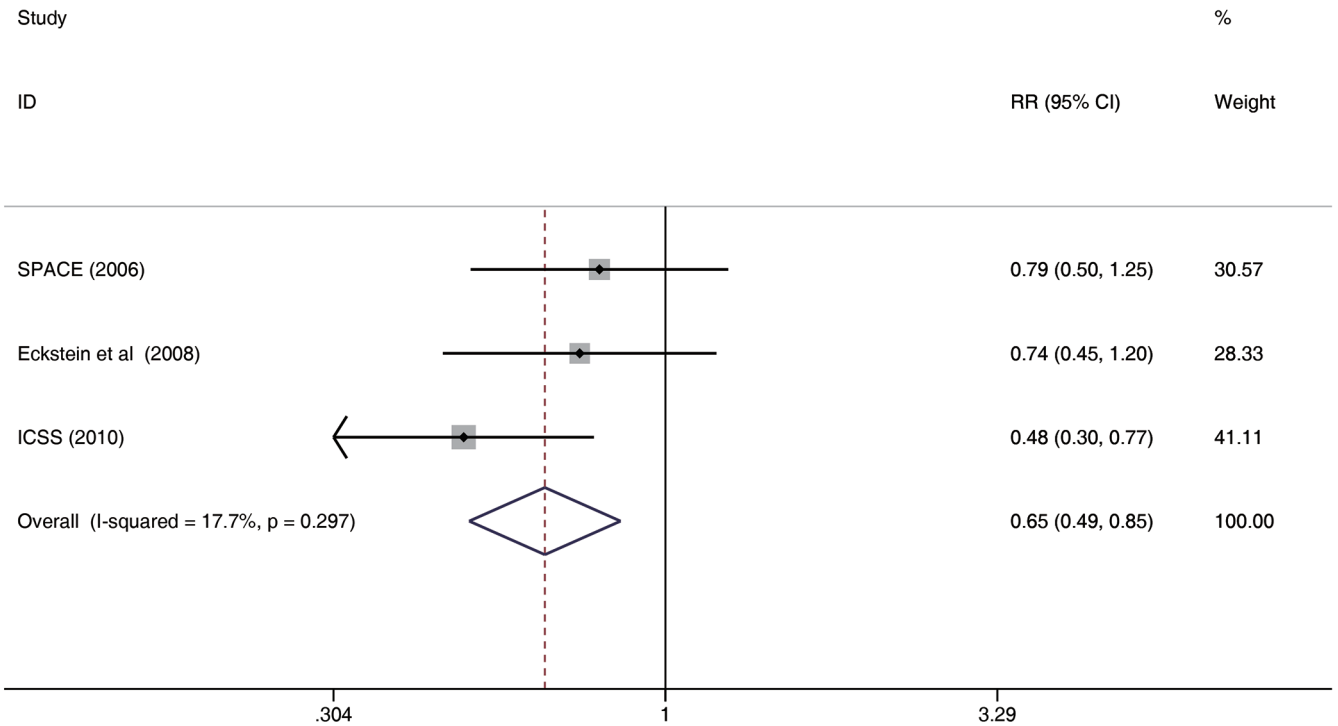

Figure S3 Forest plot of risk ratios (RR) of ipsilateral ischemic stroke with carotid endarterectomy (CEA) *vs.* carotid artery stenting (CAS; control) for patients with symptomatic carotid stenosis.

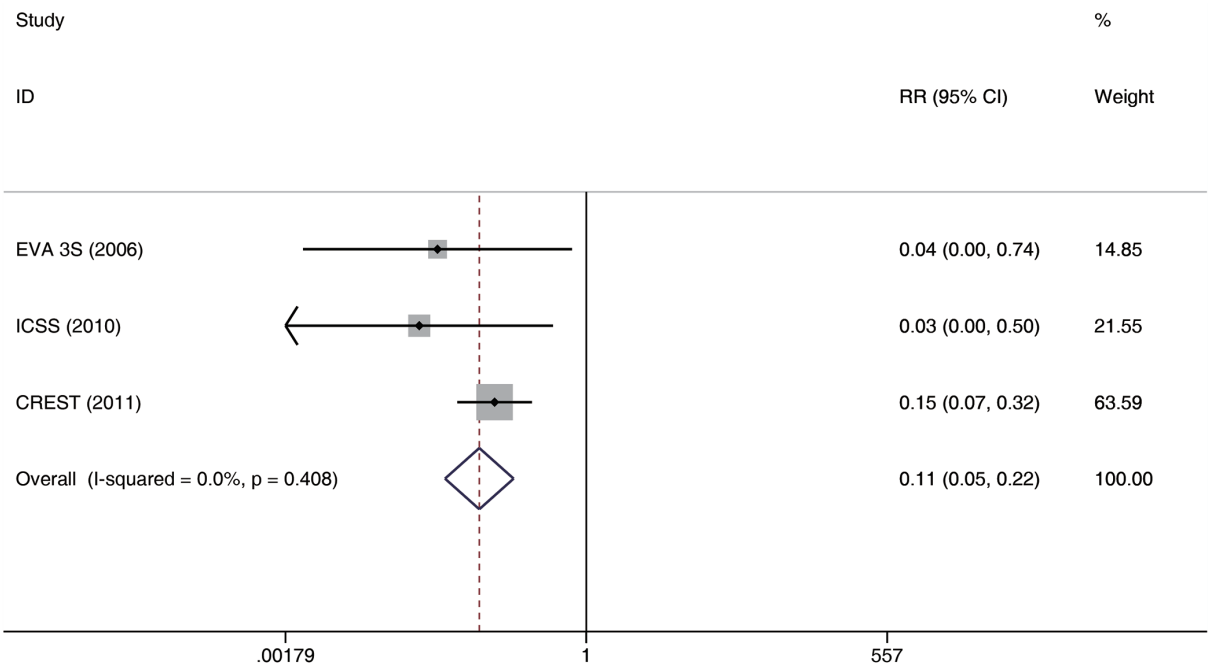

Figure S4 Forest plot of risk ratios (RR) of bradycardia or hypotension with carotid endarterectomy (CEA) *vs.* carotid artery stenting (CAS; control) for patients with symptomatic carotid stenosis.

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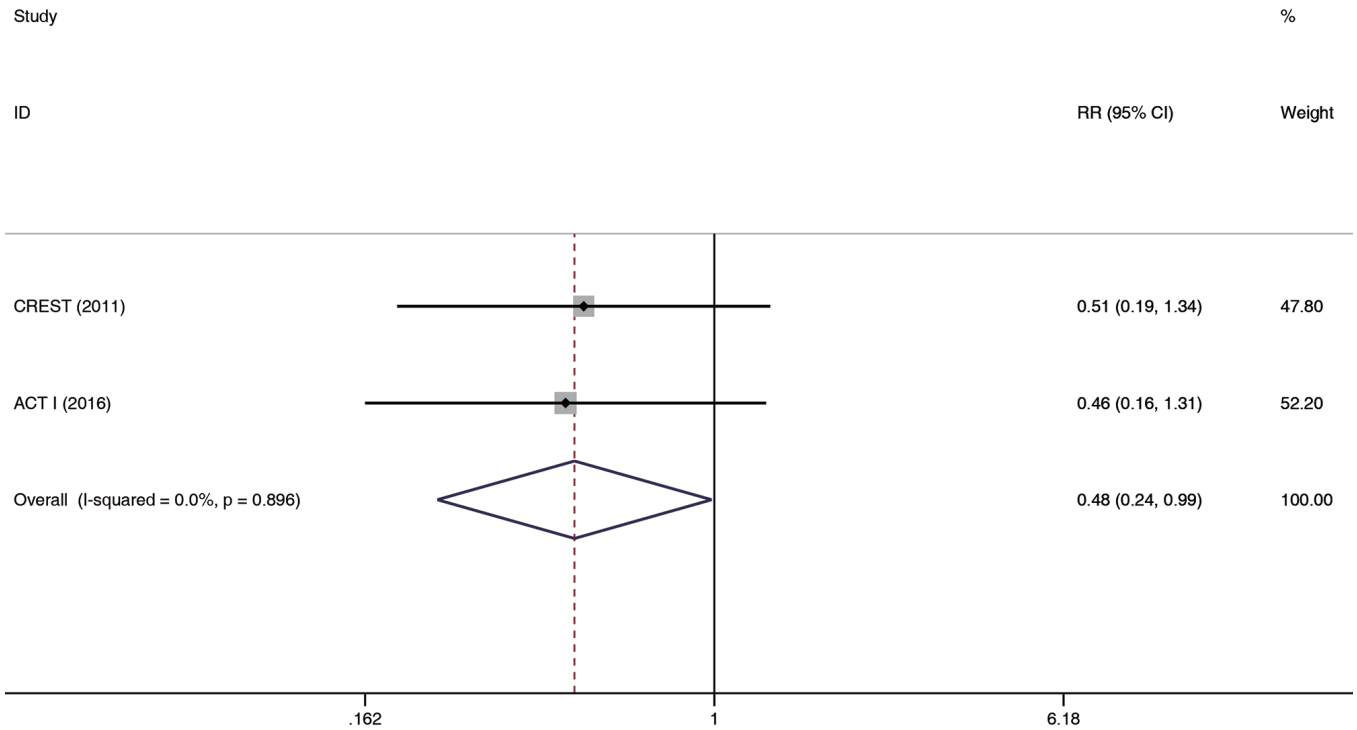

Figure S5 Forest plot of risk ratios (RR) of periprocedural minor stroke with carotid endarterectomy (CEA) *vs.* carotid artery stenting (CAS; control) for patients with asymptomatic carotid stenosis.

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