A systematic review supporting the Society for Vascular Surgery Guidelines on the management of carotid artery disease

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ABSTRACT

Background: To support the development of guidelines on the management of carotid disease, a writing committee from the Society for Vascular Surgery has commissioned this systematic review.

Methods: We searched multiple data bases for studies addressing five questions: medical management vs carotid revascularization (CEA) in asymptomatic patients, CEA vs carotid artery stenting (CAS) in symptomatic low surgical risk patients, the optimal timing of revascularization after acute stroke, screening high-risk patients for carotid disease, and the optimal sequence of interventions in patients with combined coronary and carotid disease. Studies were selected and appraised by pairs of independent reviewers. Meta-analyses were performed when feasible.

Results: Medical management compared with carotid interventions in asymptomatic patients was associated with better early outcome during the first 30 days. However, CEA was associated with significantly lower long-term rate of stroke/death at 5 years. In symptomatic low-risk surgical patients, CEA was associated with a lower risk of stroke, but a significant increase in myocardial infarction compared with CAS during the first 30 days. When the long-term outcome of transfemoral CAS vs CEA in symptomatic patients were examined using preplanned pooled analysis of individual patient data from four randomized trials, the risk of death or stroke within 120 days of the index procedure was 5.5% for CEA and 8.7% for CAS, which lends support that, over the long term, CEA has a superior outcome compared with transfemoral CAS. When managing acute stroke, the comparison of CEA during the first 48 hours to that between day 2 and day 14 did not reveal a statistically significant difference on outcomes during the first 30 days. Registry data show good results with CEA performed in the first week, but not within the first 48 hours. A single risk factor, aside from peripheral artery disease, was associated with low carotid screening yield. Multiple risk factors greatly increase the yield of screening. Evidence on the timing of interventions in patients with combined carotid and coronary disease was sparse and imprecise. Patients without carotid symptoms, who had the carotid intervention first, compared with a combined carotid intervention and coronary artery bypass grafting, had better outcomes.

Conclusions: This updated evidence summary supports the Society for Vascular Surgery clinical practice guidelines for commonly raised clinical scenarios. CEA was superior to medical therapy in the long-term prevention of stroke/death over medical therapy. CEA was also superior to transfemoral CAS in minimizing long-term stroke/death for symptomatic low risk surgical patients. CEA should optimally be performed between 2 and 14 days from the onset of acute stroke. Having multiple risk factors increases the value of carotid screening. (J Vasc Surg 2022;75:99S-108S.)

Keywords: Systematic review; Meta-analysis; Carotid artery disease; Carotid endarterectomy; Carotid artery stenting; Screening; Management

Extracranial carotid artery disease occurs owing to progression of atheromatous plaque which mainly affects the carotid bifurcation, and results in narrowing or blockade of the arterial lumen. This can be an asymptomatic process and found incidentally, or the patient may present with an ischemic stroke or transient ischemic attack. Stroke is one of the leading causes of morbidity, disability and mortality. It is the cause for about 140,000 deaths each year in the United States.[1] Poststroke care in the United States is a huge economic burden and can reach $4850 per patient month.[2]

From the Evidence-Based Practice Research Program,[a] Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery,[b] and Mayo Clinic Libraries,[c] Mayo Clinic, Rochester; and the Department of Surgery, West Virginia University, Charleston.[d]

Author conflict of interest: none.

Funded by a grant from the Society for Vascular Surgery.

Additional material for this article may be found online at www.jvascsurg.org.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2021.06.001

Table. Research questions

Patient	Intervention	Comparison	Outcomes	Study design	Subgroups
Question 1. What is the comparative effectiveness of medical management vs carotid intervention in asymptomatic patients?					
Asymptomatic patients above 70% stenosis	Medical management	CEA or CAS	Stroke, ipsilateral stroke, death (or mortality), MI, combined	RCTs or observational	30 day, >30 day, 5 years or more
Question 2. What is the comparative effectiveness of carotid endarterectomy vs carotid artery stenting in symptomatic patients?					
Symptomatic patients	CEA	CAS	Stroke, ipsilateral stroke, death (or mortality), MI	RCTs	30 day, >30 day, 5 years or more
Question 3. What is the optimal timing of carotid intervention after acute stroke?					
Patients with acute stroke with >50% carotid stenosis	Intervention (CEA or CAS) <2 days	Intervention 2-14 days, >14 days	Improvement, deterioration, death (perioperative, 30 days) cerebral hem or hyperperfusion, MI, new stroke	RCT or observational	CEA, CAS
Question 4. Which high-risk patients should be screened for carotid disease?					
Patients with risk factors for atherosclerosis (ie, HTN, smokers, hypercholesterolemia, PAD, CAD, DM, RF)	Screening carotid duplex/Doppler	No screening	Prevalence of >50% stenosis, mortality, stroke	Any (comparative or noncomparative)	Risk factors
Question 5. In patients with combined coronary/carotid disease, what is the optimal sequence for intervention?					
Patients with combined coronary/carotid disease	(1) Combined carotid intervention + CABG	(2) CABG first (3) Carotid intervention first	Stroke, death, MI, combined	RCT or observational	Symptomatic, asymptomatic, CEA vs CAS

CABG, Coronary artery bypass grafting; *CAD*, coronary artery disease; *CAS*, carotid artery stenting; *CEA*, carotid endarterectomy; *DM*, diabetes mellitus; *HTN*, hypertension; *MI*, myocardial infarction; *PAD*, peripheral arterial disease; *RCT*, randomized, controlled trial; *RF*, renal failure.

Three main therapeutic strategies exist for patients with carotid artery disease, including medical management, carotid endarterectomy (CEA) and carotid artery stenting (CAS). Medical management is recommended in all cases (with CEA, CAS, or alone) and includes antiplatelet medications (aspirin, dipyridamole, ticlopidine, and clopidogrel), high-potency statins, oral diabetic medication or insulin, hypertensive medications, smoking cessation, and lifestyle modifications.

Controversies and debates exist on various aspects of the management of carotid disease, starting with knowing which patients should be screened for carotid disease. In terms of treatment, an important question is under which circumstances to use these treatment options, particularly as it relates to whether the patient is symptomatic or not. The issue of optimal timing of carotid intervention after acute stroke is equally important. In patients with combined coronary and carotid disease, the optimal sequence for intervention is also unclear.

The Society for Vascular Surgery (SVS) has determined this topic to be in need for updated clinical practice guidelines and identified several decision-making dilemmas that patients and surgeons face in practice. To support the guideline development process and summarize the evidence base, we conducted this systematic review and meta-analysis.

METHODS

This report was written in accordance with the PRISMA statement.[3] The specific questions of this review and the explicit inclusion and exclusion criteria were developed by a committee from the SVS charged with developing clinical practice guidelines on the management of carotid disease.

Eligibility criteria. The committee prioritized five questions, which are presented using the PICO format (patient, intervention, comparison, outcomes) along with the eligibility criteria in the Table. The five questions addressed medical management vs carotid revascularization (CEA) in asymptomatic patients, CEA vs CAS in symptomatic low surgical risk patients, the optimal timing of revascularization after acute stroke, screening high-risk patients for carotid disease, and the optimal sequence of interventions in patients with combined coronary and carotid disease.

Data sources and search strategies. The search strategy first identified existing systematic reviews to determine the feasibility and the approach for the project. When a high credibility review was identified, we updated the review. Dedicated searches for original studies were then designed for each question. The databases included MEDLINE, Embase, Cochrane Central

Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Scopus. Searches were completed in August 2019 for questions 1 and 3, and in July 2019 for questions 2, 4, and 5. The search strategy was designed and conducted by medical reference librarians with input from the investigators. Controlled vocabulary supplemented with key words was used to search for studies of interest without language restrictions. The actual strategy listing all search terms used and how they are combined is available in the Appendix (online only).

Study selection and data extraction. Studies obtained by the search strategies, reference mining of systematic reviews, and those suggested by the committee were reviewed independently by two reviewers. We first reviewed abstracts and in a second phase we reviewed full-text articles if included or had a conflict at the abstract level. Data from included studies were abstracted by pairs of independent reviewers using different standardized piloted Excel sheets for each question. Disagreements were resolved via consensus.

We extracted data on patient characteristics (eg number of patients, mean age, gender, mean body mass index, comorbidities, and details of medical therapy) and outcomes of interest (stroke, ipsilateral stroke, death, myocardial infarction [MI], cerebral hemorrhage, cerebral hyperperfusion, and prevalence of >50% carotid stenosis).

Methodologic quality and certainty of the evidence. The risk of bias in the included studies was assessed by two independent reviewers. This task was carried out using a standardized form based on the Newcastle Ottawa scale for observational studies[4] and the Cochrane tool for risk of bias assessment of randomized controlled trials (RCTs).[5] For uncontrolled studies, we used an adaptation of the Newcastle Ottawa scale.[6] Any discrepancy between a pair of reviewers was solved by consensus or by a third reviewer. We rated the certainty of evidence using the GRADE approach[7] as adapted by the SVS.[8,9] We considered an estimate to be imprecise if its confidence interval (CI) overlapped both, benefits and harms.[10]

Statistical analysis. For comparative studies, we calculated the relative risk (RR) from each study and estimated the 95% CI and pooled across studies using the DerSimonian and Laird random effects model. For noncomparative studies, an overall event rate was calculated and transformed using the Freeman-Tukey arcsine method, and pooled using the DerSimonian and Laird random effects model. The random effects model was chosen a priori because of anticipated heterogeneity across study populations and settings. Heterogeneity was evaluated using the I^2 index and Cochrane Q test. All statistical analyses were conducted using R version 3.6.1 (The R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study selection

We reviewed 5935 citations and 898 systematic reviews. The study selection process for the five questions is depicted in the Supplementary Figure (online only). We finally included 96 studies (question one, 6 studies[11-16]; question two, 9 RCTs[17-25]; question three, 8 studies[26-33]; question four, 47 studies[34-80]; and question five, 26 studies[81-106]). A detailed description of the included study characteristics for each of the questions and their risk of bias is available in Supplementary Tables II and III, (online only) respectively.

Question 1: Medical management vs CEA in asymptomatic patients

We included four RCTs and two observational studies. Most of the studies had a low risk of bias based on each corresponding bias assessment tool. One RCT[13] had a moderate risk of bias owing to lack of blinding of outcome assessors. The studies reported on 5498 patients (mean age, 70 years; 67% males) with a varying prevalence of comorbidities (commonly coronary artery disease, hypertension, and hypercholesterolemia). Patients in all studies received aggressive medical treatment following up-to-date national and international guidelines. Those treatments were focused on antiplatelet therapy, antihypertensive therapy, and lipid-lowering therapy.

Thirty-day outcomes. Medical management was associated with a significant decrease in strokes and combined stroke/death at 30 days compared with CEA (3 studies; RR, 0.26; 95% CI, 0.08-0.87 [Supplementary Table I, online only], and RR, 0.24; 95% CI, 0.11-0.53 [Supplementary Table I, online only], respectively). Certainty in evidence was moderate, reduced owing to methodologic limitations.

Mortality estimate was highly imprecise to derive conclusions (3 studies; RR, 0.17; 95% CI, 0.00-33.71) (Supplementary Table I, online only). The estimate for the outcome of MI and ipsilateral stroke was highly imprecise to derive conclusions. Certainty in evidence was very low, decreased owing to methodologic limitations and severe imprecision.

Outcomes at longest follow-up. Kolos et al 2015[12] demonstrated that, at the 3.3-year follow-up, medical therapy was associated with significantly higher risk of stroke/death (RR, 5.81; 95% CI, 1.38-24.45; Supplementary Table I, online only). After 5 years of follow-up, medical therapy was associated with a higher risk of stroke (ACST 2004[11]) (RR, 2.86; 95% CI, 2.02-4.03; Supplementary Table I, online only) and ipsilateral stroke (ACST 2004[11]) (RR, 4.77; 95% CI, 2.63-8.64) (Supplementary Table I, online only). Certainty in these estimates was moderate to high. The estimates for the outcomes of death, stroke, stroke/death, MI, and ipsilateral stroke at the 1-year follow-up were reported by Reiff et al[13] and were highly

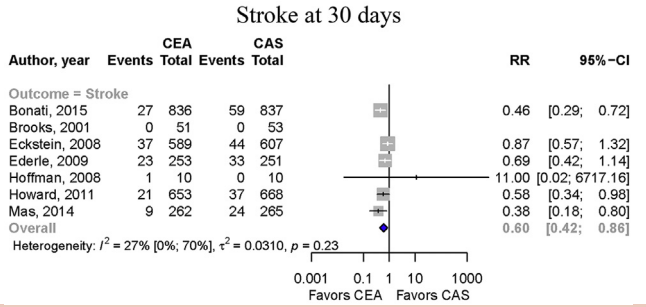

Fig 1. Forest plot representing the overall relative risk (*RR*) and associated 95% confidence intervals (CIs; horizontal lines) of stroke at 30 days for carotid endarterectomy (*CEA*) compared with carotid artery stenting (*CAS*). The grey squares indicate the weights used in the meta-analysis.

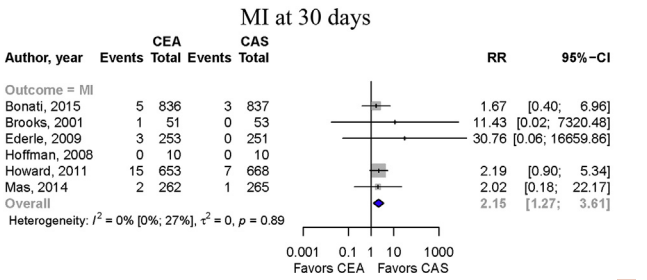

Fig 2. Forest plot representing the overall relative risk (*RR*) and associated 95% confidence intervals (CIs; horizontal lines) of myocardial infarction (*MI*) at 30 days for carotid endarterectomy (*CEA*) compared with carotid artery stenting (*CAS*). The grey squares indicate the weights used in the meta-analysis.

imprecise to derive conclusions. A meta-analysis was not feasible on stroke outcomes owing to the heterogeneity of reporting and follow-up durations.

Howard et al[107] conducted a systematic review and meta-analysis that analyzed the correlation between the degree of asymptomatic carotid stenosis and ipsilateral stroke in patients treated with contemporary best medical therapy. The ipsilateral stroke rate was significantly greater for patients with 80% to 99% carotid stenosis than those with 50% to less than 80% stenosis (18% vs 1%; $P < .0001$). Patients with 70% to 99% carotid stenosis had a higher risk of ipsilateral stroke than those with 50% to less than 70% stenosis ($P < .0001$). These studies suggest that the benefit of CEA might be underestimated in patients with severe stenosis (>70%).[107]

Question 2: CEA vs CAS in symptomatic low risk surgical patients

We included nine RCTs (published in 25 different publications). Four RCTs had a low overall risk of bias, three had a moderate risk of bias mainly owing to lack of blinding of outcome assessors, and two had a high risk of bias owing to a lack of blinding of outcome assessors, and inadequate random sequence generation, allocation concealment and possible selective reporting. The studies reported on 5486 patients (mean age, 69 years; 75% males). The most common comorbidities in this group of patients are hypertension, hyperlipidemia, and coronary artery disease.

Outcomes at 30 days. CEA was associated with a significant reduction in stroke and a significant increase in the risk of MI at 30 days compared with CAS (7 studies; RR, 0.60; 95% CI, 0.42-0.86; Fig 1) and (6 studies; RR, 2.15; 95% CI, 1.27-3.61; Fig 2), respectively. Certainty in evidence was high.

Estimates were highly imprecise to derive conclusions about the outcomes of death, ipsilateral stroke and death/stroke at 30 days (8 studies; RR, 0.63; 95% CI, 0.31-1.29; Supplementary Table I, online only), (4 studies; RR, 0.65; 95% CI, 0.22-1.93; Supplementary Table I, online only), and (4 studies; RR, 0.68; 95% CI, 0.38-1.24; Supplementary Table I, online only), respectively. Certainty in evidence was very low, reduced owing to methodologic limitations and severe imprecision.

Outcomes at 5 years. When the long-term outcome of transfemoral CAS vs CEA in symptomatic patients were examined using a preplanned pooled analysis of individual patient data from four randomized trials,[108] the risk of death or stroke within 120 days of the index procedure was 5.5% (4.7%-6.5%) for CEA and 8.7% (7.6%-9.9%) for CAS. The primary event outcome and ipsilateral postprocedural stroke at 5 years was 8.3% (7.25%-9.6%) for CEA vs 11.4% (10.1%-12.8%) for CAS (Supplementary Table I, online only).

Question 3: Timing of intervention in stroke

We included seven observational studies and one RCT. As for the observational studies, three of them had an overall low risk of bias and four had a moderate risk of bias mainly because of inadequate follow-up and inadequate comparability of cohorts baseline prognostic factors. The one RCT had an overall moderate risk of bias owing to unclear random sequence generation and lack of blinding of outcome assessors. The studies reported on 9882 patients (mean age, 70 years; 63% males). Hypertension and hypercholesterolemia were the most common comorbidities.

Outcomes at 30 days. A meta-analysis did not show a statistically significant difference in death and cerebral hemorrhage at 30 days between CEA performed at less than 2 days vs 2 to 14 days (3 studies; RR, 1.23; 95% CI, 0.48-3.17; Supplementary Table I, online only) and (2 studies; RR, 0.83; 95% CI, 0.00-13096.54; Supplementary Table I, online only). However, the results of the two larger series suggest worse outcomes with early intervention (<2 days). The study by Tanious et al[17] showed that the risk of cerebral hyperperfusion was numerically higher in patients who had CEA in less than 2 days vs 2 to 14 days (RR, 1.63; 95% CI, 0.34-7.84; Supplementary Table I,

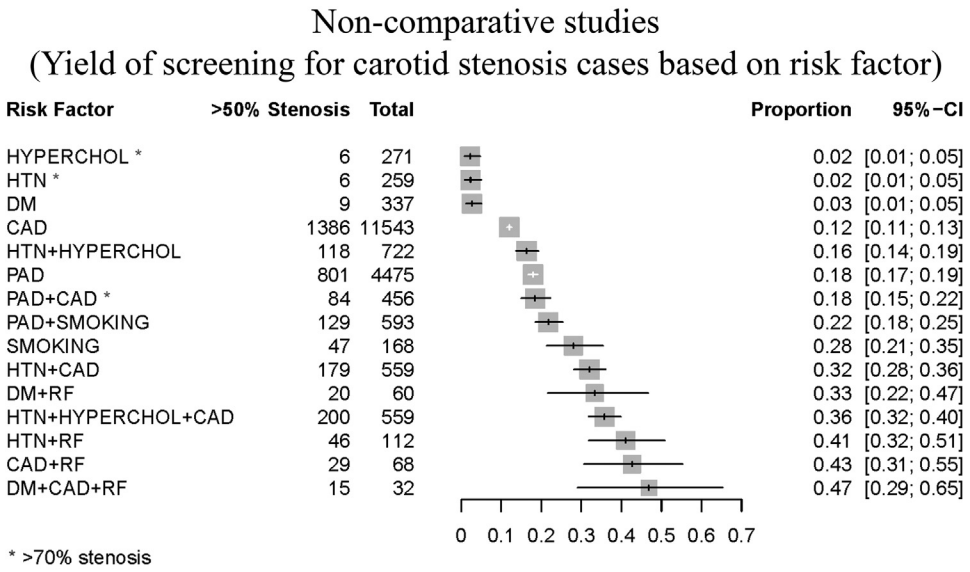

Fig 3. Forest plot representing the overall event rates (proportions) and associated 95% confidence intervals (CIs; horizontal lines) of higher than 50% stenosis stratified by various risk factors.

online only). In the series by Avgerinos et al, stroke rate was nonsignificantly higher in patients who had CEA in less than 2 days vs those who had CEA in 2 to 5 days (RR, 1.80; 95% CI, 0.74-4.39; Supplementary Table I, online only) and it was statistically significantly higher in patients with less than 2 days vs more than 6 days (RR, 4.16; 95% CI, 1.62-10.67; Supplementary Table I, online only). Similarly, Avgerinos et al[25] showed that death was nonsignificantly higher in patients who had CEA in less than 2 days vs more than 6 days (RR, 2.97; 95% CI, 0.27-32.48; Supplementary Table I, online only). Other registry/Vascular Quality Initiative data have shown good results with CEA performed in the first week, but not within the first 48 hours.[31,109-111] Multivariate analysis of Vascular Quality Initiative data demonstrated that when performing CEA between 3 and 7 days after a stroke, compared with first 48 hours after a stroke, was protective for postoperative complication ($P = .028$) and postoperative stroke/death ($P = .003$). No significant differences were noted for CAS outcomes when performed less than 2 days vs between 2 and 14 days. Other outcomes and outcomes related to other time points are available in Supplementary Table I, (online only). Certainty in evidence was very low in all these outcomes, decreased owing to methodologic limitations and severe imprecision.

Question 4: Screening high-risk patients

We included 47 observational studies, most of which were single-arm noncomparative studies. Thus, they were evaluated on the following domains: representativeness of study population, ascertainment of exposure, length of follow-up and adequacy of follow-up. Nine studies had an overall low risk of bias, 10 had a high risk, and 28 had a moderate risk of bias. The studies reported on 32,641 patients (mean age, 65 years; 71% males). Patients had hypertension, smoking, hypercholesterolemia, peripheral artery disease, coronary artery disease, and diabetes.

The yield of screening for carotid stenosis (defined as the presence of >50% stenosis) stratified by various risk factors is depicted in Fig 3. The highest yield was for a combination of diabetes, coronary artery disease, and renal failure (47%; 95% CI, 29%-65%), followed by coronary artery disease and renal failure (43%). Having a single risk factor such as isolated hyperlipidemia, hypertension, or diabetes was associated with low yield (2%, 2%, and 3%, respectively), whereas peripheral artery disease alone was associated with a yield of 18%. The certainty in the yield of screening outcome is likely to be moderate or high.

Comparative studies did not show a statistically significant difference between the screened and unscreened populations in terms of death or stroke (2 studies; RR, 0.38; 95% CI, 0.00-1432.82; Supplementary Table I, online only) and (2 studies; RR, 0.62; 95% CI, 0.00-1024.93; Supplementary Table I, online only); respectively. Certainty in evidence was very low owing to severe imprecision.

Question 5: Optimal sequence for carotid intervention in patients with combined carotid and coronary disease

We included 26 studies, 2 of which were RCTs and 24 were observational studies. One RCT had a low risk of bias, and the other one had a moderate risk owing to unclear blinding of outcome assessors. Ten of the observational studies had a low overall risk of bias and 14 had a moderate risk of bias. The studies reported on 53,577 patients (mean age, 70 years; 72% males). Common comorbidities were hypertension,

hypercholesterolemia, diabetes, a history of MI, and smoking.

Carotid endarterectomy.

Combined CEA and coronary artery bypass grafting vs coronary artery bypass grafting first. Estimates were highly imprecise to derive conclusions about the outcomes of death (10 studies; RR, 0.58; 95% CI, 0.32-1.05; Supplementary Table I, online only), stroke (9 studies; RR, 0.87; 95% CI, 0.34-2.22; Supplementary Table I, online only), and MI (9 studies; RR, 0.64; 95% CI, 0.09-4.34; Supplementary Table I, online only). Other outcomes are shown in Supplementary Table I, (online only).

Combined CEA and coronary artery bypass grafting vs CEA first. Estimates were highly imprecise to derive conclusions about the outcomes of death (17 studies; RR, 1.34; 95% CI, 0.78-2.29; Supplementary Table I, online only), stroke (16 studies; RR, 1.50; 95% CI, 1.30-1.72; Supplementary Table I, online only), MI (14 studies; RR, 0.85; 95% CI, 0.45-1.62; Supplementary Table I, online only), and combined death/stroke (2 studies; RR, 1.46; 95% CI, 0.06-38.22; Supplementary Table I, online only).

Coronary artery bypass grafting first vs CEA first. Estimates were highly imprecise to derive conclusions about the outcomes of death (8 studies; RR, 0.94; 95% CI, 0.44-2.01; Supplementary Table I, online only), stroke (7 studies; RR, 1.40; 95% CI, 0.64-3.06; Supplementary Table I, online only), and MI (8 studies; RR, 0.51; 95% CI, 0.22-1.18; Supplementary Table I, online only).

Carotid artery stenting.

Combined coronary artery bypass grafting and CAS vs CAS first. Estimates were highly imprecise to derive conclusions about the outcome of death (2 studies; RR, 4.62; 95% CI, 0.72-29.87; Supplementary Table I, online only). Other outcomes are presented in Supplementary Table I, online only.

Asymptomatic carotid disease. We evaluated in sensitivity analyses cohorts of asymptomatic carotid stenosis. The majority of patients included in this analysis had combined CEA and coronary artery bypass grafting (CABG) compared with CEA first. The combined approach compared with the carotid intervention first was associated with a significant increase in stroke (4 studies; RR, 1.42; 95% CI, 1.16-1.73; Supplementary Table I, online only) and in death/stroke (2 studies; RR, 1.28; 95% CI, 1.10-1.49; Supplementary Table I, online only). There was no statistically significant difference in death (4 studies; RR, 1.54; 95% CI, 0.23-10.31; Supplementary Table I, online only). Supplementary Table I, (online only) outlines the outcomes for comparing a combined approach in this subgroup to the patients in whom CABG was done first. The exclusion of mixed series (in which the carotid intervention was CAS or CEA) provides the same conclusions.

Symptomatic carotid disease. We evaluated in sensitivity analyses cohorts of symptomatic carotid stenosis in which patients were treated with a combined CEA and CABG approach vs CABG first (ie, no CAS studies). Estimates were highly imprecise to derive conclusions about all outcomes. The results are summarized in the Supplementary Table I, (online only). Certainty in evidence was very low in all these outcomes that relate to intervention timing, reduced owing to methodologic limitations and severe imprecision.

Data suggests CEA before or concomitant with CABG in symptomatic patients with significant carotid stenosis of 50% to 99%, who require both CABG and CEA, to potentially lower risk of stroke and stroke/death. Meanwhile, for patients who have severe asymptomatic stenosis or contralateral occlusion or severe (70%-99%) bilateral asymptomatic carotid stenosis CEA before or concomitant with CABG is preferable.

DISCUSSION

Main findings. This systematic review addressed five important dilemmas that patients and surgeons face in daily practice. In brief, medical management compared with carotid interventions (CEA) in asymptomatic patients was associated with better early outcome during the first 30 days. However, CEA was associated with significantly better stroke/death rates in the long-term at 5 years. In symptomatic low surgical risk patients, CEA was associated with lower risk of stroke, but a significant increase in MI compared with CAS during the first 30 days. The long-term outcome of transfemoral CAS vs CEA in symptomatic patients suggests that the risk of death or stroke within 120 days of the index procedure was higher for CAS. The primary event outcome and ipsilateral postprocedural stroke at 5 years was also higher for CAS, which lends support that, over the long term, CEA has superior outcome than transfemoral CAS. When managing acute stroke, the comparison of CEA during the first 48 hours to that between day 2 and day 14 did not reveal a statistically significant difference on outcomes during the first 30 days. Although we did not find comparative evidence to support screening for carotid disease (ie, screening vs no screening), we were able to stratify patients based on risk factors and provide estimates of screening yield. These estimates will be highly relevant for shared decision-making. A single risk factor, aside from peripheral artery disease, was associated with low yield. Multiple risk factors greatly increase the yield of screening and can justify a screening recommendation. Evidence on the timing of interventions in patients with combined carotid and coronary disease was sparse and imprecise. Patients without carotid symptoms who had the carotid intervention first, compared with a combined carotid intervention and CABG, had better outcomes.

Clinical implications. This systematic review/meta-analysis analyzes five important clinical questions/issues in the management of extracranial carotid artery disease: medical management vs CEA in asymptomatic patients,

CEA vs CAS in symptomatic low risk surgical patients, timing of intervention in stroke, screening high risk patients, and the optimal sequence for carotid intervention in patients with combined carotid and coronary disease. The recommendations are addressed in a separate document, "Society for Vascular Surgery Clinical Practice Guidelines for Management of Extracranial Cerebrovascular Disease."[112] Furthermore, a separate comprehensive implementation document will address these issues in further details and cover other important clinical issues in extracranial cerebrovascular disease management.[113]

Strengths and limitations. The strength of this systematic review and meta-analyses includes following rigorous procedures, such as selecting and appraising studies by pairs of independent reviewers, the comprehensive search that included several databases, and collaboration with content experts from the SVS. Clear limitations of the evidence base are however present. Comparative studies about the timing of carotid intervention after acute stroke and the optimal sequence of intervention in patients with combined carotid and coronary disease are needed. The estimates in these comparisons were highly imprecise. Considering that blinding of patients and surgeons is not feasible in studies of carotid disease, we encourage the blinding of outcome assessors and data analysts, which is possible and highly desirable to decrease the risk of bias. Studies that compare the outcomes and cost effectiveness of carotid screening are also needed.

CONCLUSIONS

This systematic review supports the SVS clinical practice guidelines for commonly raised clinical scenarios in the management of extracranial carotid disease. CEA was superior to medical therapy in the long-term prevention of stroke/death over medical therapy. CEA was also superior to transfemoral CAS in minimizing long-term stroke/death for symptomatic low risk surgical patients. CEA should optimally be performed between 2 and 14 days from the onset of acute stroke. This systematic review demonstrates that the presence of multiple risk factors increases the value of carotid screening.

Future clarification of some of these issues, particularly with advances in medical therapy (including the use of statins), might further impact the benefit of medical therapy. Additionally, analysis of current medical therapy will be better understood vs carotid intervention once several currently ongoing randomized trials (eg, CREST2, SPACE2) are completed. Similarly, with the introduction of transcarotid artery revascularization,[114] the role of CAS in treating both symptomatic/asymptomatic patients would need to be clarified over the long-term. Other larger studies regarding the timing of carotid intervention after acute stroke will be very beneficial.

AUTHOR CONTRIBUTIONS

Conception and design: BH, MF, AA, MM
Analysis and interpretation: BH, MF, TN, MM
Data collection: BH, MF, TN, MA, KM, RA, SHS, RR, MS, SS, LH, LP, AA, MM
Writing the article: BH, MM
Critical revision of the article: BH, MF, TN, MA, KM, RA, SHS, RR, MS, SS, LH, LP, AA, MM
Final approval of the article: BH, MF, TN, MA, KM, RA, SHS, RR, MS, SS, LH, LP, AA, MM
Statistical analysis: BH
Obtained funding: MM
Overall responsibility: MM

REFERENCES

1. Centers for Disease Control. Stroke fact sheet. Available at: www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_stroke.htm. Accessed June 16, 2020.
2. Rajsic S, Gothe H, Borba H, Sroczynski G, Vujicic J, Toell T, et al. Economic burden of stroke: a systematic review on post-stroke care. Eur J Health Econ 2019;20:107-34.
3. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.
4. Wells Ga, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed August 2, 2017.
5. Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011. Available at: www.handbook.cochrane.org.
6. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. BMJ Evid Based Med 2018;23:60-3.
7. Murad MH. Clinical practice guidelines: a primer on development and dissemination. Mayo Clin Proc 2017;92:423-33.
8. Murad MH, Montori VM, Sidawy AN, Ascher E, Meissner MH, Chaikof EL, et al. Guideline methodology of the Society for Vascular Surgery including the experience with the GRADE framework. J Vasc Surg 2011;53:1375-80.
9. Murad MH, Swiglo BA, Sidawy AN, Ascher E, Montori VM. Methodology for clinical practice guidelines for the management of arteriovenous access. J Vasc Surg 2008;48(5 Suppl):26S-30S.
10. Alper BS, Oettgen P, Kunnamo I, Iorio A, Ansari MT, Murad MH, et al. Defining certainty of net benefit: a GRADE concept paper. BMJ Open 2019;9:e027445.
11. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995;273:1421-8.
12. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomized controlled trial. Lancet 2004;363:1491-502.
13. Kolos I, Troitskiy A, Balakhonova T, Shariya M, Skrypnik D, Tvorogova T, et al. Modern medical treatment with or without carotid endarterectomy for severe asymptomatic carotid atherosclerosis. J Vasc Surg 2015;62:914-22.
14. Reiff T, Eckstein H, Mansmann U, Jansen O, Fraedrich G, Mudra H, et al. Angioplasty in asymptomatic carotid artery stenosis vs endarterectomy compared to best medical treatment: one-year interim results of SPACE-2. Int J Stroke 2019;15. 1747493019833017.
15. Sato K, Fujiyoshi K, Hoshi K, Noda C, Yamaoka-Tojo M, Ako J, et al. Low stroke rate of carotid stenosis under the guideline-oriented medical treatment compared with surgical treatment. Int Heart J 2016;57:80-6.
16. Lin CJ, Chang FC, Chou KH, Tu PC, Lee YH, Lin CP, et al. Intervention versus aggressive medical therapy for cognition in severe

asymptomatic carotid stenosis. AJNR Am J Neuroradiol 2016;37:1889-97.
17. Hoffmann SE, Taschner C, Mendelowitsch A, Merlo A, Radue EW, Lyrer P, et al. Carotid artery stenting versus carotid endarterectomy - a prospective randomised controlled single-centre trial with long-term follow-up (BACASS). Swiss Arch Neurol Psychiatr 2008;159:84-9.
18. Brooks WH, McClure RR, Jones MR, Coleman TC, Breathitt L. Carotid angioplasty and stenting versus carotid endarterectomy: randomized trial in a community hospital. J Am Coll Cardiol 2001;38:1589-95.
19. Brott TG, Hobson RW, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010;363:11-23.
20. Eckstein H-H, Ringleb P, Allenberg J-R, Berger J, Fraedrich G, Hacke W, et al. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomised trial. Lancet Neurol 2008;7:893-902.
21. Ederle J, Bonati LH, Dobson J, Featherstone RL, Gaines PA, Beard JD, et al. Endovascular treatment with angioplasty or stenting versus endarterectomy in patients with carotid artery stenosis in the Carotid And Vertebral Artery Transluminal Angioplasty Study (CAVATAS): long-term follow-up of a randomised trial. Lancet Neurol 2009;8:898-907.
22. International Carotid Stenting Study investigators, Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. Lancet 2010;375:985-97.
23. Mas J-L, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin J-P, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med 2006;355:1660-71.
24. Naylor AR. Randomized study of carotid angioplasty and stenting versus carotid endarterectomy: a stopped trial. J Vasc Surg 1998;28:326-34.
25. Steinbauer MGM, Pfister K, Greindl M, Schlachetzki F, Borisch I, Schuirer G, et al. Alert for increased long-term follow-up after carotid artery stenting: results of a prospective, randomized, single-center trial of carotid artery stenting vs carotid endarterectomy. J Vasc Surg 2008;48:93-8.
26. Avgerinos ED, Farber A, Abou Ali AN, Rybin D, Doros G, Eslami MH. Early carotid endarterectomy performed 2 to 5 days after the onset of neurologic symptoms leads to comparable results to carotid endarterectomy performed at later time points. J Vasc Surg 2017;66:1719-26.
27. Azzini C, Gentile M, De Vito A, Traina L, Sette E, Fainardi E, et al. Very early carotid endarterectomy after intravenous thrombolysis. Eur J Vasc Endovasc Surg 2016;51:482-6.
28. Barbetta I, Carmo M, Mercandalli G, Lattuada P, Mazzaccaro D, Settembrini AM, et al. Outcomes of urgent carotid endarterectomy for stable and unstable acute neurologic deficits. J Vasc Surg 2014;59:440-6.
29. Brandl R, Brauer RB, Maurer PC. Urgent carotid endarterectomy for stroke in evolution. Vasa 2001;30:115-21.
30. Hlavica M, Berberat J, Ineichen BV, Añon J, Diepers M, Nedeltchev K, et al. Emergent vs elective stenting of carotid stenosis with intraluminal carotid thrombus. J Neuroradiol 2017;44:254-61.
31. Mihindu E, Mohammed A, Smith T, Brinster C, Sternbergh WC, Bazan HA. Patients with moderate to severe strokes (NIHSS score >10) undergoing urgent carotid interventions within 48 hours have worse functional outcomes. J Vasc Surg 2019;69:1471-81.
32. Tanious A, Pothof AB, Boitano LT, Pendleton AA, Wang LJ, deBorst GJ. Timing of carotid endarterectomy after stroke: retrospective review of prospectively collected national database. J Vasc Surg 2018;68:1955-6.
33. Welsh S, Mead G, Chant H, Picton A, O'Neill PA, McCollum CN. Early carotid surgery in acute stroke: a multicentre randomised pilot study. Cerebrovasc Dis 2004;18:200-5.
34. Ahn SS, Baker JD, Walden K, Moore WS. Which asymptomatic patients should undergo routine screening carotid duplex scan? Am J Surg 1991;162:180-4.
35. Aiello F, Meltzer A, Cohen B, Espiritu M, Burmeister J, Hoque R, et al. Risk factors for prevalence and progression of asymptomatic carotid disease in patients with peripheral arterial disease. J Vasc Surg 2012;55:69S.
36. Anastasiadis K, Karamitsos TD, Velissaris I, Makrygiannakis K, Kiskinis D. Preoperative screening and management of carotid artery disease in patients undergoing cardiac surgery. Perfusion 2009;24:257-62.
37. Ascher E, Hingorani A, Yorkovich W, Ramsey PJ, Salles-Cunha S. Routine preoperative carotid duplex scanning in patients undergoing open heart surgery: is it worthwhile? Ann Vasc Surg 2001;15:669-78.
38. Bae H-J, Yoon B-W, Kang D-W, Koo J-S, Lee S-H, Kim K-B, et al. Correlation of coronary and cerebral atherosclerosis: difference between extracranial and intracranial arteries. Cerebrovasc Dis 2006;21:112-9.
39. Berens ES, Kouchoukos NT, Murphy SF, Wareing TH. Preoperative carotid artery screening in elderly patients undergoing cardiac surgery. J Vasc Surg 1992;15:313-21; discussion: 322-3.
40. Bishara RA, Taha W, Alfarouk MO, Milik IA, Wilson N. Screening for significant carotid artery disease among a cohort of 1,000 Egyptian patients. Vascular 2008;16:35-40.
41. Cheng SWK, Wu LLH, Lau H, Ting ACW, Wong J. Prevalence of significant carotid stenosis in Chinese patients with peripheral and coronary artery disease. Aust NZ J Surg 1999;69:44-7.
42. Cheng Y, Gao J, Wang J, Wang S, Peng J. Risk factors for carotid artery stenosis in Chinese patients undergoing coronary artery bypass graft interventions. Medicine 2015;94:e1119.
43. Choo KS. Clinical utility of preoperative carotid duplex ultrasonography prior to operation for peripheral artery disease. Ultrasound Med Biol 2017;43:S249.
44. Chun LJ, Tsai J, Tam M, Prema J, Chen LH, Patel KK. Screening carotid artery duplex in patients undergoing cardiac surgery. Ann Vasc Surg 2014;28:1178-85.
45. Cornily J-C, Le Saux D, Vinsonneau U, Bezon E, Le Ven F, Le Gal G, et al. Assessment of carotid artery stenosis before coronary artery bypass surgery. Is it always necessary? Arch Cardiovasc Dis 2011;104:77-83.
46. de Virgilio C, Toosie K, Arnell T, Lewis RJ, Donayre CE, Baker JD, et al. Asymptomatic carotid artery stenosis screening in patients with lower extremity atherosclerosis: a prospective study. Ann Vasc Surg 1997;11:374-7.
47. Dharmasaroja PA, Piyayotai D, Hutayanon P, Buakhamsri A, Intharakham K. Extracranial carotid stenosis and peripheral arterial disease in Thai patients with coronary artery disease. Angiology 2010;61:329-32.
48. Drohomirecka A, Kołtowski L, Kwinecki P, Wronecki K, Cichoń R. Risk factors for carotid artery disease in patients scheduled for coronary artery bypass grafting. Kardiol Pol 2010;68:789-94.
49. Fassiadis N, Adams K, Zayed H, Goss D, Deane C, MacCarthy P, et al. Occult carotid artery disease in patients who have undergone coronary angioplasty. Interact Cardiovasc Thorac Surg 2008;7:855-7.
50. Fowl R, Marsch J, Love M, Patterson R, Shukla R, Kempczinski R. Prevalence of hemodynamically significant stenosis of the carotid artery in an asymptomatic veteran population. Surg Gynecol Obstet 1991;172:13-6.
51. Gentile AT. Prevalence of asymptomatic carotid stenosis in patients undergoing infrainguinal bypass surgery. Arch Surg 1995;130:900.
52. Helfre M, Grange C, Riche B, Maucort-Boulch D, Thivolet C, Vouillarmet J. Usefulness of a systematic screening of carotid atherosclerosis in asymptomatic people with type 2 diabetes for cardiovascular risk reclassification. Ann Endocrinol (Paris) 2017;78:14-9.
53. Hill AB, Obrand D, Steinmetz K. The utility of selective screening for carotid stenosis in cardiac surgery patients. J Cardiovasc Surg 1999;40:8.
54. House A. Asymptomatic carotid artery stenosis associated with peripheral vascular disease: a prospective study. Cardiovasc Surg 1999;7:44-9.
55. Ignat'ev IM. Asymptomatic stenoses of carotid arteries. Angiol Sosud Khir 2012;18:72-84.
56. Stephens J, Abdel-Aziz K. Are asymptomatic Hollenhorst plaques a reliable predictor of ipsilateral carotid stenosis and medium term stroke risk? Eur J Neurol 2010;17(Suppl 3):351-625.

57. Jackson VP, Bendick PJ. Duplex ultrasound screening for carotid arteriosclerotic disease in asymptomatic patients. J Ultrasound Med 1985;4:411-5.
58. Kaul S, Alladi S, Mridula KR, Bandaru VS, Umamashesh M, Anjanikumar D, et al. Prevalence and risk factors of asymptomatic carotid artery stenosis in Indian population: an 8-year follow-up study. Neurol India 2017;65:279.
59. Kawarada O, Yokoi Y, Morioka N, Nakata S, Higashiue S, Mori T, et al. Carotid stenosis and peripheral artery disease in Japanese patients with coronary artery disease undergoing coronary artery bypass grafting. Circ J 2003;67:1003-6.
60. Klop RBJ, Eikelboom BC, Taks ACJM. Screening of the internal carotid arteries in patients with peripheral vascular disease by colour-flow duplex scanning. Eur J Vasc Surg 1991;5:41-5.
61. Kurvers HAJM, van der Graaf Y, Blankensteijn JD, Visseren FLJ, Eikelboom BC. Screening for asymptomatic internal carotid artery stenosis and aneurysm of the abdominal aorta: comparing the yield between patients with manifest atherosclerosis and patients with risk factors for atherosclerosis only. J Vasc Surg 2003;37:1226-33.
62. Lin JC, Kabbani LS, Peterson EL, Masabni K, Morgan JA, Brooks S, et al. Clinical utility of carotid duplex ultrasound prior to cardiac surgery. J Vasc Surg 2016;63:710-4.
63. Lin R, Hingorani A, Marks N, Ascher E, Jimenez R, Aboian E, et al. Screening for carotid artery stenosis and renal artery stenosis in patients undergoing tunneled cuffed hemodialysis catheter placement. Vasc Endovascular Surg 2012;46:364-8.
64. Mackaay AJC, Beks PJ, Dur AHM, Bischoff M, Scholma J, Heine RJ, et al. The distribution of peripheral vascular disease in a Dutch Caucasian population: comparison of type II diabetic and non-diabetic subjects. Eur J Vasc Endovasc Surg 1995;9:170-5.
65. Marek J, Mills JL, Harvich J, Cui H, Fujitani RM. Utility of routine carotid duplex screening in patients who have claudication. J Vasc Surg 1996;24:572-9.
66. Miralles M, Corominas A, Cotillas J, Castro F, Clara A, Vidal-Barraquer F. Screening for carotid and renal artery stenoses in patients with aortoiliac disease. Ann Vasc Surg 1998;12:17-22.
67. Miura T, Soga Y, Doijiri T, Goya M, Yokoi H, Iwabuchi M, et al; Kokura Memorial Hospital, Kitakyushu, Japan. Prevalence of extra-coronary artery disease in patients with coronary artery disease undergoing coronary intervention. Eur Heart J 2010;31:297-587.
68. Narayan P, Khan MW, Das D, Guha Biswas R, Das M, Rupert E. Carotid artery screening at the time of coronary artery bypass - does it influence neurological outcomes? Int J Cardiol 2017;243:140-4.
69. Pilcher JM, Danaher J, Khaw K-T. The prevalence of asymptomatic carotid artery disease in patients with peripheral vascular disease. Clin Radiol 2000;55:56-61.
70. Planas-Ballvé A, Crespo AM, Aguilar LM, Hernández-Pérez M, Canento T, Dorado L, et al. The Barcelona-Asymptomatic Intracranial Atherosclerosis study: subclinical intracranial atherosclerosis as predictor of long-term vascular events. Atherosclerosis 2019;282:132-6.
71. Posacioğlu H, İlamoğlu F, Çalkavur T, Yağdi T, Atay Y, Özbaran M, et al. Predictive values of risk factors in carotid duplex scanning before peripheral vascular surgery. Int J Angiology 2001;10:250-3.
72. Moraca RJ, Wanamaker K, Nitzberg D, Bailey SH, Benckart D, McGregor W, et al. The role of routine carotid artery duplex in patients referred for coronary artery bypass grafting. International Stroke Conference, February 1-2, 2012, New Orleans, Louisiana. Available at: https://www.ahajournals.org/doi/abs/10.1161/str.43.suppl_1.a3878.
73. Rockman CB, Jacobowitz GR, Gagne PJ, Adelman MA, Lamparello PJ, Landis R, et al. Focused screening for occult carotid artery disease: patients with known heart disease are at high risk. J Vasc Surg 2004;39:44-50.
74. Lezama L, Santiago G, Nafria G, Novel A, Garcia T, Ruiz C, et al. Stroke and mortality after cardiac surgery and its relationship to severe carotid. In: Stückle D, editor. European Stroke Conference. 24th Conference, Vienna, Austria, May 13-15, 2015: Abstract e-Book. Vienna, Austria: Karger; 2015. Cerebrovascular Diseases Conference: 24th European Stroke Conference, May 13-15, 2015, Vienna, Austria. Available at: https://doi.org/10.1159/000431011.
75. Sayed A, Ahmed S, Abdelalim A, Nagah M, Khairy H. Is peripheral arterial disease associated with carotid artery disease in Egyptians? A pilot study. Egypt J Neurol Psychiatr Neurosurg 2016;53:12.
76. Chumpita S, Supot S, Nijasri C. Prevalence of extracranial internal carotid and intracranial large arteries stenosis in patients with suspected coronary artery disease who underwent coronary angiography in Chulalongkorn Hospital. In: Stückle D, editor. Vienna, Austria: Karger; 2012.
77. Valentine R. Utility of carotid duplex in young adults with lower extremity atherosclerosis: how aggressive should we be in screening young patients? Cardiovasc Surg 1997;5:408-13.
78. Wanamaker KM, Moraca RJ, Nitzberg D, Magovern GJ. Contemporary incidence and risk factors for carotid artery disease in patients referred for coronary artery bypass surgery. J Cardiothorac Surg 2012;7:78.
79. Yamamoto K, Miyata T, Nagayoshi M, Akagi D. Carotid endarterectomy may reduce the high stroke rate for patients with the disease of abdominal aorta and peripheral arteries. Int Angiol 2006;25:35.
80. Yun W-S, Rho Y-N, Park U-J, Lee K-B, Kim D-I, Kim Y-W. Prevalence of asymptomatic critical carotid artery stenosis in Korean patients with chronic atherosclerotic lower extremity ischemia: is a screening carotid duplex ultrasonography worthwhile? J Korean Med Sci 2010;25:1167.
81. Abbasi K, Araghi MF, Zafarghandi M, Karimi A, Ahmadi H, Marzban M, et al. Concomitant carotid endarterectomy and coronary artery bypass grafting versus staged carotid stenting followed by coronary artery bypass grafting. J Cardiovasc Surg (Torino) 2008;49:285-8.
82. Bernhard VM. Carotid artery stenosis: association with surgery for coronary artery disease. Arch Surg 1972;105:837.
83. Brow T, Kakkar V, Pepper J, Das S. Toward a rational management of concomitant carotid and coronary artery disease. J Cardiovasc Surg 1999;40:837.
84. Carrel T, Stillhard G, Turina M. Combined carotid and coronary artery surgery: early and late results. Cardiology 1992;80:118-25.
85. Chiappini B, Dell' Amore A, Di Marco L, Di Bartolomeo R, Marinelli G. Simultaneous carotid and coronary arteries disease: staged or combined surgical approach? J Card Surg 2005;20:234-40.
86. Faggioli GL, Curl GR, Ricotta JJ. The role of carotid screening before coronary artery bypass. J Vasc Surg 1990;12:724-31.
87. Feldman DN, Swaminathan RV, Geleris JD, Okin P, Minutello RM, Krishnan U, et al. Comparison of trends and in-hospital outcomes of concurrent carotid artery revascularization and coronary artery bypass graft surgery. JACC Cardiovasc Interv 2017;10:286-98.
88. Giangola G, Migaly J, Riles TS, Lamparello PJ, Adelman MA, Grossi E, et al. Perioperative morbidity and mortality in combined vs staged approaches to carotid and coronary revascularization. Ann Vasc Surg 1996;10:138-42.
89. Hempe S, Moza A, Goetzenich A, Tewarie L, Bleilevens C, Autschbach R, et al. Synchronous or staged carotid endarterectomy and coronary artery bypass grafting? Propensity score matched study. Heart Surg Forum 2018;21:E359-64.
90. Hertzer NR, Loop FD, Taylor PC, Beven EG. Staged and combined surgical approach to simultaneous carotid and coronary vascular disease. Surgery 1978;84:803-11.
91. Hudorovic N. Reduction in hospitalisation rates following simultaneous carotid endarterectomy and coronary artery bypass grafting; experience from a single centre. Interact Cardiovasc Thorac Surg 2006;5:367-72.
92. Illuminati G, Ricco J-B, Caliò F, Pacilè MA, Miraldi F, Frati G, et al. Short-term results of a randomized trial examining timing of carotid endarterectomy in patients with severe asymptomatic unilateral carotid stenosis undergoing coronary artery bypass grafting. J Vasc Surg 2011;54:993-9.
93. Iyem H, Buket S. Early results of combined and staged coronary bypass and carotid endarterectomy in advanced age patients in single Centre. Open Cardiovasc Med J 2009;3:8-14.
94. Kovacevic P, Redzek A, Kovacevic-Ivanovic S, Velicki L, Ivanovic V, Kieffer E. Coronary and carotid artery occlusive disease: single center experience. Eur Rev Med Pharmacol Sci 2012;16:483-90.
95. Newman DC, Hicks RG, Horton DA. Coexistent carotid and coronary arterial disease. Outcome in 50 cases and method of management. J Cardiovasc Surg 1987;28:599-606.

96. Oz K, Aydın Ü, Kyaruzi M, Karaman Z, Göksel OS, Yeniterzi M, et al. Staged or combined approach for carotid endarterectomy in patients undergoing coronary artery bypass grafting: a 5-year-long experience. Heart Surg Forum 2016;19:E276-81.
97. Peric M, Huskic R, Nezic D, Nastasic S, Popovic Z, Bojic M. Cardiac events after combined surgery for coronary and carotid artery disease. Eur J Cardiothorac Surg 1997;11:1074-80.
98. Rosenthal D, Lamis PA. Carotid and coronary arterial disease. Am Surg 1984;50:233-5.
99. Şaşkın H, Duzyol C, Ozcan KS, Aksoy R, Idiz M. Is carotid artery stenting an alternative to simultaneous carotid endarterectomy performed for carotid artery stenosis in patients undergoing isolated coronary bypass surgery? Heart Surg Forum 2015;18:E211-8.
100. Takach TJ, Reul GJ, Cooley DA, Duncan JM, Ott DA, Livesay JJ, et al. Is an integrated approach warranted for concomitant carotid and coronary artery disease? Ann Thorac Surg 1997;64:16-22.
101. Timaran CH, Mantese VA, Malas M, Brown OW, Lal BK, Moore WS, et al. Differential outcomes of carotid stenting and endarterectomy performed exclusively by vascular surgeons in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). J Vasc Surg 2013;57:303-8.
102. Urschel H, Razzuk M, Gardner M. Management of concomitant occlusive disease of the carotid and coronary arteries. J Thorac Cardiovasc Surg 1976;72:829-34.
103. Weimar C, Bilbilis K, Rekowski J, Holst T, Beyersdorf F, Breuer M, et al. Safety of simultaneous coronary artery bypass grafting and carotid endarterectomy versus isolated coronary artery bypass grafting. Stroke 2017;48:2769-75.
104. Xiang B, Luo X, Yang Y, Qiu J, Zhang J, Li L, et al. Midterm results of coronary artery bypass graft surgery after synchronous or staged carotid revascularization. J Vasc Surg 2019;700:1942-9.
105. Yang T, Zhang L, Wang X, Dong H, Jiang X, Sun H. Revascularization by carotid artery stenting and off-pump coronary artery bypass: carotid and coronary revascularization. ANZ J Surg 2016;86:602-7.
106. Ziada KM, Yadav JS, Mukherjee D, Lauer MS, Bhatt DL, Kapadia S, et al. Comparison of results of carotid stenting followed by open heart surgery versus combined carotid endarterectomy and open heart surgery (coronary bypass with or without another procedure). Am J Cardiol 2005;96:519-23.
107. Howard DP, Gaziano L, Rothwell PM, Study OV. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. Lancet Neurol 2021;20:193-202.
108. Brott TG, Calvet D, Howard G, Gregson J, Algra A, Becquemin J-P, et al. Long-term outcomes of stenting and endarterectomy for symptomatic carotid stenosis: a preplanned pooled analysis of individual patient data. Lancet Neurol 2019;18:348-56.
109. Loftus I, Paraskevas K, Johal A, Waton S, Heikkila K, Naylor A, et al. Editor's choice—delays to surgery and procedural risks following carotid endarterectomy in the UK National Vascular Registry. Eur J Vasc Endovasc Surg 2016;52:438-43.
110. Rantner B, Schmidauer C, Knoflach M, Fraedrich G. Very urgent carotid endarterectomy does not increase the procedural risk. Eur J Vasc Endovasc Surg 2015;49:129-36.
111. Strömberg S, Gelin J, Österberg T, Bergström GM, Karlström L, Österberg K, et al. Very urgent carotid endarterectomy confers increased procedural risk. Stroke 2012;43:1331-5.
112. AbuRahma AF, Avgerinos EM, Change RW, Darling RC 3rd, Duncan AA, Forbes TL, et al. Society for Vascular Surgery clinical practice guidelines for management of extracranial cerebrovascular disease. J Vasc Surg 2021 June 18. [Epub ahead of print].
113. AbuRahma AF, Avgerinos EM, Chang RW, Darling RC 3rd, Duncan AA, Forbes TL, et al. Updated Society for Vascular Surgery implementation document for management of extracranial cerebrovascular disease. J Vasc Surg 2020 Jun 18. [Epub ahead of print].
114. Naazie IN, Cui CL, Osaghae I, Murad MH, Schermerhorn M, Malas MB. A systematic review and meta-analysis of transcarotid artery revascularization with dynamic flow reversal versus transfemoral carotid artery stenting and carotid endarterectomy. Ann Vasc Surg 2020;69:426-36.

Submitted Feb 11, 2021; accepted Jun 1, 2021.

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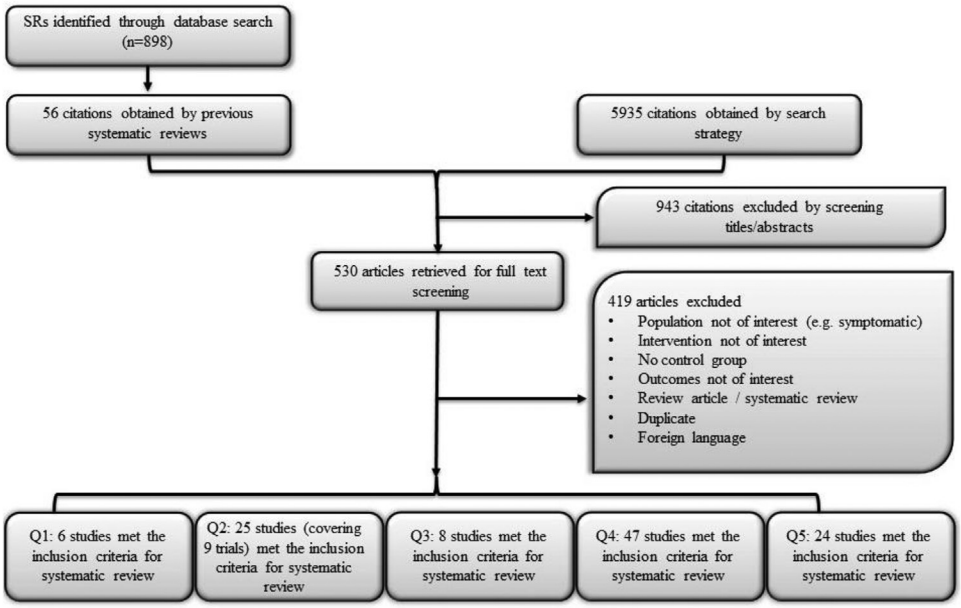

Supplementary Figure (online only). Process of studies selection.

Supplementary Table I (online only). Summary results of meta-analysis of included studies

Outcome	Intervention vs comparison	Author, year	Group 1	Group 2	Total	RR (95% CI)
Question 1: Medical management vs carotid intervention in asymptomatic patients						
Death at 30 days	Medical management vs CEA	ACST, 2004	1560	1560	3120	0.13 (0.03-0.58)
		Reiff et al,[1] 2019	113	400	513	NA
		Walker et al,[3] 1995	834	825	1659	0.33 (0.03-3.16)
		Overall	**2507**	**2785**	**5292**	**0.17 (0-33.71), I^2 = 0%**
Stroke at 30 days	Medical management vs CEA	ACST, 2004	1560	1560	3120	0.31 (0.16-0.62)
		Reiff et al,[1] 2019	113	400	513	0.07 (0-36.11)
		Walker et al,[3] 1995	834	825	1659	0.12 (0.03-0.5)
		Overall	**2507**	**2785**	**5292**	**0.26 (0.08-0.87), I^2 = 0%**
Stroke/death at 30 days	Medical management vs CEA	ACST, 2004	1560	1560	3120	0.28 (0.14-0.53)
		Reiff et al,[1] 2019	113	400	513	0.07 (0-36.11)
		Walker et al,[3] 1995	834	825	1659	0.16 (0.05-0.53)
		Overall	**2507**	**2785**	**5292**	**0.24 (0.11-0.53), I^2 = 0%**
Ipsilateral stroke at 30 days	Medical management vs CEA	Reiff et al,[1] 2019	113	203	316	0.2 (0.011-3.66)
Ipsilateral stroke at 30 days	Medical management vs CAS	Reiff et al,[1] 2019	113	197	310	0.16 (0.0088-2.83)
MI at 30 days	Medical management vs CEA/CAS	Reiff et al,[1] 2019	113	400	513	NA
Ipsilateral stroke at 30 days	Medical management vs CEA/CAS	Reiff et al,[1] 2019	113	400	513	0.04 (0.0001-19.71)
Death at 5 years	Medical management vs CEA/CAS	ACST, 2004	1560	1560	3120	0.95 (0.81-1.11)
		Walker et al,[3] 1995	834	825	1659	1.06 (0.8-1.41)
		Overall	**2394**	**2385**	**4779**	**0.97 (0.53-1.8), I^2 = 0%**
Death at 1 year	Medical management vs CAS	Reiff et al,[1] 2019	113	197	310	3.49 (0.649-18.74)
Stroke at 1 year	Medical management vs CAS	Reiff et al,[1] 2019	113	197	310	0.22 (0.028-1.72)
Stroke at 3 months	Medical management vs CAS	Lin et al,[2] 2016	15	25	40	NA
Ipsilateral stroke at 1 year	Medical management vs CAS	Reiff et al,[1] 2019	113	197	310	0.29 (0.035-2.38)
Ipsilateral stroke at 3 months	Medical management vs CAS	Lin et al,[2] 2016	15	25	40	NA
MI at 1 year	Medical management vs CAS	Reiff et al,[1] 2019	113	197	310	1.74 (0.035-86.95)
MI at 3 months	Medical management vs CAS	Lin et al,[2] 2016	15	25	40	NA
Death at 1 year	Medical management vs CEA	Reiff et al,[1] 2019	113	203	316	1.44 (0.39-5.24)
Death at 3.3 years	Medical management vs CEA	Kolos et al,[4] 2015	24	31	55	5.17 (0.617-43.28)
Stroke at 1 year	Medical management vs CEA	Reiff et al,[1] 2019	113	203	316	0.22 (0.028-1.77)
Stroke at 3.3 years	Medical management vs CEA	Kolos et al,[4] 2015	24	31	55	6.46 (0.81-51.69)
Stroke at 5 years	Medical management vs CEA	ACST, 2004	1560	1560	3120	2.86 (2.02-4.03)
Stroke/death at 1 year	Medical management vs CEA	Reiff et al,[1] 2019	113	203	316	0.36 (0.04-3.04)
Stroke/death at 5 years	Medical management vs CEA	Walker et al,[3] 1995	182	192	374	2.37 (0.74-7.57)

Supplementary Table I (online only). Continued.

Outcome	Intervention vs comparison	Author, year	Group 1	Group 2	Total	RR (95% CI)
Stroke/death at 3.3 years	Medical management vs CEA	Kolos et al,[4] 2015	24	31	55	5.81 (1.38-24.45)
Ipsilateral stroke at 1 year	Medical management vs CEA	Reiff et al,[1] 2019	113	203	316	0.45 (0.051-3.97)
Ipsilateral stroke at 3.3 years	Medical management vs CEA	Kolos et al,[4] 2015	24	31	55	6.46 (0.81-51.69)
Ipsilateral stroke at 5 years	Medical management vs CEA	ACST, 2004	1560	1560	3120	4.77 (2.6338-8.6359)
MI at 1 year	Medical management vs CEA	Reiff et al,[1] 2019	113	203	316	0.6 (0.0245-14.5234)
Question 2: CEA vs CAS in symptomatic patients						
Death at 30 days	CEA vs CAS	Bonati et al,[16] 2015	836	837	1673	0.36 (0.12-1.14)
		Brooks et al,[20] 2001	51	53	104	11.43 (0.02-7320.48)
		Eckstein et al,[21] 2008	589	607	1196	0.86 (0.26-2.8)
		Ederle et al,[24] 2009	253	251	504	0.57 (0.17-1.91)
		Hoffman et al,[27] 2008	10	10	20	NA
		Howard et al,[33] 2011	653	668	1321	0.03 (0-17.9)
		Mas et al,[28] 2014	262	265	527	1.52 (0.26-9.01)
		Naylor,[31] 1998	10	7	17	NA
		Overall	**2664**	**2698**	**5362**	**0.63 (0.31-1.29), I^2 = 0%**
Ipsilateral stroke at 30 days	CEA vs CAS	Bonati et al,[16] 2015	836	837	1673	0.47 (0.29-0.76)
		Eckstein et al,[21] 2008	589	607	1196	0.9 (0.59-1.4)
		Hoffman et al,[27] 2008	10	10	20	11 (0.02-6717.16)
		Naylor,[31] 1998	10	7	17	0.01 (0-6.69)
		Overall	**1445**	**1461**	**2906**	**0.65 (0.22-1.93), I^2 = 53%**
Death/stroke at 30 days	CEA vs CAS	Eckstein et al,[21] 2008	589	607	1196	0.89 (0.59-1.35)
		Ederle et al,[24] 2009	253	251	504	0.99 (0.59-1.68)
		Featherstone et al,[18] 2016	821	828	1649	0.46 (0.30-0.72)
		Howard et al,[33] 2011	653	668	1321	0.54 (0.32-0.90)
		Overall	**2316**	**2354**	**4670**	**0.68 (0.38-1.24), I^2 = 60%**
Death at 5 years	CEA vs CAS	Ederle et al,[24] 2009	253	251	504	1 (0.82-1.22)
		Howard et al,[33] 2011	653	668	1321	0.03 (0-17.9)
		Mas et al,[28] 2014	262	265	527	0.94 (0.68-1.31)
		Steinbauer et al,[40] 2008	42	42	84	1.3 (0.64-2.63)
		Overall	**1210**	**1226**	**2436**	**1 (0.81-1.22), I^2 = 0%**
Ipsilateral stroke at 5 years	CEA vs CAS	Ederle et al,[24] 2009	253	251	504	0.91 (0.41-2.02)
		Mas et al,[28] 2014	262	265	527	1.52 (0.43-5.31)
		Steinbauer et al,[40] 2008	42	42	84	0.02 (0-12.74)
		Overall	**557**	**558**	**1115**	**1.01 (0.23-4.42), I^2 = 4%**

Outcome	Intervention vs comparison	CEA total No. of patients	CEA risk (95% CI)	CAS total No. of patients	CAS risk (95% CI)
Stroke/death at 120 days	CEA vs CAS	2361	5.5% (4.7% to 6.5%)	2393	8.7% (7.6% to 9.9%)
Stroke/death and ipsilateral stroke at 5 years	CEA vs CAS	2168	8.3% (7.2% to 9.6%)	2121	11.4% (10.1% to 12.8%)

Outcome	Intervention vs Comparison	Author, Year	Group 1	Group 2	Total	RR (95% CI)
Question 3: Timing of intervention in stroke						
Death at 30 days	CEA <2 days vs 2-14 days	Azzini et al,[6] 2016	22	12	34	6.02 (0.01-3755.64)

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Supplementary Table I (online only). Continued.

Outcome	Intervention vs Comparison	Author, Year	Group 1	Group 2	Total	RR (95% CI)
		Barbetta et al,[7] 2014	25	27	52	0.1 (0-62.15)
		Tanious et al,[8] 2018	649	3707	4356	1.24 (0.63-2.45)
		Overall	**696**	**3746**	**4442**	**1.23 (0.48-3.17), I^2 = 0%**
Cerebral hemorrhage	CEA <2 days vs 2-14 days	Azzini et al,[6] 2016	22	12	34	1.09 (0.11-10.83)
		Barbetta et al,[7] 2014	25	27	52	0.1 (0-62.15)
		Overall	**47**	**39**	**86**	**0.83 (0-13096.54), I^2 = 0%**
MI	CEA <2 days vs 2-14 days	Azzini et al,[6] 2016	22	12	34	6.0226 (0.0097-3755.6400)
Stroke	CEA <2 days vs 2-14 days	Barbetta et al,[7] 2014	25	27	52	0.72 (0.13-3.96)
Cerebral hyperperfusion	CEA <2 days vs 2-14 days	Tanious et al,[8] 2018	649	3707	4356	1.632 (0.34-7.84)
Death (perioperative)	CEA <2 days vs 2-5 days	Avgerinos et al,[9] 2017	96	322	418	0.6708 (0.079-5.670)
Death 30 days	CEA <2 days vs 2-5 days	Avgerinos et al,[9] 2017	96	322	418	0.559 (0.068-4.587)
Stroke	CEA <2 days vs 2-5 days	Avgerinos et al,[9] 2017	96	322	418	1.8061 (0.740-4.399)
MI	CEA <2 days vs 2-5 days	Avgerinos et al,[9] 2017	96	322	418	1.1181 (0.23-5.45)
Death (perioperative)	CEA <2 days vs >6 days	Avgerinos et al,[9] 2017	96	571	667	2.974 (0.27-32.48)
Death 30 days	CEA <2 days vs >6 days	Avgerinos et al,[9] 2017	96	571	667	0.9913 (0.12-8.14)
Stroke	CEA <2 days vs >6 days	Avgerinos et al,[9] 2017	96	571	667	4.1635 (1.62-10.67)
MI	CEA <2 days vs >6 days	Avgerinos et al,[9] 2017	96	571	667	2.3792 (0.47-12.09)
Death (perioperative)	CEA 2-5 days vs >6 days	Avgerinos et al,[9] 2017	322	571	893	4.4332 (0.87-22.72)
Death 30 days	CEA 2-5 days vs >6 days	Avgerinos et al,[9] 2017	322	571	893	1.7733 (0.58-5.45)
Stroke	CEA 2-5 days vs >6 days	Avgerinos et al,[9] 2017	322	571	893	2.3053 (1.02-5.20)
MI	CEA 2-5 days vs >6 days	Avgerinos et al,[9] 2017	322	571	893	2.128 (0.65-6.92)
Death 30 days	CAS <2 days vs 2-14 days	Hlvacia et al,[10] 2017	6	5	11	NA
Stroke	CAS <2 days vs 2-14 days	Hlvacia et al,[10] 2017	6	5	11	NA
Death (perioperative)	CAS <2 days vs 2-14 days	Hlvacia et al,[10] 2017	6	5	11	NA
Question 4: Screening high high-risk patients - comparative studies						
Death	Screened vs unscreened	Berens et al,[44] 1992	1087	97	1184	0.2 (0.13-0.31)
		Lin et al,[2] 2016	515	2718	3233	0.73 (0.49-1.09)
		Overall	**1602**	**2815**	**4417**	**0.38 (0-1432.82), I^2 = 95%**
Stroke	Screened vs unscreened	Berens et al,[44] 1992	1087	97	1184	0.33 (0.14-0.79)
		Lin et al,[2] 2016	515	2718	3233	1.06 (0.59-1.90)
		Overall	**1602**	**2815**	**4417**	**0.62 (0-1024.93), I^2 = 79%**
Question 5: Optimal sequence for intervention in patients with combined carotid and coronary disease[a]						

Supplementary Table I (online only). Continued.

Outcome	Intervention vs Comparison	Author, Year	Group 1	Group 2	Total	RR (95% CI)
Death	CEA and CABG combined vs CABG first	Bernhard,[92] 1972	15	1	16	NA
		Brow et al,[93] 1999	23	9	32	4.33 (0.01-2681.88)
		Chiappini et al,[95] 2005	140	40	180	0.51 (0.18-1.45)
		Giangola et al,[98] 1996	28	12	40	NA
		Hudorovic,[101] 2006	30	23	53	0.38 (0.11-1.37)
		Illuminati et al,[12] 2011	94	91	185	0.97 (0.06-15.25)
		Newman et al,[14] 1987	10	12	22	NA
		Peric et al,[105] 1997	37	38	75	1.03 (0.22-4.77)
		Rosenthal et al,[107] 1984	22	8	30	NA
		Urschel et al,[110] 1976	7	17	24	NA
		Overall	**406**	**251**	**657**	**0.58 (0.32-1.05), I^2 = 0%**
Stroke	CEA and CABG combined vs CABG first	Bernhard,[92] 1972	15	1	16	1.53 (0-643.18)
		Brow et al,[93] 1999	23	9	32	8.27 (0.02-4492.74)
		Chiappini et al,[95] 2005	140	40	180	1.29 (0.29-5.71)
		Giangola et al,[98] 1996	28	12	40	17.65 (0.03-9025.25)
		Hudorovic,[101] 2006	30	23	53	NA
		Illuminati et al,[12] 2011	94	91	185	0.01 (0-6.96)
		Peric et al,[105] 1997	37	38	75	0.62 (0.16-2.40)
		Rosenthal et al,[107] 1984	22	8	30	NA
		Urschel et al,[110] 1976	7	17	24	0.22 (0-133.65)
		Overall	**396**	**239**	**635**	**0.87 (0.34-2.22), I^2 = 0%**
MI	CEA and CABG combined vs CABG first	Bernhard,[92] 1972	15	1	16	NA
		Brow et al,[93] 1999	23	9	32	4.33 (0.01-2681.88)
		Chiappini et al,[95] 2005	140	40	180	0.29 (0.04-1.96)
		Giangola et al,[98] 1996	28	12	40	NA
		Hudorovic,[101] 2006	30	23	53	0.26 (0.06-1.15)
		Newman et al,[14] 1987	10	12	22	NA
		Peric et al,[105] 1997	37	38	75	2.05 (0.55-7.61)
		Rosenthal et al,[107] 1984	22	8	30	NA
		Urschel et al,[110] 1976	7	17	24	NA
		Overall	**312**	**160**	**472**	**0.64 (0.09-4.34), I^2 = 45%**

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Supplementary Table I (online only). Continued.

Outcome	Intervention vs Comparison	Author, Year	Group 1	Group 2	Total	RR (95% CI)
Stroke/death	CEA and CABG combined vs CABG first	Weimar et al,[11] 2017	65	62	127	1.7885 (0.82-3.92)[b]
Stroke	CEA and CABG combined vs CABG first	Weimar et al,[11] 2017	65	62	127	2.6231 (0.88-7.80)[b]
Death	CEA and CABG combined vs CABG first	Weimar et al,[11] 2017	65	62	127	2.1462 (0.6966-6.610)[b]
MI	CEA and CABG combined vs CABG first	Weimar et al,[11] 2017	65	62	127	0.0308 (0.0001-16.5500)[b]
Stroke/death	CEA and CABG combined vs CABG first	Illuminati et al,[12] 2011	94	91	185	0.121 (0.015-0.950)
Death	CEA and CABG combined vs CEA first	Bernhard,[92] 1972	15	15	30	0.02 (0-9.83)
		Brow et al,[93] 1999	23	3	26	1.48 (0-857.08)
		Carrel et al,[94] 1992	52	45	97	0.72 (0.24-2.21)
		Chiappini et al,[95] 2005	140	22	162	0.47 (0.14-1.61)
		Faggioli, 1990	2	17	19	NA
		Feldman, 2017	15,402	6297	21,699	1.16 (1, 1.34)
		Giangola, 1996	28	17	45	0.03 (0, 16.02)
		Hempe, 2018	307	16	323	0.78 (0.11, 5.55)
		Hertzer, 1978	115	59	174	2.57 (0.31, 21.46)
		Kovacevic, 2012	112	726	838	5.4 (2.39, 12.21)
		Lyem et al,[102] 2009	40	40	80	0.75 (0.18-3.14)
		Newman et al,[14] 1987	10	28	38	NA
		Oz et al,[104] 2016	108	204	312	2.83 (0.48-16.7)
		Peric et al,[105] 1997	37	81	118	1.31 (0.33-5.21)
		Rosenthal et al,[107] 1984	22	14	36	0.06 (0-36.3)
		Takach et al,[109] 1997	255	257	512	2.52 (0.80-7.93)
		Urschel et al,[110] 1976	7	8	15	NA
		Overall	**16,675**	**7849**	**24,524**	**1.34 (0.78-2.29), I^2 = 46%**
Stroke	CEA and CABG combined vs CEA first	Bernhard,[92] 1972	15	15	30	21 (0.04-11476.96)
		Brow et al,[93] 1999	23	3	26	2.82 (0.01-1433.88)
		Carrel et al,[94] 1992	52	45	97	1.3 (0.23-7.43)
		Chiappini et al,[95] 2005	140	22	162	1.41 (0.19-10.62)
		Faggioli et al,[96] 1990	2	17	19	NA
		Feldman et al,[97] 2017	15,402	6297	21,699	1.47 (1.20-1.79)
		Giangola et al,[98] 1996	28	17	45	2.43 (0.30-19.97)
		Hempe et al,[99] 2018	307	16	323	8.44 (0.02-4146.38)
		Hertzer et al,[100] 1978	115	59	174	2.57 (0.58-11.33)

Supplementary Table I (online only). Continued.

Outcome	Intervention vs Comparison	Author, Year	Group 1	Group 2	Total	RR (95% CI)
		Kovacevic et al,[103] 2012	112	726	838	1.3 (0.38-4.41)
		Lyem et al,[102] 2009	40	40	80	0.67 (0.12-3.78)
		Oz et al,[104] 2016	108	204	312	4.72 (0.93-23.94)
		Peric et al,[105] 1997	37	81	118	0.94 (0.26-3.43)
		Rosenthal et al,[107] 1984	22	14	36	NA
		Takach et al,[109] 1997	255	257	512	2.02 (0.70-5.81)
		Urschel et al,[110] 1976	7	8	15	NA
		Overall	**16,665**	**7821**	**24,486**	**1.5 (1.3-1.72), I^2 = 0%**
MI	CEA and CABG combined vs CEA first	Bernhard,[92] 1972	15	15	30	0.03 (0-16.82)
		Brow et al,[93] 1999	23	3	26	1.48 (0-857.08)
		Carrel et al,[94] 1992	52	45	97	0.02 (0-11.05)
		Chiappini et al,[95] 2005	140	22	162	0.1 (0.02-0.59)
		Giangola et al,[98] 1996	28	17	45	0.01 (0-6.06)
		Hempe et al,[99] 2018	307	16	323	2.67 (0.01-1368.95)
		Hertzer et al,[100] 1978	115	59	174	1.03 (0.41-2.60)
		Lyem et al,[102] 2009	40	40	80	2 (0.19-21.18)
		Newman et al,[14] 1987	10	28	38	NA
		Oz et al,[104] 2016	108	204	312	1.26 (0.36-4.37)
		Peric et al,[105] 1997	37	81	118	1.64 (0.61-4.39)
		Rosenthal et al,[107] 1984	22	14	36	0.06 (0-36.3)
		Takach et al,[109] 1997	255	257	512	1.01 (0.46-2.20)
		Urschel et al,[110] 1976	7	8	15	0.1 (0-62.09)
		Overall	**1159**	**809**	**1968**	**0.85 (0.45-1.62), I^2 = 21%**
Death/stroke	CEA and CABG combined vs CEA first	Feldman et al,[97] 2017	1047	6297	7344	1.26 (1.12-1.42)
		Takach et al,[109] 1997	255	257	512	2.27 (1-5.12)
		Overall	**1302**	**6554**	**7856**	**1.46 (0.06-38.22), I^2 = 49%**
Death	CABG first vs CEA first	Bernhard,[92] 1972	1	15	16	0.27 (0-103.45)
		Brow et al,[93] 1999	9	3	12	NA
		Chiappini et al,[95] 2005	40	22	62	0.92 (0.24-3.48)
		Giangola et al,[98] 1996	12	17	29	0.07 (0-36.68)
		Newman et al,[14] 1987	12	28	40	NA
		Peric et al,[105] 1997	38	81	119	1.28 (0.32-5.08)
		Rosenthal et al,[107] 1984	8	14	22	0.16 (0-96.74)

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Supplementary Table I (online only). Continued.

Outcome	Intervention vs Comparison	Author, Year	Group 1	Group 2	Total	RR (95% CI)
		Urschel et al,[110] 1976	17	8	25	NA
		Overall	**137**	**188**	**325**	**0.94 (0.44-2.01), I^2 = 0%**
Stroke	CABG first vs CEA first	Bernhard,[92] 1972	1	15	16	NA
		Brow et al,[93] 1999	9	3	12	NA
		Chiappini et al,[95] 2005	40	22	62	1.1 (0.11-11.46)
		Giangola et al,[98] 1996	12	17	29	0.13 (0-79.8)
		Peric et al,[105] 1997	38	81	119	1.52 (0.52-4.49)
		Rosenthal et al,[107] 1984	8	14	22	NA
		Urschel et al,[110] 1976	17	8	25	5.21 (0.01-3197.17)
		Overall	**125**	**160**	**285**	**1.4 (0.64-3.06), I^2 = 0%**
MI	CABG first vs CEA	Bernhard,[92] 1972	1	15	16	0.44 (0-177.27)
		Brow et al,[93] 1999	9	3	12	NA
		Chiappini et al,[95] 2005	40	22	62	0.37 (0.07-2.03)
		Giangola et al,[98] 1996	12	17	29	0.03 (0-13.86)
		Newman et al,[14] 1987	12	28	40	NA
		Peric et al,[105] 1997	38	81	119	0.8 (0.22-2.85)
		Rosenthal et al,[107] 1984	8	14	22	0.16 (0-96.74)
		Urschel et al,[110] 1976	17	8	25	0.04 (0-26.42)
		Overall	**137**	**188**	**325**	**0.51 (0.22-1.18), I^2 = 0%**
Death	CAS and CABG combined vs CAS first	Xiang et al,[111] 2019	5	208	213	4.62 (0.72-29.87)
		Yang et al,[13] 2016	20	39	59	NA
		Overall	**25**	**247**	**272**	**4.62 (0.72-29.87), I^2 = NA%**
Stroke	CAS and CABG combined vs CAS first	Yang et al,[13] 2016	20	39	59	21.398 (0.034-13554.280)
MI	CAS and CABG combined vs CAS first	Yang et al,[13] 2016	20	39	59	0.1768 (0.0003-112.0200)
Stroke/death/MI	CAS and CABG combined vs CAS first	Yang et al,[13] 2016	20	39	59	1.95 (0.13-29.57)
Death	CEA/CAS and CABG combined vs CABG first in asymptomatic patients	Illuminati et al,[12] 2011	94	91	185	0.9681 (0.062-15.250)
Stroke	CEA/CAS and CABG combined vs CABG first in asymptomatic patients	Illuminati et al,[12] 2011	94	91	185	0.0136 (0.00-6.96)
Stroke/death	CEA/CAS and CABG combined vs CABG first in asymptomatic patients	Illuminati et al,[12] 2011	94	91	185	0.121 (0.015-0.950)
Stroke/death	CEA/CAS and CABG combined vs CABG first in asymptomatic patients	Weimar et al,[11] 2017	65	62	127	1.7885 (0.82-3.92)[b]
Stroke	CEA/CAS and CABG combined vs CABG first in asymptomatic patients	Weimar et al,[11] 2017	65	62	127	2.6231 (0.882-7.800)[b]

Supplementary Table I (online only). Continued.

Outcome	Intervention vs Comparison	Author, Year	Group 1	Group 2	Total	RR (95% CI)
Death	CEA/CAS and CABG combined vs CABG first in asymptomatic patients	Weimar et al,[11] 2017	65	62	127	2.1462 (0.697-6.610)[b]
MI	CEA/CAS and CABG combined vs CABG first in asymptomatic patients	Weimar et al,[11] 2017	65	62	127	0.0308 (0.0001-16.5500)[b]
Death	CEA/CAS and CABG combined vs carotid intervention first in asymptomatic patients	Faggioli et al,[96] 1990	2	17	19	NA
		Feldman et al,[97] 2017	15,402	7099	22,501	1.23 (1.07-1.42)
		Kovacevic et al,[103] 2012	112	726	838	5.4 (2.39-12.21)
		Timaran,[113] 2008	26,197	887	27,084	1.04 (0.78-1.39)
		Overall	**41,713**	**8729**	**50,442**	**1.54 (0.23-10.31), I^2 = 86%**
Stroke	CEA/CAS and CABG combined vs carotid intervention first in asymptomatic patients	Faggioli et al,[96] 1990	2	17	19	NA
		Feldman et al,[97] 2017	15,402	7099	22,501	1.38 (1.14-1.66)
		Kovacivoc et al,[103] 2012	112	726	838	1.3 (0.38-4.41)
		Timaran,[113] 2008	26,197	887	27,084	1.65 (1.08-2.53)
		Overall	**41,713**	**8729**	**50,442**	**1.42 (1.16-1.73), I^2 = 0%**
Death/stroke	CEA/CAS and CABG combined vs carotid intervention first in asymptomatic patients	Feldman et al,[97] 2017	15,402	7099	22,501	1.29 (1.15-1.45)
		Timaran et al,[113] 2008	26,197	887	27,084	1.25 (0.98-1.60)
		Overall	**41,599**	**7986**	**49,585**	**1.28 (1.1-1.49), I^2 = 0%**
Death	CEA/CAS and CABG combined vs CABG first in symptomatic patients	Newman et al,[14] 1987	10	12	22	NA
MI	CEA/CAS and CABG combined vs CABG first in symptomatic patients	Newman et al,[14] 1987	10	12	22	NA
Death	CEA/CAS and CABG combined vs carotid intervention first in symptomatic patients	Newman et al,[14] 1987	10	28	38	NA
MI	CEA/CAS and CABG combined vs carotid intervention first in symptomatic patients	Newman et al,[14] 1987	10	28	38	NA
Death	CABG first vs carotid intervention first in symptomatic patients	Newman et al,[14] 1987	12	28	40	NA
MI	CABG first vs carotid intervention first in symptomatic patients	Newman et al,[14] 1987	12	28	40	NA

CABG, Coronary artery bypass grafting; *CAS*, carotid artery stenting; *CEA*, carotid endarterectomy; *CI*, confidence interval; *MI*, myocardial infarction; *RR*, relative risk.
[a]Studies did not report symptom status from cardiac point of view. Symptomatology in this report refers to carotid related symptoms.
[b]CEA and CABG combined vs isolated CABG.

Supplementary Table II (online only). Characteristics of included studies

Author, year (trial name) geographic area	Total No. of patients (A) medical management (B) CEA/CAS	Mean age, years	Male sex, %	Mean BMI	Comorbidities	Medical therapy
Question 1: Medical management vs carotid intervention in asymptomatic patients						
ACST, 2004[5] (ACST trial) UK	(A) 1560 (B) 1560	NR	(A) 65.5 (B) 65.4	NR	(A) DM 19.6%, CAD 26.8% (B) DM 20.2%, CAD 26.3%	Antiplatelet therapy, antihypertensive treatment, and lipid-lowering therapy
Kolos et al,[4] 2015 (AMTEC trial) Russia	(A) 24 (B) 31	(A) 66.1 (B) 67	(A) 83 (B) 65	(A) 26.8 (B) 29.9	(A) CAD 75%, smoking 46%, MI 38%, stroke 8%, previous PCI/CABG 58%, DM 21%, CKD 4% (B) CAD 68%, smoking 68%, MI 26%, stroke 23%, previous PCI/CABG 48%, DM 29%, CKD 0%	All patients received antiplatelet therapy with aspirin at a dose of 81-325 mg/dL, aggressive therapy to lower LDL cholesterol levels with atorvastatin (10-80 mg/dL), with a target LDL level of <2.6 mmol/L (ideally <2.0 mmol/L), and antihypertensive therapy with amlodipine (5-10 mg/dL) and losartan (50-100 mg/dL) to lower the BP to a target level of <140/90 mm Hg, and hydrochlorothiazide (12.5 mg/dL) was added if the target BP was not achieved
Lin et al,[2] 2016 Taiwan	(A) 15 (B) 25	(A) 68.8 (B) 71.4	(A) 73 (B) 84	NR	(A) HTN 80%, DM 47%, hypercholesterolemia 60%, smoking 33%, AF 6.6% (B) HTN 80%, DM 36%, hypercholesterolemia 68%, smoking 36%, AF 0%	Aggressive medical treatment (dual antiplatelets if tolerated or at least 1 antiplatelet, statin therapy goal of LDL <100 mg/dL, DM treatment goal of HbA1c <7%, HTN treatment goal of SBP of <140 mm Hg, smoking cessation
Reiff et al, 2019[1] (SPACE-2 trial) Germany	(A) 113 (B) 400	(A) 68 (B) 70	(A) 87 (B) 73.5	(A) 27 (B) 27	(A) HTN 90.3%, DM 35.4%, CAD 35.4%, hypercholesterolemia 80.5%, Current smoker 21.2% (B) HTN 89.2%, DM 27.7%, CAD 35.5%, hypercholesterolemia 79%, current smoker 19%	Up-to-date medication following national and international guidelines, Not specified
Sato et al,[15] 2016 Japan	(A) 64 (B) 47	(A) 77.5 (B) 68.9	(A) 76.6 (B) 94.5	(A) 23.1 (B) 23.9	(A) HTN 89.1%, hypercholesterolemia 70.3%, DM 50%, AF 7.81%, stroke before 6 months 12.5%, CAD 73.4%, PAD 28.1%, AAA 4.69% (B) HTN 70.2%, hypercholesterolemia 61.7%, DM 17%, AF 8.51%, stroke before 6 months 12.8%, CAD 54.4%, PAD 14.9%, AAA 6.38%	Guideline-oriented medical treatment, not specified
Walker et al,[3] 1995 (ACAS trial) USA and Canada	(A) 834 (B) 825	NR	(A) 66 (B) 66	NR	(A) CAD 69%, HTN 64%, cancer 10%, DM 21%, lung disease 5%, current smoker 24%, previous contralateral CEA 19%, TIA or stroke 27% (B) CAD 69%, HTN 64%, cancer 12%, DM 25%, lung disease 6%, current smoker 28%, previous contralateral CEA 20%, TIA or stroke 22%	325 mg of regular or enteric-coated aspirin daily, the recommendations of the ACAS Risk Factor Reduction Committee were followed for diastolic and systolic HTN, diabetes mellitus, abnormal lipid levels, excessive consumption of ethanol, and tobacco use

Author, year (trial name) geographic area	Total No. of patients (A) CEA (B) CAS	Mean age, years	Male sex, %	Mean BMI	Comorbidities (CEA)	Comorbidities (CAS)	Comments
Question 2: CEA vs CAS in symptomatic patients							
Bonati et al,[16] 2015 Huibers, 2015[17] Featherstone et al,[18] 2016 ICSS,[19] 2010 (ICSS) International, multicenter	(A) 857 (B) 853	(A) 70 (B) 70	(A) 71 (B) 70	NR	HTN 70%, CHF 5%, Angina in past 6 months 9%, MI 18%, CABG 14%, AF 7%, DM 22%, PAD 16%, hyperlipidemia 66%, current smoker 23%, ex-smoker 49%	HTN 69%, CHF 3%, Angina in past 6 months 10%, MI 18%, CABG 13%, AF 7%, DM 22%, PAD 16%, hyperlipidemia 61%, current smoker 24%, ex-smoker 48%	

Supplementary Table II (online only). Continued.

Author, year (trial name) geographic area	Total No. of patients (A) CEA (B) CAS	Mean age, years	Male sex, %	Mean BMI	Comorbidities (CEA)	Comorbidities (CAS)	Comments
Brooks et al,[20] 2001 USA	(A) 51 (B) 53	(A) 69.6 (B) 66.4	NR	NR	HTN 94.1%, DM 23.5% smoking: 78.4% CAD 60.8%	HTN 84.9%, DM 35.9%, smoking: 71.7%, CAD 73.6%	
Eckstein et al,[21] 2008 Ringaleb et al,[22] 2004[22] Ringaleb et al,[23] 2006 (SPACE) Europe, multicenter	(A) 589 (B) 607	(A) 68.7 (B) 68.1	(A) 72 (B) 72	(A) 26.7 (B) 27.2	HTN 76%, DM 29%, coronary heart disease 24%, previous or present smoker 70%	HTN 75%, DM 26%, coronary heart disease 21%, previous or present smoker 71%	Data mostly from Eckstein et al,[21] 2008 and Ringaleb, 2004[22]
Ederle et al,[24] 2009 Brown et al,[25] 2001 Bonati et al,[26] 2014 (CAVATAS) International, multicenter	(A) 253 (B) 251	(A) 67 (B) 67	(A) 70 (B) 69	NR	HTN 58%, DM 13%, smoker 78%, MI 17% AF 5%, PAD 20%, CAD 37%	HTN 53%, DM 14%, smoker 77%, MI 19%, AF 5%, PAD 24%, CAD 39%	Data mainly from Ederle et al,[24] 2009 and Brown, 2001[25]
Hoffman et al,[27] 2008 (BACASS) Switzerland	(A) 10 (B) 10	(A) 71 (B) 69	(A) 90 (B) 80	NR	HTN 80%, smoking 60%, HLD 60%, DM 30%, CAD 40%	HTN 70%, smoking 50%, HLD 70%, DM 30%, CAD 20%	
Mas et al,[28] 2014 Mas et al,[29] 2006 Mas et al,[30] 2008 (EVA-3s) France, multicenter	(A) 262 (B) 265	(A) 70.2 (B) 69.1	(A) 77.9 (B) 72.8	(A) 26.3 (B) 26.1	HTN 72.5%, DM 25.6%, hypercholesterolemia 55.7%, tobacco use 24.5%, stroke 19.8%, TIA 22.9%, MI 13.4%, PAD 11.5%, CHF 2.7%, PCI/CABG 13.4%, contralateral CEA/CAS 3.8%	HTN 72.8%, DM 22.3%, hypercholesterolemia 58.1%, tobacco use 23.3%, stroke 13.2%, TIA 25.7%, MI 10.6%, PAD 15.1%, CHF 2.6%, PCI/CABG 13.2%, contralateral CEA/CAS 2.3%	
Naylor,[31] 1998 UK	(A) 10 (B) 7	(A) 66.7 (B) 68	(A) 40 (B) 71.4	NR	NR	NR	Initial number of patients randomized is 23 (CES 12, CAS 11), information is available only for patients who received the treatment. The trial was officially abandoned in April 1997, because of problems with informed consent to future patients.
Silver, 2011[32] Howard et al,[33] 2011 Brott et al,[34] 2010 Meschia et al,[35] 2015 Jones et al,[36] 2018 Howard et al,[37] 2015 Timaran et al,[38] 2013 Blackshear et al,[39] 2011 (CREST) USA and Canada	(A) 653 (B) 668	(A) 68.8 (B) 68.8	(A) 65.4 (B) 64.1	NR	HTN 84.4%, DM 27.5%, dyslipidemia 81.1%, current smoker 29.6%, CAD 39.3%, CABG 17.0%	HTN 83.6%, DM 28.7%, dyslipidemia 76.9%, current smoker 26.8%, CAD 36.6%, CABG 16.8%	Data mainly from Silver, 2011[32] (baseline characteristics) and Howard et al,[33] 2011 (outcomes)
Steinbauer et al,[40] 2008 Germany	(A) 44 (B) 43	(A) 68.4 (B) 67.9	NR	NR	HTN 77.3%, current or past smoker 40.91%, CAD 45.5%, DM 34.1%, hypercholesterolemia 52.3%, PAD 18.2%	HTN 79.1%, current or past smoker 44.2%, CAD 41.9%, DM 44.2%, hypercholesterolemia 51.2%, PAD 18.6%	

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) <2 days (B) 2-14 days (C) >14 days	Mean age, years	Male sex, %	Comorbidities
Question 3: Timing of intervention in stroke						
Avgerinos et al,[9] 2017 USA	The Vascular Study Group of New England registry was queried from 2003 to 2014 to identify CEA procedures. The analysis included only CEA for symptomatic stroke with a known LOS	Asymptomatic, combined CEA and cases with missing LOS were excluded. We also excluded cases performed for minor or major strokes occurring >1 month from symptoms and cases performed for TIAs	(A) 96 (B) 322 (2-5 days) (C) 571 (>6 days)	(A) 70.1 (B) 69.9 (C) 69.4	(A) 68.8 (B) 65.2 (C) 66.1	(A) HTN 91.7%, DM 28.1%, CHF 11.5%, COPD 24%, CAD 36.5% (B) HTN 82.6%, DM 28.3%, CHF 6.5%, COPD 19.6%, CAD 22% (C) HTN 87%, DM 32.3%, CHF 8.4%, COPD 21.2%, CAD 27.2%

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Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) <2 days (B) 2-14 days (C) >14 days	Mean age, years	Male sex, %	Comorbidities
Azzini et al,[6] 2016 Italy	Patients with stroke and CAS who underwent intravenous therapy and CEA after intravenous therapy	NR	(A) 22 (B) 12	(A) 66.5 (B) 68	(A) 82 (B) 67	NR
Barbetta et al,[7] 2014 Italy	Patients who presented with an acute onset of a neurologic deficit	NR	(A) 25 (B) 27	70	71.1	HTN 83.3, DM 27.7, CAD 30, PAD 15.5, HLD 53.3, smoking 62.2
Brandl et al,[41] 2001 Germany	Patients admitted for CEA	Patients were considered not eligible for CEA, if they had an intracerebral hemorrhage and/or early signs of territorial infarcts with disturbance of the blood-brain barrier were present	(A) 16 (C) 217	(A) 69.9 (C) NR	(A) 75 (C) NR	NR
Hlvacia et al,[10] 2017 Switzerland	Consecutive cases with acute symptomatic carotid stenosis with ICA thrombus that received endovascular treatment	N/A	(A) 6 (B) 5	70	82	NR
Mihindu et al,[42] 2019 USA	CEA or CAS performed during the index hospitalization after presentation with a TIA or an acute stroke in patients with >50% common or internal carotid stenosis	Elective carotid interventions for asymptomatic or symptomatic carotid stenosis were excluded	(A) 55 (B) 64	68.3	68.3	Hypercholesterolemia 93.3%, MI 28.6%, DM 34.2%, CRF 25.8%
Tanious et al,[8] 2018 USA	The Vascular Quality Initiative was queried for all symptomatic patients who presented with a stroke and underwent CEA between the years 2012 and 2017	Patients were excluded if they had missing data, were asymptomatic on presentation, or presented with symptoms of TIAs or amaurosis fugax. In addition, patients who underwent emergency surgery, concomitant cardiac surgery, and those with an occluded ipsilateral ICA were also excluded	(A) 649 (B) 3707 (C) 4048	(A) 69 (B) 70 (C) 69.9	(A) 65.5 (B) 63.1 (C) 62.2	(A) Obesity 35.4%, DM 12.3%, anemia 12.6%, HTN 85.7%, CAD 20.6%, CHF 5.4%, ESRD 0.9%, COPD 16.5% (B) Obesity 34.1%, DM 15.2%, anemia 14.7%, HTN 87.4%, CAD 20.8%, CHF 10.1%, ESRD 0.8%, COPD 19.8% (C) Obesity 32.6%, DM 14.4%, anemia 12.5%, HTN 86.7%, CAD 21.5%, CHF 9.4%, ESRD 0.9%, COPD 21.7%
Welsh et al,[43] 2004 UK	Only patients with acute stroke randomized within 7 days of the onset of symptoms were included	Focal neurologic deficits lasting <24 h, patients unfit for surgery and those with a Barthel score of <18 before stroke (measured by a Barthel Activities of Daily Living score) were not included. Patients with cerebral hemorrhage or intracranial space-occupying lesion on CT scan and any medical condition that precluded surgery were also ineligible.	(A) 19 (C) 21	69	(A) 58 (C) 57	(A) HTN 42%, DM 5%, cardiac disease 37%, claudication 16%, previous stroke 15.7% (C) HTN 33%, DM 5%, cardiac disease 19%, claudication 5%, previous stroke 4.7%

Author, year geographic area	Inclusion criteria	Total No. of patients (A) screened (B) unscreened	Mean age, years	Male sex, %	Mean BMI	Comorbidities
Question 4: Screening high risk patients (comparative studies)						
Berens et al,[44] 1992 USA	Patients who were ≥65 years of age undergoing a cardiac surgical procedure	(A) 1087 (B) 97	(A) 72 (B) NR	(A) 59 (B) NR	NR	(A) CAD 89.3%, HTN 64%, DM 27%, PAD 10%, stroke 7.1%, renal disease 2.5% (B) NR

Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Total No. of patients (A) screened (B) unscreened	Mean age, years	Male sex, %	Mean BMI	Comorbidities
Lin et al,[45] 2016 USA	Patients were those who underwent open heart surgery	(A) 515 (B) 2718	(A) 64.6 (B) 63.1	(A) 72 (B) 64.8	(A) 28.8 (B) 29.2	(A) CAD 59.4%, current smoker: 37.7%, DM 36.7%, dyslipidemia 68.7%, HTN 80.2%, infectious endocarditis: 3.7%, chronic lung disease: 21%, cerebrovascular disease 10.9%, prior CVA: 8.2%, prior TIA 2.9% (B) CAD 52.1% current smoker 37.7%, DM 36.7%, dyslipidemia 58.4%, HTN 83.3%, infectious endocarditis 3.9%, chronic lung disease 21.8%, cerebrovascular disease 12.7%, prior CVA 7.2%, Prior TIA 3.3%

Author, year geographic area	Inclusion criteria	Exclusion criteria	No. of patients	Mean age, years	Male sex, %	Comorbidities
Question 4: Screening high-risk patients (noncomparative studies)						
Ahn et al,[46] 1991 USA	Carotid duplex scans performed in the vascular laboratory between 1985 and 1989. Patients who underwent a screening carotid duplex scan as part of their initial evaluation for PAD, despite having no signs or symptoms of any carotid artery disease.	Scans performed for any focal or nonfocal neurologic symptoms including TIAs, strokes, amaurosis fugax, retinal stroke, dizziness, vertigo, syncope, tinnitus, blurred vision, mental status changes, eye pain, or even headaches were excluded. Scans that were performed for any signs of carotid artery disease including a decreased carotid pulse, cervical bruit, pulsatile neck mass, or Hollenhorst's plaque were also eliminated. Scans that were performed in patients with carotid artery disease previously documented by an abnormal duplex scan or angiogram and/or previous carotid surgery were excluded.	78	70	69	PAD 100%, smoking 79%, CAD 59%, HTN 52%, DM 26%, HLD 56%
Aiello et al,[47] 2012 USA	Patients with PAD undergoing peripheral vascular studies and carotid duplex ultrasound examination	NR	542	72	54.2	PAD 100%
Anastasiadis et al,[48] 2009 Greece	Patients who underwent open heart surgery who had no symptoms suggestive ofcarotid artery disease.	NR	307	65.4	76.2	HTN 67.8%, lipidemia 51.8%, DM 33.6%, smoking 40.7%, history of stroke 6.5%
Ascher et al,[49] 2001 USA	Patients underwent CABG and/or VR. 98% underwent CABG	history of stroke, TIAs, or amaurosis fugax, history of CEA	3708	68	83	DM 33%, smoking 53%, HTN 59%
Bae et al,[50] 2006 Korea	NR	NR	246	59.2	75.2	HTN 50%, DM 26.8%, HLD 34.1%, smoking 52%, history of stroke 13%
Bishara et al,[51] 2008 Egypt	Patients with one of the following risk factors: DM, ischemic heart disease, HTN, smoking, and dyslipidemia.	NR	617	60.4	56.7	DM, HTN, HLD, smoking, CAD

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Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	No. of patients	Mean age, years	Male sex, %	Comorbidities
Cheng et al,[52] 1999 China	Patients who were without cerebrovascular symptoms but who were at risk of carotid atherosclerosis: patients with symptomatic PVD; patients with AAA from the department of surgery; and patients with symptomatic CAD referred from cardiology and cardiothoracic surgery.	Patients who had previous carotid surgery	456	68.9	63.4	PAD 100%, CAD 100%
Cheng et al,[53] 2015 China	Patients who underwent CABG	Patients undergoing emergency CABG or cardiac valve procedures	1558	61.54	77.2	CAD 100%, HTN 66.6%, DM 35.1%, history of stroke 12.5%, CKD 1.3%, COPD 0.4%, History of smoking 52.8%, AF 2.7%, previous PCI 13.6%, previous stent 10.4%, in-stent restenosis 4.5%, history of MI 32.9%
Choo et al,[54] 2017 South Korea	Consecutive neurologically asymptomatic patients who had undergone preoperative carotid duplex ultrasound examination for PAD	NR	231	69.5	87.4	PAD 100%
Chun et al,[55] 2014 USA	Patients who had undergone preoperative carotid artery duplex ultrasound examination before scheduled cardiac surgery	Patients who needed emergency cardiac surgery	722	70.2	66.2	DM 44.5%, HTN 88.8%, HLD 90.9%, CKD/ESRD 37%, COPD 10.5%, PAD 20.2%, CAD 74.7%, CVA/TIA 18.3%, MI: 28.9%
Cornily et al,[56] 2011 France	Patients undergoing CAB with no other concomitant cardiac procedure (such as valve replacement/repair, aneurysmectomy, atrial septal defect closure) patients with either CVD or PVD, diabetes mellitus, carotid bruit and/or aged >70 years	Aortic stenosis even if not significant (bruit of aortic stenosis can hide a carotid bruit); need for emergency surgery; and carotid evaluation performed in another center.=	121	NR	NR	PAD, DM, HTN, HLD, smoking
de Virgilio et al,[57] 1997 USA	Patients presenting with complaints related to lower extremity atherosclerotic disease (claudication, ischemic rest pain, ischemic ulcer, or gangrene)	Patients who had a history of stroke, TIA, amaurosis fugax, prior CEA, nonatherosclerotic vascular disease, or presented with urgent life or limb threatening problems	89	66	100	HTN 60%, DM 42%, PAD 100%
Dharmasaroja et al,[58] 2010 Thailand	Patients who had coronary angiography	Patients withnormal coronary arteries	177	65	53.6	HTN 67%, DM 38%, HLD 64%, smoking 19%, PAD 38.4, CAD 100%
Drohomirecka et al,[59] 2010 Poland	Patient scheduled for CABG	Patients with a history of previous CEA or carotid stenting	682	63.2	79.5	HTN 74.3%, DM 31.4%, CAD 100%, CKD 5.4%, prior CVA 10.3%
Fassiadis et al,[60] 2008 UK	Patients aged between 65 and 75 years who underwent previous coronary angioplasty	NR	117	71	68.7	HLD 53.8%, HTN 47%, DM 24%, smoking 11.1%, previous regular smoker 58.1%, MI 40%

Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	No. of patients	Mean age, years	Male sex, %	Comorbidities
Fowl et al,[61] 1991 USA	Any veteran who was visiting the hospital for nonvascular problems. At a later stage, routine carotid artery examinations were limited to only those veterans who were regularly observed in the Vascular Laboratory for PVD of the lower extremity.	Patients with known symptomatic carotid artery disease treated either medically or surgically.	116	64.4	94.8	PAD 100%, HTN 45.7%, DM 28.5%, cardiac disease 36.2%, smoking 96.6%
Gentile,[62] 1995 USA	Neurologically asymptomatic patients undergoing lower extremity revascularization	Patients with a history of previous CEA or symptomatic cerebrovascular disease, including stroke, TIA, and nonhemispheric symptoms, patients who underwent emergency operations, and patients with nonatherosclerotic disease	225	67	52	PAD 100%
Helfre et al,[63] 2017 France	People with type 2 diabetes who had a routine screening by carotid artery Doppler ultrasound examination	Patients with a history of coronary vascular disease, cerebral infarction or PAD	337	61.1	55.1	DM 100%, HTN 27.3%, retinopathy 20.1%, neuropathy 27.9%, nephropathy 37.4%
Hill et al,[64] 1999 Canada	Patients scheduled for elective cardiac surgery (185 coronary artery bypass, 4 valve replacements and 11 combined valve and coronary artery operations)	Patients who required transplant, urgent or emergency surgery	200	NR	81	Smoking 52%, neurologic history 7%,DM 22%, HLD 31%, PAD 20%
House,[65] 1999 Australia	Patients with PVD	Patients with previous stroke, extracranial vascular surgery or cerebrovascular symptoms	486	70.6	63	PAD 100%, smoking 70%, cholesterol: 59%, HTN 58%, heart disease: 49%, renal disease: 26%, DM 18%, COPD 18%
Ignatiev,[66] 2012 Russia	Patients aged >50 years old and having neither transient nor persistent neurologic symptomatology with no history of previously endured ischemic stroke	NR	485	58.8	79	HTN, CAD, DM, PAD, smoking
Jackson et al,[67] 1985 USA	Asymptomatic patients who underwent duplex carotid screening	NR	254	64.8	62	HTN 63%, DM 27%, CAD or PAD 44%
Kaul et al,[68] 2017 India	Individuals with no present or past history of stroke or TIA, and age more than 40 years	Individuals with present or past history of cardiovascular disease (angina, myocardial ischemia), cerebrovascular disease (stroke or TIA), vascular diseases of the eye, PVDs, and age below 40 years	1500	58.1	67.7	HTN 35.9%, DM 23.2%, dyslipidemia 17.4%
Kawarada et al,[69] 2003 Japan	Patients who underwent elective CABG at Kishiwada Tokushukai hospital	NR	380	66	77.1	HTN 52.3%, HLD 32.1%, DM 40.3%, stroke 18.9%, hemodialysis 6.8%, PAD 15.3%, CAD 100%
Klop et al,[70] 1991 the Netherlands	Patients with PAD	NR	416	66.9	67.8	PAD 100%, HTN 35.3%, Cardiac disease 24.8%, DM 15.4%, hypercholesterolemia (13.8% was assessed in only 288 patients), smoking 61.1%

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Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	No. of patients	Mean age, years	Male sex, %	Comorbidities
Kurvers et al,[71] 2003 the Netherlands	Patients enrolled in the Second Manifestations of Arterial disease study, a single-center, prospective cohort study of patients referred to the Vascular Center of the University Medical Center	Patients >79 years and those with terminal malignancy	1668	54	64.4	PAD 24%, CAD 31%, DM 13%, HTN 16%, HLD 16%
Lara et al,[72] 2015 Spain	Consecutive patients with a duplex ultrasound screening for carotid artery disease before their admission to the department of cardiovascular surgery (CABG and heart valve replacement)	NR	725	NR	NR	CAD 87.2%
Lin et al,[73] 2012 USA	Patients who underwent tunneled cuffed hemodialysis catheter placement	NR	123	73	58	DM 49%, HTN 91%, CAD 55%
Mackaay et al,[74] 1995 the Netherlands	Dutch Caucasian inhabitants	NR	461	Range: 50-75	48	DM 37.5%, PAD 24.9%
Marek et al,[75] 1996 USA	Patients who were referred with claudication and no history of cerebrovascular symptoms or previous carotid surgery	NR	188	64.2	75.5	DM 28.7%, HTN 64.9%, HLD 55.9%, CAD 24.0%, PAD 100%
Miralles et al,[76] 1998 Spain	Consecutive patients selected for elective aortoiliac surgery, no patient had undergone previous diagnostic or therapeutic procedures in the renal arteries	patients previously referred for neurologic symptoms	168	62.8	95.8	HTN 44%, DM 25.6%, hypercholesterolemia 22%, hypertriglyceridemia 13.1%, hypercholesterolemia plus hypertriglyceridemia 15.5%, CAD 25.6%, aortic aneurysm 34.5%, renal failure 18.5%, arterial occlusive disease 65.5%
Miura,[77] 2010 Japan	Consecutive CAD patients who underwent PCI	NR	2179	70	76	CAD 100%, MD 44%, HTN 78%, CRF 9%, stroke 12%, PAD 19.2%
Moraca et al,[78] 2012 USA	Patients with screening preoperative carotid duplex referred for CABG	NR	559	67	75.7	CAD 100%, DM 36.3%, COPD 23.1%, CVA 5.4%, HTN 94.3%, PVD 14.8%, CKD 13.2%, CHF 13.4%
Narayan et al,[79] 2017 India	Patients presenting for primary CABG, patients with elective presentation	History of pericarditis, median sternotomy, thoracotomy, chest irradiation, or pleurodesis; associated valvular pathology requiring a combined procedure; re-operative surgery	4364	NR	NR	CAD 100%, DM 45.5%, smoker 45.3%, PAD 5.2%, HTN 70.1%, previous CVA 2%
Pilcher et al,[80] 2000 UK	PAD with uncomplicated limb ischemia	Patients with any history of neurologic symptoms, previous stroke, or previous CEA or complicated limb ischemia were excluded	200	68.8	61	HTN 42%, CAD 59%, hypercholesterolemia 16%, DM 20%, previous or current smoking 94.5%, previous smoking 58%

Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	No. of patients	Mean age, years	Male sex, %	Comorbidities
Planas-Ballvé et al,[81] 2019 Spain	Random population sample of 933 Caucasian patients older than 50 years with a moderate-high vascular risk (assessed by REGICOR score, which is the Framingham risk score validated for the Spanish population and calculated based on age, sex, diabetes, smoking, BP and cholesterol levels) and without history of stroke, coronary disease or severe disability	NR	933	66.4	63.7	HTN 56.4%, DM 26.8%, dyslipidemia 54.6%
Posacioglu et al,[82] 2001 Turkey	Patients admitted for peripheral vascular reconstruction	NR	108	NR	97.2	PAD 100%, HTN 43.5%, DM 30.6%, HLD 40.7%, CAD 62%, stroke 3.7%
Rockman et al,[83] 2004 USA	≥60 years old and had ≥1 of the following risk factors: history of cardiac disease, diagnosed HTN, history of smoking, and family history of stroke	NR	610	70.8	36.6	Smoker 9.5%, HTN 62%, CAD 17.4%, hypercholesterolemia 44.6%
Sayed et al,[84] 2016 Egypt	Patients presenting to the Vascular Surgery Division, Kasr Al-Ainy University Hospitals with PAD	Patients with PAD owing to causes other than atherosclerosis	37	60.41	78.4	PAD 100%, HTN 27%, DM 59.5%, obesity 18.9%, stroke or TIA 32.4%, CAD 43.3%
Stephens et al,[85] 2010 UK	Asymptomatic diabetic patients referred from the diabetic retinal screening program over a 9-year period	NR	36	70.6	63.9	DM 100%
Sutthapas,[86] 2012 Thailand	Consecutive patients with angiographically documented CAD	NR	320	NR	NR	CAD 100%
Valentine,[87] 1997 USA	Men with premature PVD	NR	76	47	100	HTN 45%, DM 14%, dyslipidemia 36%, CAD 61%, PAD 100%
Wanamaker et al,[88] 2012 USA	Patients who underwent isolated CABG	NR	673	67	76	CHF 13%, HTN 94%, COPD 23%, CVA 5.4%, PAD 15%, CKD 13%, MI 45%, HLD 85%, DM 36%, previous PCI 27%
Yamamoto et al,[89] 2006 Japan	Surgical candidates with abdominal aortic disease or PAD for elective surgery	Patients with known carotid stenosis and those owing to undergo operation in emergency	406	NR	83.7	DM 30.2%, HTN 70.6%, HLD 35%, smoking 78%
Yun et al,[90] 2010 Korea	Arterial bypass patients owing to chronic atherosclerotic lower extremity ischemia	History of cerebrovascular symptoms or previous carotid surgery	340	65.7	92.4	Smoking 56.8%, HTN 52.4%, DM 32.6%, CAD 27.1%, CRF 7.1%, hypercholesterolemia 13.8%, PAD 100%

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) combined (B) CABG first (C) carotid first	Mean age, years	Male sex, %	Comorbidities
Question 5: Optimal sequence for intervention in patients with combined carotid and coronary disease						
Abbasi et al,[91] 2008 Iran	Patient who had significant carotid artery stenosis and were candidates for CABG	Patients reluctant to participate; patients with previous major CVA, significant bilateral carotid stenosis and intracranial lesions	(A) 19 (C) 28	(A) 67.4 (C) 65.6	(A) 57.9 (C) 46.4	(A) HTN 78.9%, DM 26.3%, smoking 36.8%, CRF 5.3%, hypercholesterolemia 57.9%, TIA/stroke 15.8% (C) HTN 60.7%, DM 42.9%, smoking 21.4%, CRF 3.6%, hypercholesterolemia 82.7%, TIA/stroke 35.7%

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Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) combined (B) CABG first (C) carotid first	Mean age, years	Male sex, %	Comorbidities
Bernhard,[92] 1972 USA	Patients with coronary revascularization who also had associated significant extracranial cerebrovascular arteriosclerosis	N/A	(A) 15 (B) 1 (C) 15	58	58.06	NR
Brow et al,[93] 1999 UK	Patients with CAD who underwent carotid endarterectomy	NR	(A) 23 (B) 9 (C) 3	(A) 67 (B) NR (C) NR	(A) 78.3 (B) 88.9 (C) 100	(A) HTN 39%, PAD 47%, hypercholesterolemia 35% (B) NR (C) NR
Carrel et al,[94] 1992 Switzerland	Patients with coronary and carotid artery disease who underwent either combined or staged CEA+CABG	NR	(A) 52 (C) 45	(A) 60.5 (C) NR	(A) 84.6 (C) NR	(A) Nicotine abuse 67.2%, adiposity 57.8%, HTN 51.8%, COPD 42.2%, DM 15.4%, PAD 15.4%, CRF 5.7% (C) NR
Chiappini et al,[95] 2005 Italy	Patient who underwent both CABG and CEA, either as a single-stage or as a two-stage procedure	NR	(A) 140 (B) 40 (C) 22	(A) 67.1 (B) 63.2 (C) NR	(A) 88.6 (B) 79 (C) NR	(A) History of smoking 42.8%, HTN 71.4%, DM 25%, main left CAD 30%, HLD 17.8%, PAD 24.3%, CRF 10%, unstable angina 28.6%, obesity 10.7%, previous MI 42.8%, previous TIA/stroke 28.6%, COPD 12.9% (B) History of smoking 32.3%, HTN 83.9%, DM 41.9%, obesity 83.9%, HLD 32.3%, previous MI 29%, previous TIA/stroke 24.9%, PAD 20.9% CRF 4.8%, unstable angina 19.4%, COPD 9.6% (C) NR
Faggioli et al,[96] 1990 USA	Data from all patients undergoing CAB were reviewed	N/A	(A) 2 (C) 17	63.45	Predominantly male	Hypercholesterolemia, HTN, DM
Feldman et al,[97] 2017 USA	Patients who underwent CABG, as a combined (CEA+CABG) or staged (CEA+CABG or CAS+CABG) procedure	Any patients who underwent CEA or CAS after CABG, patients undergoing CAS and CABG on the same day	(A) 15402 (C) 7099	(A) 69.7 (C) 69.2	(A) 68.9 (C) 67.9	(A) HTN 73.9%, DM 38.1%, anemia 18.6%, collagen vascular disease 1.5%, CHF 2.4%, chronic pulmonary disease 29.8%, coagulopathy 15.9%, liver disease 0.8%, obesity 11.7%, PAD 32.5%, CRF 15.2%, previous PCI 6.4%, previous CABG 1.8% (C) HTN 75.3%, DM 38.8%, anemia 20.4%, collagen vascular disease: 1.4%, CHF 4.1%, chronic pulmonary disease 31.2%, coagulopathy 12.3%, liver disease 0.9%, obesity 13.4%, PAD 31.8%, CRF 16.4%, previous PCI 7.5%, previous CABG 1.6%
Giangola et al,[98] 1996 USA	Patients who had undergone both CEA and CABG either as simultaneous or staged procedure	NR	(A) 28 (B) 12 (C) 17	(A) 70.5 (B) 74.5 (C) NR	(A) 58 (B) 76 (C) NR	(A) MI 7.1%, crescendo angina 66.7%, CHF 7.1%, left main vessel or triple-vessel disease 17.9%, CVA 17.9% (B) MI 8.3%, crescendo angina 75%, CHF 16.7%, CVA 16.7% (C) MI: 5.8%, crescendo angina 64.7%, CHF 11.8%, left main vessel or triple-vessel disease 17.6%, CVA 17.6%

Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) combined (B) CABG first (C) carotid first	Mean age, years	Male sex, %	Comorbidities
Hempe et al,[99] 2018 Germany	Patients who underwent elective or urgent CABG and CEA, either as synchronous CABG+CEA or staged procedure (CEA followed by CABG within the same hospitalization)	NR	(A) 307 (C) 16	(A) 69.2 (C) 67.5	(A) 76.5 (C) 75	(A) COPD 21.8%, PAD 25.7%, DM 28.3%, smoking 15.7%, CVA 15.7%, MI 36.1%, PCI 34.4%, kidney disease 16.1% (C) COPD 31.3%, PAD 37.5%, DM 43.8%, smoking 68.8%, CVA: 18.8%, MI 50%, PCI 37.5%, kidney disease 12.5%
Hertzer et al,[100] 1978 USA	Patients who underwent staged or combined repair of significant simultaneous carotid and coronary atherosclerosis	N/A	(A) 115 (C) 59	(A) 59.4 (C) 57.2	79.31	NR
Hudorovic,[101] 2006 Croatia	Patients who underwent reverse-staged or simultaneous off-pump CABG/CEA	NR	(A) 30 (B) 23	(A) 64.9 (B) 66	(A) 80 (B) 87	(A) previous MI 50%, DM 16.7%, HLD 36.7%, HTN 43.3%, history of smoking 50%, obesity 6.7%, CRF 16.7%, COPD 13.3% (B) previous MI 56.5%, DM 17.4%, HLD 34.8%, HTN 47.8%, history of smoking 52.2%, obesity 8.7%, CRF 17.4%, COPD 13%
Illuminati et al,[12] 2011 Italy	Elective CABG for triple-vessel or left main trunk symptomatic CAD associated with unilateral, asymptomatic carotid stenosis >70% on preoperative color duplex ultrasound scans, and with the absence of significant atherosclerotic disease of the ascending aorta, aortic arch, and supra-aortic trunks at helical CT scan	Patients undergoing urgent CABG, defined as any revascularization performed outside normal operating hours or displacing other patients from the surgical schedule Also excluded were patients undergoing CABG with intra-aortic balloon pump, off-pump CABG, or other associated cardiac operations such as valvuloplasty or valvular replacement	(A) 94 (B) 91	(A) 67 (B) 66	(A) 62.8 (B) 67	(A) HTN 80.9%, HLD 27.7%, DM 26.6%, COPD 38.3%, PAD 13.8%, CRF 3.2%, smoker 47.9% (B) HTN 78%, HLD 33%, DM 23.1%, COPD 41.8%, PAD 12.1%, CRF 4.4%, smokers 51.6%
Iyem et al,[102] 2009 Turkey	Patients with predominant ischemic heart disease	NR	(A) 40 (C) 40	(A) 69 (C) 71	(A) 80 (C) 85	(A) CVA 15%, PAD 5%, COPD 52.5%, peptic/gastric ulcer 7.5%, DM 85%, HTN 82.5%, HLD 85%, smoking 92.5%, preoperative MI 17.5%, AF 2.5%, left main CAD 22.5%, unstable angina pectoris 17.5% (C) CVA 17.5%, PAD 2.5%, COPD 60%, peptic/gastric ulcer 5%, cancer 2.5%, DM 90%, HTN 80%, HLD 77.5%, smoking 95%, preoperative MI 15%, AF 7.5%, left main CAD 20%, unstable angina pectoris 22.5%
Kovacevic et al,[103] 2012 Serbia	Patients operated of occlusive coronary and carotid artery disease	Patients who did not meet the inclusion criteria were excluded from the study	(A) 112 (C) 726	62.6	66.8	HTN 63.7%, DM 37.3%, MI 17.8%, ejection fraction <30%: 28%
Newman et al,[14] 1987 USA	The last 50 patients requiring operations on both coronary and carotid arterial disease	N/A	(A) 10 (B) 12 (C) 28	59.5	62	Smoking 50%, HTN 62%, HLD 28%, DM 24%; renal dysfunction 14%

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Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) combined (B) CABG first (C) carotid first	Mean age, years	Male sex, %	Comorbidities
Oz et al,[104] 2016 Turkey	patients who were scheduled for CEA and CABG (either staged or concomitant)	Patients who are candidates for emergency or off-pump CABG; patient with paraganglioma in addition to carotid stenosis	(A) 108 (C) 204	(A) 63.7 (C) 63.8	(A) 69.4 (C) 70.6	(A) HTN 87.3%, DM 25%, renal dysfunction 13.9% COPD 38.9%, PAD 19.4%, stroke 6.5% (C) HTN 88.2%, DM 23.5%, renal dysfunction 18.6%, COPD 34.3%, PAD 21.6%, stroke: 5.9%
Peric et al,[105] 1997 Peric et al, 1998[106] Yugoslavia	Patients who underwent both CABG and CEA, either as a single-stage, or as a two-stage procedure	NR	(A) 48 (B) 50 (C) 103	(A) 59.3 (B) NR (C) NR	(A) 75.1 (B) NR (C) NR	(A) Previous MI 64.6%, Unstable angina pectoris 66.7%, triple vessel CAD 100%, left main CAD 35.4% (B) Previous MI 78%, Unstable angina pectoris 72%, triple vessel CAD 100%, left main CAD 36% (C) Previous MI 61.2%, Unstable angina pectoris 16.5%, triple vessel CAD 99%, left main CAD 5.8%
Rosenthal et al,[107] 1984 USA	Patients with coexistent carotid and coronary arterial disease	NR	(A) 22 (B) 8 (C) 14	NR	NR	NR
Saskin et al,[108] 2015 Turkey	Patients who received isolated CABG and carotid artery interventions for carotid artery stenosis together with CAD, either simultaneous CEA with coronary bypass surgery or staged carotid artery stenting with coronary bypass surgery	Patients with congenital heart disease (atrial septal defect, ventricular septal defect etc.), valvular heart disease, and disease of the aorta who underwent surgery	(A) 71 (C) 31	(A) 64.7 (C) 67.1	(A) 77.5 (C) 77.4	(A) HTN 78.9%, DM 45.1%, smoking 64.8%, HLD 18.3%, PAD 18.3%, COPD 2.8%, three vessel CAD 76.1%, MI history 35.2% (C) HTN 80.6%, DM 77.4%, smoking 61.3%, HLD 58.1%, PAD 22.6%, COPD 25.8%, three-vessel CAD 71%, MI history 16.1%
Takach et al,[109] 1997 USA	Patients with concomitant, severe coronary and carotid artery occlusive disease who underwent coronary revascularization and CEA procedures either in staged or simultaneous sequence.=	NR	(A) 255 (C) 257	(A) 65.6 (C) 64.3	(A) 65.5 (C) 74.7	(A) HTN 66.3%, smoking 29.4%, CHF 11.8%, MI 31.8%, PAD 32.9%, DM 25.9%, COPD 12.9%, CRF 3.5%, obesity 5.5%, HLD 20.8% (C) HTN 66.9%, smoking 42.0%, CHF 10.5%, MI 38.5%, PAD 29.6%, DM 19.8%, COPD 9.7%, CRF 1.9%, obesity 4.7%, HLD 20.2%
Timaran,[113] 2008 USA	Patients who underwent CAS before CABG and combined CEA-CABG	Patients from federal and prison hospitals	(A) 26197 (C) 887	(A) 72 (C) 69	(A) 67 (C) 52.8	(A) HTN 63%, DM 32.4%, chronic lung disease 26.9%, MI 20.4%, CHF 2.7% CRF 6.3% (C) HTN 68.9%, DM 28%, chronic lung disease 28.5%, MI 29.7%, CHF 2.3%, CRF 9.7%
Urschel et al,[110] 1976 USA	Patients with both severe coronary and carotid occlusive disease	N/A	(A) 7 (B) 17 (C) 8	59	84.38	NR

Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) combined (B) CABG first (C) carotid first	Mean age, years	Male sex, %	Comorbidities
Weimar et al,[11] 2017 Europe	Asymptomatic (past 180 days) ICA stenosis ≥80% (following criteria of the European Carotid Surgery Trial, main criterion: in-stenosis peak systolic velocity ≥300 cm/s, corresponding to ≥70% NASCET [North American Symptomatic CEA Trial], carotid artery stenosis treatable with CEA, negative pregnancy test in premenopausal women, written informed consent and full legal capacity, ability of the patient to participate in follow-up examinations	Nonatherosclerotic stenosis (eg, dissection, floating thrombus, fibromuscular dysplasia, tumor, and postradiation), complete occlusion or previous stenting of the carotid artery to be treated, additional higher grade intracranial or intrathoracic stenosis (tandem stenosis), recent (past 180 days) ischemic symptoms ipsilateral to carotid stenosis or occlusion, contralateral carotid occlusion or other known indication for carotid revascularization (apart from scheduled CABG), MI (NSTEMI or STEMI) within the past 7 days (reduced to 48 hours for NSTEMI after the first amendment) or hemodynamically unstable patients, known high risk for cardiogenic embolism requiring anticoagulation (mechanical heart valve, chronic atrial fibrillation [omitted after the first amendment], left ventricular thrombus, left ventricular aneurysm), evidence for intracranial bleeding within the past 90 days, modified Rankin Scale score of >3 or severe aphasia, patients unlikely to survive >1 year because of concomitant diseases, planned combined cardiac valve replacement or any other cardiac surgery beyond CABG (±CEA) during the procedure, major surgery (apart from study procedures) planned within 8 weeks from randomization, and participation in another clinical trial	(A) 65 (B) 62 (Isolated CABG)	(A) 69.7 (B) 69.3	(A) 83.1 (B) 83.9	(A) HTN 89.2%, DM 31.7%, HLD 72.3%, current smoker 23.4% (B) HTN 88.7%, DM 38.7%, HLD 69.4%, current smoker 25.8%
Xiang et al,[111] 2019 China	Patients who underwent carotid revascularization within 90 days before receiving CABG	Intolerance to heparin and antiplatelet drugs, intraluminal carotid artery thrombus, chronic carotid total occlusion, history of ischemic major stroke within 3 months, severe comorbidity in patients not tolerant to percutaneous intervention, any other illness that impeded their ability to provide informed consent, and patients who had a previous open heart surgery	(A) 37 (C) 208	(A) 66.6 (C) 64.7	(A) 78.1 (C) 80.3	(A) Smoking 56.3%, HTN 81.3%, DM 37.5%, hypercholesterolemia 71.9%, COPD 6.3%, CRF 0%, previous stroke 12.5%, previous angina 75%, previous PCI 18.8% (C) Smoking 61.1%, HTN 72.1%, DM 37.5%, hypercholesterolemia 60.1%, COPD 28.8%, CRF 0.5%, previous stroke 18.8%, previous angina: 59.6%, previous PCI: 2.9%

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Supplementary Table II (online only). Continued.

Author, year geographic area	Inclusion criteria	Exclusion criteria	Total No. of patients (A) combined (B) CABG first (C) carotid first	Mean age, years	Male sex, %	Comorbidities
Yang et al,[13] 2016 China	Patients with coronary and carotid artery disease who underwent either hybrid or staged CAS-off-pump CABG	Coagulopathy, brain hemorrhage within 3 months, brain infarction within 2 weeks, allergy to contrast agent, carotid artery occlusion, severe renal function and hepatic function failure	(A) 20 (C) 39	(A) 67.1 (C) 68.3	(A) 80 (C) 82	(A) HTN 75%, DM 40%, hypercholesterolemia 35%, brain infarction history 40%, unstable angina 50% (C) HTN 69% DM 26%, hypercholesterolemia 64%, brain infarction history 31%, unstable angina 56%
Ziada et al,[112] 2005 USA	Patients who require coronary and carotid revascularization who underwent either CS within 90 days before open heart surgery for coronary revascularization or CEA+ open heart surgery	NR	(A) 111 (C) 56	(A) 69 (C) 70	(A) 70.2 (C) 69.6	(A) HTN 81%, DM 51.3%, history of smoking 68.5%, unstable angina pectoris 27%, CRF 14%, TIA/stroke: 23% (C) HTN 87.5%, DM 42.9%, history of smoking 69.2%, unstable angina pectoris 52%, CRF 7%, TIA/stroke: 46%

AAA, Abdominal aortic aneurysm; *AF*, atrial fibrillation; *BMI*, body mass index; *BP*, blood pressure; *CABG*, coronary artery bypass grafting; *CAD*, coronary artery disease; *CAS*, coronary artery stenting; *CEA*, carotid endarterectomy; *CHF*, congestive heart failure; *CKD*, chronic kidney disease; *COPD*, chronic obstructive pulmonary disease; CRF, chronic renal failure; *CT*, computed tomography; *CVA*, cerebrovascular accident; *DM*, diabetes mellitus; *ESRD*, end-stage renal disease; *HbA1c*, hobgoblin A1; *HLD*, hyperlipidemia; *HTN*, hypertension; *ICA*, internal carotid artery; *LDL*, low-density lipoprotein; *LOS*, length of stay; *MI*, myocardial infarction; *NR*, not reported; *NSTEMI*, non-ST segment elevation myocardial infarction; *PAD*, peripheral artery disease; *PCI*, percutaneous coronary intervention; *PVD*, peripheral vascular disease; *STEMI*, ST segment elevation myocardial infarction; *TIA*, transient ischemic attack; *VR*, valve replacement.

Supplementary Table III (online only). Risk of Bias assessment

	Selection		Outcomes					
Author, year	Random sequence generation: (A) Low risk* (B) High risk (C) Unclear	Allocation concealment: (A) Low risk* (B) High risk (C) Unclear	Blinding of participants or personnel: (A) Low risk* (B) High risk (C) Unclear	Blinding of outcome assessment: (A) Low risk* (B) High risk (C) Unclear	Incomplete outcome data: (A) Low risk* (B) High risk (C) Unclear	Reporting bias/selective reporting: (A) Low risk* (B) High risk (C) Unclear	Other Sources of bias: (A) Low risk* (B) High risk (C) Unclear	Overall risk of bias
Question 1: RCTs								
ACST, 2004[5]	A	A	C	A	A	A	A	Low
Kolos et al,[4] 2015	A	A	B	A	A	A	A	Low
Reiff et al, 2019[1]	C	C	B	B	A	A	A	Moderate
Walker et al,[3] 1995	A	A	B	A	A	A	A	Low

	Selection			Comparability	Outcome			
Author, Year	Representativeness of the exposed cohort (A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: (A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: (A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): (A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: (A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self-report (E) No description	Was follow-up long enough for outcomes to occur: (A) Yes* (B) No	Adequacy of follow-up: (A) Complete follow-up- all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) Follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Question 1: Observational studies								
Lin et al,[2] 2016	B	A	A	A	A	B	B	Low
Sato, 2016[15]	A	A	A	A	E	A	B	Low

	Selection		Outcomes					
Author, year	Random sequence generation: (A) Low risk* (B) High risk (C) Unclear	Allocation concealment: (A) Low risk* (B) High risk (C) Unclear	Blinding of participants or personnel: (A) Low risk* (B) High risk (C) Unclear	Blinding of outcome assessment: (A) Low risk* (B) High risk (C) Unclear	Incomplete outcome data: (A) Low risk* (B) High risk (C) Unclear	Reporting bias/selective reporting: (A) Low risk* (B) High risk (C) Unclear	Other sources of bias: (A) Low risk* (B) High risk (C) Unclear	Overall risk of bias
Question 2: RCTs								
Brooks et al,[20] 2001	C	C	C	C	A	C	B	High
Brott et al,[34] 2010	A	A	A	A	B	A	A	Low
Eckstein et al,[21] 2008	A	A	A	C	B	A	A	Moderate
Ederle et al,[24] 2009	A	A	A	A	A	A	A	Low
Hoffman et al,[27] 2008	C	A	A	C	A	A	C	Moderate
ICSS,[19] 2010	A	A	A	A	A	A	A	Low
Mas et al,[28] 2014	A	A	A	A	A	A	A	Low
Naylor,[31] 1998	A	A	B	C	A	A	A	Moderate
Steinbauer et al,[40] 2008	C	C	C	C	A	C	B	High

		Selection			Comparability	Outcome			
Author, year	Study design	Representativeness of the exposed cohort A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self report (E) No description	Was follow-up long enough for outcomes to occur: A) Yes: ≥1 month* (B) No: <1 month	Adequacy of follow-up: A) Complete follow-up - all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Question 3: Observational studies									
Avgerinos et al,[9] 2017	Retrospective cohort	A	A	A	A	B	A	D	Low
Azzini et al,[6] 2016	Cohort	A	A	A	C	B	A	D	Moderate
Barbetta et al,[7] 2014	Retrospective cohort	A	A	A	C	B	A	D	Moderate
Brandl, 2001[41]	Retrospective Cohort	A	A	A	C	B	A	D	Moderate
Hlvacia et al,[10] 2017	Case series	A	A	A	C	B	A	A	Low

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Supplementary Table III (online only). Continued.

		Selection			Comparability	Outcome			
Author, year	Study design	Representativeness of the exposed cohort A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self report (E) No description	Was follow-up long enough for outcomes to occur: A) Yes: ≥1 month* (B) No: <1 month	Adequacy of follow-up: A) Complete follow-up - all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Mihindu et al,[42] 2019	Retrospective cohort	A	A	A	C	B	B	D	Moderate
Tanious et al,[8] 2018	Retrospective cohort	A	A	A	A	B	A	D	Low

	Selection		Outcomes					
Author, Year	Random sequence generation: (A) Low risk* (B) High risk (C) Unclear	Allocation concealment: (A) Low risk* (B) High risk (C) Unclear	Blinding of participants or personnel: (A) Low risk* (B) High risk (C) Unclear	Blinding of outcome assessment: (A) Low risk* (B) High risk (C) Unclear	Incomplete outcome data: (A) Low risk* (B) High risk (C) Unclear	Reporting bias/selective reporting: A) Low risk* (B) High risk (C) Unclear	Other sources of bias: A) Low risk* (B) High risk (C) Unclear	Overall risk of bias
Question 3: RCTs								
Welsh et al,[43] 2004	C	C	B	C	A	A	A	Moderate

	Selection			Comparability	Outcome			
Author, year	Representativeness of the exposed cohort (A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: (A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: (A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: (A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self report (E) No description	Was follow-up long enough for outcomes to occur: (A) Yes: ≥6 months* (B) No: <6 months	Adequacy of follow-up: (A) Complete follow-up - all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) Follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Question 4: Observational studies								
Ahn et al,[46] 1991	A	N/A	A	N/A	B	A	A	Low
Aiello et al,[47] 2012	B	N/A	C	N/A	E	Unclear	A	High
Anastasiadis et al,[48] 2009	C	N/A	A	N/A	C	N/A	N/A	High
Ascher et al,[49] 2001	A	N/A	A	N/A	C	N/A	N/A	Moderate
Bae et al,[50] 2006	A	N/A	A	N/A	C	N/A	N/A	Moderate
Berens et al,[44] 1992	A	A	B	C	C	A	A	Low
Bishara et al,[51] 2008	A	N/A	A	N/A	C	N/A	N/A	Moderate
Cheng et al,[53] 2015	A	N/A	A	N/A	B	A	A	Low
Cheng et al,[52] 1999	A	N/A	A	N/A	B	A	A	Low
Choo,[54] 2017	B	N/A	C	N/A	A	Unclear	A	Moderate
Chun et al,[55] 2014	A	N/A	A	N/A	B	A	A	Low
Cornily et al,[56] 2011	A	N/A	A	N/A	B	N/A	N/A	Moderate
de Virgilio et al,[57] 1997	B	N/A	C	N/A	A	Unclear	A	Moderate
Dharmasaroja et al,[58] 2010	A	N/A	A	N/A	C	N/A	N/A	Moderate
Drohomirecka et al,[59] 2010	A	N/A	A	N/A	B	N/A	N/A	Moderate
Fassiadis et al,[60] 2008	C	N/A	A	N/A	C	N/A	N/A	High
Fowl et al,[61] 1991	A	N/A	A	N/A	B	Unclear	D	Moderate
Gentile,[62] 1995	B	N/A	C	N/A	C	Unclear	A	Moderate
Helfre et al,[63] 2017	A	N/A	C	N/A	E	B	A	High

Supplementary Table III (online only). Continued.

	Selection			Comparability	Outcome			
Author, year	Representativeness of the exposed cohort (A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: (A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: (A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: (A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self report (E) No description	Was follow-up long enough for outcomes to occur: (A) Yes: ≥6 months* (B) No: <6 months	Adequacy of follow-up: (A) Complete follow-up - all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) Follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Hill et al,[64] 1999	A	N/A	A	N/A	C	N/A	N/A	Moderate
House,[65] 1999	A	N/A	A	N/A	B	Unclear	A	Moderate
Ignatiev,[66] 2012	A	N/A	A	N/A	C	N/A	N/A	High
Jackson et al,[67] 1985	A	N/A	C	N/A	C	A	A	Moderate
Kaul et al,[68] 2017	A	N/A	A	N/A	B	A	A	Low
Kawarada et al,[69] 2003	A	N/A	C	N/A	C	Unclear	A	Moderate
Klop et al,[70] 1991	A	N/A	A	N/A	B	Unclear	D	Moderate
Kurvers et al,[71] 2003	A	N/A	A	N/A	B	Unclear	D	Moderate
Lara,[72] 2015	B	N/A	C	N/A	E	A	A	Moderate
Lin et al,[73] 2012	B	N/A	A	N/A	B	B	A	Moderate
Lin et al,[45] 2016	A	A	A	C	B	B	A	Low
Mackaay et al,[74] 1995	A	N/A	B	N/A	C	Unclear	A	Moderate
Marek et al,[75] 1996	B	N/A	B	N/A	C	Unclear	A	Moderate
Miralles et al,[76] 1998	A	N/A	C	N/A	B	A	A	Moderate
Miura,[77] 2010	B	N/A	C	N/A	E	Unclear	A	High
Moraca et al,[78] 2012	B	N/A	C	N/A	E	Unclear	A	High
Narayan et al,[79] 2017	A	N/A	C	N/A	E	B	A	High
Pilcher et al,[80] 2000	A	N/A	A	N/A	C	N/A	N/A	Moderate
Planas-Ballvé et al,[81] 2019	A	N/A	A	N/A	B	A	A	Low
Posacioglu et al,[7] 2001	A	N/A	C	N/A	C	A	A	Moderate
Rockman et al,[83] 2004	A	N/A	A	N/A	C	N/A	N/A	Moderate
Sayed et al,[84] 2016	A	N/A	A	N/A	C	Unclear	A	Moderate
Stephens et al,[85] 2010	B	N/A	C	N/A	E	Unclear	A	High
Sutthapas et al,[86] 2012	B	N/A	C	N/A	E	Unclear	A	High
Valentine et al,[87] 1997	B	N/A	A	N/A	B	A	A	Low

(Continued on next page)

Supplementary Table III (online only). Continued.

	Selection			Comparability	Outcome			
Author, year	Representativeness of the exposed cohort (A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: (A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: (A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: (A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self report (E) No description	Was follow-up long enough for outcomes to occur: (A) Yes: ≥6 months* (B) No: <6 months	Adequacy of follow-up: (A) Complete follow-up - all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) Follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Wanamaker et al,[88] 2012	B	N/A	A	N/A	B	B	A	Moderate
Yamamoto et al,[89] 2006	A	N/A	B	N/A	C	N/A	N/A	Moderate
Yun et al,[90] 2010	A	N/A	A	N/A	B	N/A	N/A	Moderate

	Selection		Outcomes					
Author, year	Random sequence generation: (A) Low risk* (B) High Risk (C) Unclear	Allocation concealment: (A) Low risk* (B) High risk (C) Unclear	Blinding of participants or personnel: (A) Low risk* (B) High risk (C) Unclear	Blinding of outcome assessment: (A) Low risk* (B) High risk (C) Unclear	Incomplete outcome data: (A) Low risk* (B) High Risk (C) Unclear	Reporting bias/selective reporting: (A) Low risk* (B) High risk (C) Unclear	Other sources of bias: (A) Low risk* (B) High risk (C) Unclear	Overall risk of bias
Question 5: RCTs								
Illuminati et al,[12] 2011	A	A	B	C	A	A	A	Moderate
Weimar et al,[11] 2017	A	A	B	A	A	A	A	Low

		Selection			Comparability	Outcome			
Author, year	Study design	Representativeness of the exposed cohort (A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: (A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: (A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: (A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self-report (E) No description	Was follow-up long enough for outcomes to occur: A) Yes: ≥6 months * (B) No: <6 months	Adequacy of follow-up: (A) Complete follow-up - all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) Follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Question 5: Observational studies									
Abbasi et al,[91] 2008	Cohort	A	A	A	A	B	B	A	Low
Bernhard,[92] 1972	Case series	A	A	C	C	B	A	D	Moderate
Brow et al,[93] 1999	Retrospective cohort	B	A	A	C	B	A	B	Low
Carrel et al,[94] 1992	Retrospective cohort	A	A	C	C	E	A	C	Moderate
Chiappini et al,[95] 2005	Retrospective cohort	A	A	C	A	D	A	B	Moderate
Faggioli et al,[96] 1990	Case series	A	A	A	C	B	B	D	Moderate
Feldman et al,[97] 2017	Retrospective cohort	B	A	A	A	B	B	A	Low
Giangola et al,[98] 1996	Retrospective cohort	A	A	B	B	B	B	A	Low
Hempe et al,[99] 2018	Retrospective cohort	B	A	A	A	B	B	A	Low
Hertzer et al,[100] 1978	Case series	A	A	A	A	B	B	D	Moderate

Supplementary Table III (online only). Continued.

		Selection			Comparability	Outcome			
Author, year	Study design	Representativeness of the exposed cohort (A) Truly representative* (B) Somewhat representative* (C) No description of the derivation of the cohort	Selection of the nonexposed cohort: (A) Drawn from the same community as the exposed cohort* (B) Drawn from general population (matched for important criteria)* (C) No description of the derivation of the nonexposed cohort	Ascertainment of exposure: (A) Secure record* (B) written self-report* (C) No description	Comparability of cohorts on the basis of the design or analysis (matching/confounder adjustment): A) Study controls for age and sex* (B) Study controls for BMI and comorbidities* (C) No description	Assessment of outcome: (A) Independent blind assessment* (B) Record linkage* (C) Standard procedure well described* (D) Self-report (E) No description	Was follow-up long enough for outcomes to occur: A) Yes: ≥6 months * (B) No: <6 months	Adequacy of follow-up: (A) Complete follow-up - all patients accounted for* (B) Patients lost to follow-up unlikely to introduce bias -small number lost- >80% follow-up, or description of those lost* (C) Follow-up rate <80% and no description of those lost (D) No statement	Overall risk of bias
Hudorovic,[101] 2006	Retrospective cohort	A	A	A	A	B	A	A	Low
Iyem et al,[102] 2009	Retrospective cohort	B	A	C	A	B	B	A	Moderate
Kovacevic et al,[103] 2012	Retrospective cohort	A	A	A	C	B	B	D	Moderate
Newman et al,[14] 1987	Case series	A	A	A	C	B	A	D	Moderate
Oz et al,[104] 2016	Prospective cohort	A	A	B	A	B	A	A	Low
Peric et al,[105] 1997	Retrospective cohort	A	A	C	A	E	B	A	Moderate
Rosenthal et al,[107] 1984	Retrospective cohort	A	A	C	C	E	B	A	Moderate
Saskin, 2015[108]	Retrospective cohort	A	A	A	A	B	A	A	Low
Takach et al,[109] 1997	Retrospective cohort	A	A	A	C	B	B	A	Moderate
Timaran,[113] 2008	Cross-sectional	A	A	A	C	B	B	A	Moderate
Urschel et al,[110] 1976	Case series	A	A	C	C	B	B	D	Moderate
Xiang et al,[111] 2019	Retrospective cohort	B	A	C	A	C	A	A	Low
Yang et al,[13] 2016	Prospective cohort	A	A	C	A	C	A	A	Low
Ziada, 2005[112]	Retrospective cohort	B	A	A	C	B	B	A	Moderate

BMI, Body mass index; *N/A*, not applicable.

APPENDIX (online only).

Actual Search Strategies

Question 1: Medical management vs carotid intervention in asymptomatic patients

Database(s): Embase 1988 to 2019 Week 33, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations 1996 to August 22, 2019, EBM Reviews - Cochrane Central Register of Controlled Trials July 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to August 21, 2019.

Search Strategy:

1	asymptomatic diseases/	10597
2	asymptomatic.ti,ab,hw,kw.	336353
3	1 or 2	336353
4	exp Carotid Stenosis/	46337
5	carotid artery obstruction/	25245
6	carotid artery disease/	21918
7	(carotid adj1 (arter* or stenosis)).ti,ab,hw,kw.	213263
8	or/4-7	213263
9	3 and 8	16015
10	exp endarterectomy/	34806
11	(carotid adj2 endarterectom*).ti,ab,hw,kw.	31347
12	10 or 11	39920
13	carotid artery stent/	1088
14	exp Carotid Arteries/	112308
15	exp Stents/	240571
16	(carotid adj2 stent*).ti,ab,hw,kw.	14474
17	14 and 15	8431
18	13 or 16 or 17	19587
19	exp *angioplasty/	70066
20	carotid angioplasty/	639
21	"carotid angioplast*".ti,ab,hw,kw.	2964
22	or/19-21	71434
23	("best medical therap*" or "no surgery").ti,ab,hw,kw.	175005
24	((conservative or medical) adj (manag* or treat* or therap*)).ti,ab,hw,kw.	359760
25	(statin* or antiplatelet*).ti.	59470
26	Platelet Aggregation Inhibitors/	74332
27	(platelet* adj1 aggregat* adj1 inhibit*).ti,ab,hw,kw.	43743
28	Antihypertensive Agents/	129542
29	("blood pressure" adj3 lowering).ti,ab,hw,kw.	19043
30	Hypolipidemic Agents/	41120
31	or/23-30	819988
32	12 or 18 or 22 or 31	922243
33	9 and 32	8697
34	limit 33 to (english language and yr="2016 -Current") [Limit not valid in CDSR; records were retained]	1551
35	34 not ((exp animals/ or exp nonhuman/) not exp humans/)	1546
36	35 not ((case* adj3 report*).ti,ab,hw,kw. or case report/)	1389
37	35 and ((clinical or intervention* or evaluation or validation or cohort or comparative or prospective* or retrospective or "cross section*") adj4 (trial* or stud*)).ti,ab,hw,kw.	964
38	limit 35 to (clinical study or clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or observational study or pragmatic clinical trial or randomized controlled trial or systematic reviews or validation studies) [Limit not valid in Embase,CCTR,CDSR; records were retained]	299
39	or/36-38	1413
40	remove duplicates from 39	978

SCOPUS

1	TITLE-ABS-KEY (asymptomatic)
2	TITLE-ABS-KEY ((carotid W/1 (obstruct* OR stenosis)))
3	#1 and #2
4	TITLE-ABS-KEY ((carotid W/2 endarterectom*))
5	TITLE-ABS-KEY ((carotid W/2 stent*))
6	TITLE-ABS-KEY ("carotid angioplast*")
7	#4 or #5 or #6
8	#3 and #7
9	TITLE-ABS-KEY (("best medical therap*" OR "no surgery"))
10	TITLE-ABS-KEY (((conservative OR medical) W/1 (manag* OR treat* OR therap*)))
11	TITLE ((statin* OR antiplatelet*))
12	TITLE ((platelet* W/1 aggregat* W/1 inhibit*))
13	TITLE (("blood pressure" W/3 lowering))
14	#9 or #10 or #11 or #12 or #13
15	#3 and #14
16	#8 or #15
17	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
18	#16 and not ##17
19	DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh) OR DOCTYPE(ch)
20	#18 and not #19
21	LANGUAGE(english)
22	#20 and #21
23	PUBYEAR aft 2015
24	#22 and #23

Question 2: CEA vs CAS in symptomatic patients

Ovid. Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials May 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 26, 2019, Embase 1974 to 2019 July 02, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to July 02, 2019.

Search Strategy:

#	Searches	Results
1	exp Carotid Arteries/su [Surgery]	11536
2	exp Carotid Artery Diseases/su [Surgery]	27830
3	("arteria carotis" or carotid).ti,ab,hw,kw.	321971
4	1 or 2 or 3	323628
5	exp Endarterectomy, Carotid/	26276
6	exp Stents/	241364
7	exp Angioplasty/	151689
8	(angioplast* or endarterectom* or "endoluminal repair*" or endovascular* or stent*).ti,ab,hw,kw.	538781
9	5 or 6 or 7 or 8	540110
10	4 and 9	68617
11	exp Randomized Controlled Trial/	1042749
12	exp triple blind procedure/	218
13	exp Double-Blind Method/	445917
14	exp Single-Blind Method/	81911
15	exp latin square design/	363
16	exp Placebos/	394848
17	exp Placebo Effect/	11474
18	((randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (random* adj1 allocat*) or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo*).mp,pt.	2864915
19	or/11-18	2865181
20	10 and 19	5123
21	(exp animals/ or exp nonhuman/) not exp humans/	10729834
22	((alpaca or alpacas or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or carp or cats or cattle or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or lagomorph or lagomorphs or lamb or lambs or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or nematode or nematodes or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or worm or worms or xenopus or "zebra fish" or zebrafish) not (human or humans or patient or patients)).ti,ab,hw,kw.	9272186
23	20 not (21 or 22)	4996
24	limit 23 to yr="2011 -Current"	2446

Continued.

#	Searches	Results
25	limit 24 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	155
26	from 25 keep 1-7	7
27	(24 not 25) or 26	2298
28	remove duplicates from 27	1589

Scopus.

1 TITLE-ABS-KEY("arteria carotis" OR carotid)

2 TITLE-ABS-KEY(angioplast* OR endarterectom* OR "endoluminal repair*" OR endovascular* OR stent*)

3 TITLE-ABS-KEY((randomized W/3 study) OR (randomized W/3 trial) OR (randomised W/3 study) OR (randomised W/3 trial) OR "pragmatic clinical trial" OR (random* W/1 allocat*) OR (doubl* W/1 blind*) OR (doubl* W/1 mask*) OR (singl* W/1 blind*) OR (singl* W/1 mask*) OR (tripl* W/1 blind*) OR (tripl* W/1 mask*) OR (trebl* W/1 blind*) OR (trebl* W/1 mask*) OR "latin square" OR placebo* OR nocebo*)

4 PUBYEAR AFT 2010

5 1 and 2 and 3 and 4

6 TITLE-ABS-KEY((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) AND NOT (human OR humans or patient or patients))

7 5 and not 6

8 DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

9 7 and not 8

10 INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)

11 9 and not 10

Question 3: Timing of intervention in stroke

Database(s): Embase 1988 to 2019 Week 33, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations 1996 to August 20, 2019, EBM Reviews - Cochrane Central Register of Controlled Trials July 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to August 21, 2019.

Search Strategy:

1	("Carotid Artery, External"/ and stents/) or Carotid Stenosis/surgery or exp carotid artery obstruction/su or "Endarterectomy, Carotid"/ or exp Carotid Artery, External/su	28675
2	((procedure or stent* or surg* or endarterectom* or CEA or CAS or revasculari* or intervention*) adj3 (carotid or stroke or tia or "ischemic attack" or "brain infarct*" or "ischaemic attack")).ti,ab,hw,kw.	64373
3	(procedure or stent* or surg* or endarterectom* or CEA or CAS or revasculari* or intervention*).ti. and exp cerebrovascular accident/	23898
4	(procedure or stent* or surg* or endarterectom* or CEA or CAS or revasculari* or intervention*).ti. and (cereb* adj (accident or arrest or failure or injur* or insufficien* or insult* or attack or appolex*)).ti,ab,hw,kw.	19488
5	or/1-4	83123

(Continued on next page)

Continued.

6	exp "Early Medical Intervention"/ or "Time-to-Treatment"/ or exp "Time Factors"/ or (early or earlier or timing or urgent* or immediat*).ti.	1602429
7	5 and 6	6511
8	limit 7 to (english language and yr="2017 -Current") [Limit not valid in CDSR; records were retained]	1811
9	8 not ((exp animals/ or exp nonhuman/) not exp humans/)	1796
10	9 not ((case* adj3 report*).ti,ab,hw,kw. or case report/)	1715
11	9 and ((clinical or intervention* or evaluation or validation or cohort or comparative or prospective* or retrospective or "cross section*") adj4 (trial* or stud*)).ti,ab,hw,kw.	1367
12	limit 9 to (clinical study or clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or observational study or pragmatic clinical trial or randomized controlled trial or systematic reviews or validation studies) [Limit not valid in Embase,CCTR,CDSR; records were retained]	742
13	10 or 11 or 12	1740
14	remove duplicates from 13	1400

SCOPUS

1	TITLE-ABS-KEY (((procedure OR stent* OR surg* OR endarterectom* OR cea OR cas OR revasculari* OR intervention*) W/3 (carotid OR stroke OR tia OR "ischemic attack" OR "brain infarct*" OR "ischaemic attack")))
2	TITLE ((early OR earlier OR timing OR urgent* OR immediat*))
3	#1 and #2
4	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
5	#3 and not #4
6	PUBYEAR aft 2015
7	#5 and #6

Question 4: Screening high risk patients

Ovid. Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials May 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 26, 2019, Embase 1974 to 2019 July 02, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to July 02, 2019.

Search Strategy:

#	Searches	Results
1	exp Carotid Arteries/dg [Diagnostic Imaging]	16743
2	exp Carotid Artery Diseases/di, dg [Diagnosis, Diagnostic Imaging]	21616
3	("arteria carotis" or carotid).ti,ab,hw,kw.	321971
4	1 or 2 or 3	323046
5	exp Ultrasonography, Doppler, Duplex/	28503
6	("carotid duplex" or "color doppler ultraso*" or "doppler color ultraso*" or "duplex doppler ultraso*" or "duplex ultraso*").ti,ab,hw,kw.	28981
7	5 or 6	50717
8	4 and 7	8210
9	exp Mass Screening/	350627
10	screen*.ti,ab,hw,kw.	2056301
11	9 or 10	2065959
12	8 and 11	789
13	(exp animals/ or exp nonhuman/) not exp humans/	10729834
14	((alpaca or alpacas or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or carp or cats or cattle or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or lagomorph or lagomorphs or lamb or lambs or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or nematode or nematodes or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or worm or worms or xenopus or "zebra fish" or zebrafish) not (human or humans or patient or patients)).ti,ab,hw,kw.	9272186
15	12 not (13 or 14)	785
16	limit 15 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	6
17	15 not 16	779
18	remove duplicates from 17	534

Scopus.

1 TITLE-ABS-KEY("arteria carotis" or carotid)

2 TITLE-ABS-KEY("carotid duplex" OR "color doppler ultraso*" OR "doppler color ultraso*" OR "duplex doppler ultraso*" OR "duplex ultraso*")

3 TITLE-ABS-KEY(screen*)

4 1 and 2 and 3

5 TITLE-ABS-KEY((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) AND NOT (human OR humans or patient or patients))

6 4 and not 5

7 DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

8 6 and not 7

9 INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)

10 8 and not 9

Question 5: Optimal sequence for intervention in patients with combined carotid and coronary disease

Ovid. Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials May 2019, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 26, 2019, Embase 1974 to 2019 July 02, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to July 02, 2019.

Search Strategy:

#	Searches	Results
1	exp Carotid Arteries/	139002
2	exp Carotid Artery Diseases/dh, dt, rt, su, th [Diet Therapy, Drug Therapy, Radiotherapy, Surgery, Therapy]	19840
3	("arteria carotis" or carotid).ti,ab,hw,kw.	321971
4	1 or 2 or 3	322854
5	exp Coronary Disease/	527641
6	exp ischemic heart disease/	1072420
7	exp heart atrium fibrillation/	56268
8	exp Atrial Fibrillation/	110853

Continued.

#	Searches	Results
9	("acute coronary artery thrombos*" or "acute coronary syndrome*" or "acute heart muscle ischaemia*" or "acute heart muscle ischemia*" or "ampulla cardiomyopath*" or angina or "anginal attack*" or "apical ballooning" or "arteria coronaria ostium stenos*" or "atrial fibrillation*" or "atrial infarct*" or "atrium fibrillation*" or "atrium infarct*" or "auricular fibrilation*" or "auricular fibrillation*" or "auricular infarct*" or "broken heart syndrome*" or "cardiac allograft vasculopath*" or "cardiac atrial fibrillation*" or "cardiac atrial infarct*" or "cardiac atrium fibrillation*" or "cardiac atrium infarct*" or "cardiac infarct*" or "cardiac ischaemia*" or "cardiac ischemia*" or "cardiac muscle ischaemia*" or "cardiac muscle ischemia*" or "cardiac muscle necros*" or "cardiac necros*" or "cardial infarct*" or "Coronary Aneurysm*" or "coronary arterial obstruction*" or "coronary arterial thrombos*" or "coronary arterioscleros*" or "coronary artery aneurysm*" or "coronary artery anomaly" or "coronary artery atherosclerosis*" or "coronary artery calcification*" or "coronary artery constriction*" or "Coronary Artery Disease" or "coronary artery dissection*" or "coronary artery insufficienc*" or "coronary artery ischaemia*" or "coronary artery ischemia*" or "coronary artery obstruction*" or "coronary artery occlusion*" or "coronary artery occlusive disease*" or "coronary artery perforation*" or "coronary artery scleros*" or "coronary artery stenos*" or "coronary artery thrombos*" or "coronary artery vasoconstriction*" or "coronary atherosclerosis*" or "coronary bifurcation lesion*" or "coronary cardioscleros*" or "coronary constriction*" or "Coronary Disease" or "coronary heart disease*" or "coronary insufficienc*" or "coronary ischaemia*" or "coronary ischemia*" or "coronary obstruction*" or "Coronary Occlusion" or "coronary occlusive disease*" or "coronary ostial stenos*" or "coronary ostium obstruction*" or "Coronary Restenos*" or "coronary scleros*" or "Coronary Stenos*" or "coronary subclavian steal syndrome*" or "coronary syndrome*" or "Coronary Thrombos*" or "coronary vasoconstriction*" or "Coronary Vasospasm" or "Coronary-Subclavian Steal Syndrome*" or "Dressler syndrome*" or "Dresslers syndrome*" or "effort angina pectoris" or "heart anoxia" or "heart arterioscleros*" or "heart atherosclerosis*" or "heart atrial fibrillation*" or "heart atrial infarct*" or "heart atrium fibrillation*" or "heart atrium infarct*" or "heart attack*" or "heart coronary scleros*" or "heart fiber necros*" or "heart fibrillation atrium" or "heart hypoxia" or "heart infarct" or "heart infarct*" or "heart ischaemia*" or "heart ischaemic arrest*" or "heart ischaemic attack*" or "heart ischaemic time" or "heart ischemia*" or "heart ischemic arrest*" or "heart ischemic attack*" or "heart ischemic time" or "heart left ventricle infarct*" or "heart micro infarct*" or "heart muscle cell necros*" or "heart muscle hibernation*" or "heart muscle hypoxia" or "heart muscle infarct*" or "heart muscle ischaemia*" or "heart muscle ischemia*" or "heart muscle necros*" or "heart necros*" or "heart postinfarction syndrome*" or "heart reinfarct*" or "heart right ventricle infarct*" or "heart transient ischaemic attack*" or "heart transient ischemic attack*" or "heart ventricle infarct*" or "hypoxic heart" or "ischaemia heart disease*" or "ischaemic cardiac disease*" or "ischaemic cardial disease*" or "ischaemic cardiomyopath*" or "ischaemic cardiopath*" or "ischaemic heart" or "ischaemic heart arrest*" or "ischaemic heart disease*" or "ischaemic myocardium" or "ischaemic time" or "ischemia heart disease*" or "ischemic cardiac disease*" or "ischemic cardial disease*" or "ischemic cardiomyopath*" or "ischemic cardiopath*" or "ischemic heart" or "ischemic heart arrest*" or "ischemic heart disease*" or "ischemic myocardium" or "ischemic time" or "Kounis syndrome*" or "left ventricular apical ballooning" or "left ventricular apical ballooning syndrome*" or "left ventricular ballooning" or "myocardial anoxia" or "myocardial fiber necros*" or "myocardial hibernation*" or "myocardial hypoxia" or "myocardial infarct" or "myocardial infarct*" or "myocardial ischaemia*" or "myocardial ischemia*" or "myocardial necros*" or "myocardial reinfarct*" or "myocardium hypoxia*" or "myocardium infarct*" or "myocardium ischaemia*" or "myocardium ischemia*" or "myocardium necros*" or "no reflow phenomenon" or "painless cardiac ischaemia*" or "painless cardiac ischemia*" or "painless heart ischaemia*" or "painless heart ischemia*" or "painless ischaemia*" or "painless ischemia*" or "painless myocardial ischaemia*" or "painless myocardial ischemia*" or "paroxysmal atrial fibrillation*" or "post heart infarction syndrome*" or "post infarctation syndrome*" or "post infarction syndrome*" or "postinfarction syndrome*" or "postmyocard infarction syndrome*" or "postmyocardial infarction syndrome*" or "postprandial angina pectoris" or "premonitory infarction sign" or "second heart attack*" or "silent cardiac ischaemia*" or "silent cardiac ischemia*" or "silent heart ischaemia*" or "silent heart ischemia*" or "silent ischaemia*" or "silent ischemia*" or "silent myocardial ischaemia*" or "silent myocardial ischemia*" or stenocardia or "stress cardiomyopath*" or "stress induced cardiomyopath*" or "subendocardial infarct*" or "subendocardial ischaemia*" or "subendocardial ischemia*" or takotsubo or "tako-tsubo" or "takotsubo cardiomyopath*" or "takotsubo syndrome*" or "transient left ventricular apical ballooning" or "transient left ventricular apical ballooning syndrome*" or "transmural cardiac infarct*" or "transmural heart infarct*").ti,ab,hw,kw.	1648376
10	5 or 6 or 7 or 8 or 9	1660341
11	4 and 10	35844
12	exp Coronary Artery Bypass/	126970
13	("aorta coronary artery bypass*" or "aorta coronary bypass graft*" or "aorta coronary bypass*" or "aorta coronary vein bypass graft*" or "aorta coronary vein bypass*" or "aorta coronary vein shunt" or "aortic coronary artery bypass*" or "aortic coronary bypass*" or "aorticocoronary anastomosis" or "aorto coronary artery bypass*" or "aorto coronary bypass graft*" or "aorto coronary vein bypass*" or "aortocoronary anastomosis" or "aortocoronary artery bypass graft*" or "aortocoronary artery bypass*" or "aortocoronary bypass graft*" or "aortocoronary bypass*" or "aortocoronary shunt" or "aortocoronary vein bypass graft*" or "aortocoronary vein bypass*" or "aortocoronary venous bypass graft*" or "aortocoronary venous bypass*" or CABG or "coronary artery bypass grafting" or "coronary artery bypass*" or "coronary artery graft*" or "coronary bypass graft*" or "coronary bypass grafting" or "coronary bypass*" or "coronary vein bypass graft*" or "coronary venous bypass graft*" or "coronary-internal mammary artery anastomos*" or "internal mammary-coronary artery anastomos*").ti,ab,hw,kw.	186583

(Continued on next page)

Continued.

#	Searches	Results
14	12 or 13	186583
15	11 and 14	3194
16	exp meta analysis/	268673
17	exp Meta-Analysis as Topic/	58503
18	exp "systematic review"/	319167
19	exp controlled study/	6918011
20	exp Randomized Controlled Trial/	1042749
21	exp triple blind procedure/	218
22	exp Double-Blind Method/	445917
23	exp Single-Blind Method/	81911
24	exp latin square design/	363
25	exp Placebos/	394848
26	exp Placebo Effect/	11474
27	exp comparative study/	3161249
28	exp Cross-Sectional Studies/	608046
29	exp Cohort Studies/	2495260
30	exp longitudinal study/	385839
31	exp retrospective study/	1554990
32	exp prospective study/	1124740
33	exp population research/	99621
34	exp observational study/	235258
35	clinical study/	157470
36	exp Evaluation Studies/	303929
37	exp quantitative study/	38977
38	exp validation studies/	173402
39	exp quasi experimental study/	6285
40	in vivo study/	352164
41	exp panel study/	892
42	exp replication study/	2045
43	exp Feasibility Studies/	180401
44	exp correlational study/	37270
45	exp case-control studies/	1175433
46	exp confidence interval/	165843
47	exp regression analysis/	847587
48	exp proportional hazards model/	164667

Continued.

#	Searches	Results
49	((meta adj analys*) or metaanalys* or (systematic* adj3 review*) or (control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (random* adj1 allocat*) or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* adj2 study) or (intervention* adj2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") adj3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or (population adj3 (stud* or survey* or analys* or research)) or "concurrent study" or "concurrent survey" or "concurrent analysis" or (("follow-up" or followup) adj (stud* or survey or analysis)) or ((observation or observational) adj (study or survey or analysis)) or "case study" or "case series" or "clinical series" or "case studies" or "clinical study" or "clinical trial" or (("phase 0" or "phase 1" or "phase I" or "phase 2" or "phase II" or "phase 3" or "phase III" or "phase 4" or "phase IV") adj5 (trial or study)) or "evaluation study" or "evaluation survey" or "evaluation analysis" or "quantitative study" or "quantitative analys*" or "numerical study" or "validation study" or "validation survey" or "validation analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "in vivo study" or "in vivo analysis" or "panel study" or "panel survey" or "panel analysis" or "replication study" or "replication analysis " or "replication trial" or "feasibility study" or "feasibility analysis" or ((correlation* adj2 study) or (correlation* adj2 analys*)) or "case control study" or "case base study" or "case referent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or "odds ratio" or "confidence interval" or "regression analysis" or "least square" or "least squares" or (hazard* adj (model* or analys* or regression or ratio or ratios)) or "Cox model" or "Cox multivariate analyses" or "Cox multivariate analysis" or "Cox regression" or "Cox survival analyses" or "Cox survival analysis" or "Cox survival model" or "change analysis" or ((study or trial or random* or control*) and compar*)).mp,pt.	22899279
50	or/16-49	23290983
51	15 and 50	1977
52	(exp animals/ or exp nonhuman/) not exp humans/	10729834
53	((alpaca or alpacas or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or carp or cats or cattle or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or lagomorph or lagomorphs or lamb or lambs or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or nematode or nematodes or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or worm or worms or xenopus or "zebra fish" or zebrafish) not (human or humans or patient or patients)).ti,ab,hw,kw.	9272186
54	51 not (52 or 53)	1952
55	limit 54 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	26
56	from 55 keep 1-2	2
57	(54 not 55) or 56	1928
58	remove duplicates from 57	1434

Scopus.

1 TITLE-ABS-KEY("arteria carotis" or carotid)

2 TITLE-ABS-KEY("acute coronary artery thrombos*" or "acute coronary syndrome*" or "acute heart muscle ischaemia*" or "acute heart muscle ischemia*" or "ampulla cardiomyopath*" or angina or "anginal attack*" or "apical ballooning" or "arteria coronaria ostium stenos*" or "atrial fibrillation*" or "atrial infarct*" or "atrium fibrillation*" or "atrium infarct*" or "auricular fibrilation*" or "auricular fibrillation*" or "auricular infarct*" or "broken heart syndrome*" or "cardiac allograft vasculopath*" or "cardiac atrial fibrillation*" or "cardiac atrial infarct*" or "cardiac atrium fibrillation*" or "cardiac atrium infarct*" or "cardiac infarct*" or "cardiac ischaemia*" or "cardiac ischemia*" or "cardiac muscle ischaemia*" or "cardiac muscle ischemia*" or "cardiac muscle necros*" or "cardiac necros*" or "cardial infarct*" or "Coronary Aneurysm*" or "coronary arterial obstruction*" or "coronary arterial thrombos*" or "coronary arterioscleros*" or "coronary artery aneurysm*" or "coronary artery anomaly" or "coronary artery atherosclerosis*" or "coronary artery calcification*" or "coronary artery constriction*" or "Coronary Artery Disease" or "coronary artery dissection*" or "coronary artery insufficienc*" or "coronary artery ischaemia*" or "coronary artery ischemia*" or "coronary artery obstruction*" or "coronary artery occlusion*" or "coronary artery occlusive disease*" or "coronary artery perforation*" or "coronary artery scleros*" or "coronary artery stenos*" or "coronary artery thrombos*" or "coronary artery vasoconstriction*" or "coronary atherosclerosis*" or "coronary bifurcation lesion*" or "coronary cardioscleros*" or "coronary constriction*" or "Coronary Disease" or "coronary heart disease*" or "coronary insufficienc*" or "coronary ischaemia*" or "coronary ischemia*" or "coronary obstruction*" or "Coronary Occlusion" or "coronary occlusive disease*" or "coronary ostial stenos*" or "coronary ostium obstruction*" or "Coronary Restenos*" or "coronary scleros*" or "Coronary Stenos*" or "coronary subclavian steal syndrome*" or "coronary syndrome*" or "Coronary Thrombos*" or "coronary vasoconstriction*" or "Coronary Vasospasm" or "Coronary-Subclavian Steal Syndrome*" or "Dressler syndrome*" or "Dresslers syndrome*" or "effort angina pectoris" or "heart anoxia" or "heart arterioscleros*" or "heart atherosclerosis*" or "heart atrial fibrillation*" or "heart atrial infarct*" or "heart atrium fibrillation*" or "heart atrium infarct*" or "heart attack*" or "heart coronary scleros*" or "heart fiber necros*" or "heart fibrillation atrium" or "heart hypoxia" or "heart infarct" or "heart infarct*" or "heart ischaemia*" or "heart ischaemic arrest*" or "heart ischaemic attack*" or "heart ischaemic time" or "heart ischemia*" or "heart ischemic arrest*" or "heart ischemic attack*" or "heart ischemic time" or "heart left ventricle infarct*" or "heart micro infarct*" or "heart muscle cell necros*" or "heart muscle hibernation*" or "heart muscle hypoxia" or "heart muscle infarct*" or "heart muscle ischaemia*" or "heart muscle ischemia*" or "heart muscle necros*" or "heart necros*" or "heart postinfarction syndrome*" or "heart reinfarct*" or "heart right ventricle infarct*" or "heart transient ischaemic attack*" or "heart transient ischemic attack*" or "heart ventricle infarct*" or "hypoxic heart" or "ischaemia heart disease*" or "ischaemic cardiac disease*" or "ischaemic cardial disease*" or "ischaemic cardiomyopath*" or "ischaemic cardiopath*" or "ischaemic heart" or "ischaemic heart arrest*" or "ischaemic heart disease*" or "ischaemic myocardium" or "ischaemic time" or "ischemia heart disease*" or "ischemic cardiac disease*" or "ischemic cardial disease*" or "ischemic cardiomyopath*" or "ischemic cardiopath*" or "ischemic heart" or "ischemic heart arrest*" or "ischemic heart disease*" or "ischemic myocardium" or "ischemic time" or "Kounis syndrome*" or "left ventricular apical ballooning" or "left ventricular apical ballooning syndrome*" or "left ventricular ballooning" or "myocardial anoxia" or "myocardial fiber necros*" or "myocardial hibernation*" or "myocardial hypoxia" or "myocardial infarct" or "myocardial infarct*" or "myocardial ischaemia*" or "myocardial ischemia*" or "myocardial necros*" or "myocardial reinfarct*" or "myocardium hypoxia*" or "myocardium infarct*" or "myocardium ischaemia*" or "myocardium ischemia*" or "myocardium necros*" or "no reflow phenomenon" or "painless cardiac ischaemia*" or "painless cardiac ischemia*" or "painless heart ischaemia*" or "painless heart ischemia*" or "painless ischaemia*" or "painless ischemia*" or "painless myocardial ischaemia*" or "painless myocardial ischemia*" or "paroxysmal atrial fibrillation*" or "post heart infarction syndrome*" or "post infarctation syndrome*" or "post infarction syndrome*" or "postinfarction syndrome*" or "postmyocard infarction syndrome*" or "postmyocardial infarction syndrome*" or "postprandial angina pectoris" or "premonitory infarction sign" or "second heart attack*" or "silent cardiac ischaemia*" or "silent cardiac ischemia*" or "silent heart ischaemia*" or "silent heart ischemia*" or "silent ischaemia*" or "silent ischemia*" or "silent myocardial ischaemia*" or "silent myocardial ischemia*" or stenocardia or "stress cardiomyopath*" or "stress induced cardiomyopath*" or "subendocardial infarct*" or "subendocardial ischaemia*" or "subendocardial ischemia*" or takotsubo or "tako-tsubo" or "takotsubo cardiomyopath*" or "takotsubo syndrome*" or "transient left ventricular apical ballooning" or "transient left ventricular apical ballooning syndrome*" or "transmural cardiac infarct*" or "transmural heart infarct*")

3 TITLE-ABS-KEY("aorta coronary artery bypass*" OR "aorta coronary bypass graft*" OR "aorta coronary bypass*" OR "aorta coronary vein bypass graft*" OR "aorta coronary vein bypass*" OR "aorta coronary vein shunt" OR "aortic coronary artery bypass*" OR "aortic coronary bypass*" OR "aorticocoronary anastomosis" OR "aorto coronary artery bypass*" OR "aorto coronary bypass graft*" OR "aorto coronary vein bypass*" OR "aortocoronary anastomosis" OR "aortocoronary artery bypass graft*" OR

"aortocoronary artery bypass*" OR "aortocoronary bypass graft*" OR "aortocoronary bypass*" OR "aortocoronary shunt" OR "aortocoronary vein bypass graft*" OR "aortocoronary vein bypass*" OR "aortocoronary venous bypass graft*" OR "aortocoronary venous bypass*" OR CABG OR "coronary artery bypass grafting" OR "coronary artery bypass*" OR "coronary artery graft*" OR "coronary bypass graft*" OR "coronary bypass grafting" OR "coronary bypass*" OR "coronary vein bypass graft*" OR "coronary venous bypass graft*" OR "coronary-internal mammary artery anastomos*" OR "internal mammary-coronary artery anastomos*")

4 TITLE-ABS-KEY((meta W/1 analys*) OR metaanalys* OR (systematic* W/3 review*) OR (control* W/3 study) OR (control* W/3 trial) OR (randomized W/3 study) OR (randomized W/3 trial) OR (randomised W/3 study) OR (randomised W/3 trial) OR "pragmatic clinical trial" OR (random* W/1 allocat*) OR (doubl* W/1 blind*) OR (doubl* W/1 mask*) OR (singl* W/1 blind*) OR (singl* W/1 mask*) OR (tripl* W/1 blind*) OR (tripl* W/1 mask*) OR (trebl* W/1 blind*) OR (trebl* W/1 mask*) OR "latin square" OR placebo* OR nocebo* OR multivariate OR "comparative study" OR "comparative survey" OR "comparative analysis" OR (intervention* W/2 study) OR (intervention* W/2 trial) OR "cross-sectional study" OR "cross-sectional analysis" OR "cross-sectional survey" OR "cross-sectional design" OR "prevalence study" OR "prevalence analysis" OR "prevalence survey" OR "disease frequency study" OR "disease frequency analysis" OR "disease frequency survey" OR crossover OR "cross-over" OR cohort* OR "longitudinal study" OR "longitudinal survey" OR "longitudinal analysis" OR "longitudinal evaluation" OR longitudinal* OR ((retrospective OR "ex post facto") W/3 (study OR survey OR analysis OR design)) OR retrospectiv* OR "prospective study" OR "prospective survey" OR "prospective analysis" OR prospectiv* OR (population W/3 (stud* or survey* or analys* or research)) OR "concurrent study" OR "concurrent survey" OR "concurrent analysis" OR (("follow-up" or followup) W/1 (stud* or survey or analysis)) OR ((observation or observational) W/1 (study or survey or analysis)) OR "case study" OR "case series" OR "clinical series" OR "case studies" OR "clinical study" OR "clinical trial" OR (("phase 0" or "phase 1" or "phase I" or "phase 2" or "phase II" or "phase 3" or "phase III" or "phase 4" or "phase IV") W/5 (trial or study)) OR "evaluation study" OR "evaluation survey" OR "evaluation analysis" OR "quantitative study" OR "quantitative analys*" OR "numerical study" OR "validation study" OR "validation survey" OR "validation analysis" OR "quasi experimental study" OR "quasi experimental analysis" OR "quasiexperimental study" OR "quasiexperimental analysis" OR "in vivo study" OR "in vivo analysis" OR "panel study" OR "panel survey" OR "panel analysis" OR "replication study" OR "replication analysis " OR "replication trial" OR "feasibility study" OR "feasibility analysis" OR ((correlation* W/2 study) OR (correlation* W/2 analys*)) OR "case control study" OR "case base study" OR "case referrent study" OR "case referent study" OR "case referent study" OR "case compeer study" OR "case comparison study" OR "matched case control" OR "multicenter study" OR "multi-center study" OR "odds ratio" OR "confidence interval" OR "regression analysis" OR "least square" OR "least squares" OR (hazard* W/1 (model* OR analys* OR regression or ratio or ratios)) OR "Cox model" OR "Cox multivariate analyses" OR "Cox multivariate analysis" OR "Cox regression" OR "Cox survival analyses" OR "Cox survival analysis" OR "Cox survival model" OR "change analysis" OR ((study OR trial OR random* OR control*) AND compar*))

5 1 and 2 and 3 and 4

6 TITLE-ABS-KEY((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) AND NOT (human OR humans or patient or patients))

7 5 and not 6

8 DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

9 7 and not 8
10 INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
11 9 and not 10

REFERENCES

1. Reiff T, Eckstein H, Mansmann U, Jansen O, Fraedrich G, Mudra H, et al. Angioplasty in asymptomatic carotid artery stenosis vs endarterectomy compared to best medical treatment: one-year interim results of SPACE-2. Int J Stroke 2019;15. 174749301983301.
2. Lin CJ, Chang FC, Chou KH, Tu PC, Lee YH, Lin CP, et al. Intervention versus aggressive medical therapy for cognition in severe asymptomatic carotid stenosis. AJNR Am J Neuroradiol 2016;37:1889-97.
3. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995;273:1421-8.
4. Kolos I, Troitskiy A, Balakhonova T, Shariya M, Skrypnik D, Tvorogova T, et al. Modern medical treatment with or without carotid endarterectomy for severe asymptomatic carotid atherosclerosis. J Vasc Surg 2015;62:914-22.
5. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomized controlled trial. Lancet 2004;363:1491-502.
6. Azzini C, Gentile M, De Vito A, Traina L, Sette E, Fainardi E, et al. Very early carotid endarterectomy after intravenous thrombolysis. Eur J Vasc Endovasc Surg 2016;51:482-6.
7. Barbetta I, Carmo M, Mercandalli G, Lattuada P, Mazzaccaro D, Settembrini AM, et al. Outcomes of urgent carotid endarterectomy for stable and unstable acute neurologic deficits. J Vasc Surg 2014;59:440-6.
8. Tanious A, Pothof AB, Boitano LT, Pendleton AA, Wang LJ, deBorst GJ. Timing of carotid endarterectomy after stroke: retrospective review of prospectively collected national database. J Vasc Surg 2018;68:1955-6.
9. Avgerinos ED, Farber A, Abou Ali AN, Rybin D, Doros G, Eslami MH. Early carotid endarterectomy performed 2 to 5 days after the onset of neurologic symptoms leads to comparable results to carotid endarterectomy performed at later time points. J Vasc Surg 2017;66:1719-26.
10. Hlavica M, Berberat J, Ineichen BV, Añon J, Diepers M, Nedeltchev K, et al. Emergent vs elective stenting of carotid stenosis with intraluminal carotid thrombus. J Neuroradiol 2017;44:254-61.
11. Weimar C, Bilbilis K, Rekowski J, Holst T, Beyersdorf F, Breuer M, et al. Safety of simultaneous coronary artery bypass grafting and carotid endarterectomy versus isolated coronary artery bypass grafting. Stroke 2017;48:2769-75.
12. Illuminati G, Ricco J-B, Caliò F, Pacilè MA, Miraldi F, Frati G, et al. Short-term results of a randomized trial examining timing of carotid endarterectomy in patients with severe asymptomatic unilateral carotid stenosis undergoing coronary artery bypass grafting. J Vasc Surg 2011;54:993-9.
13. Yang T, Zhang L, Wang X, Dong H, Jiang X, Sun H. Revascularization by carotid artery stenting and off-pump coronary artery bypass: carotid and coronary revascularization. ANZ J Surg 2016;86:602-7.
14. Newman DC, Hicks RG, Horton DA. Coexistent carotid and coronary arterial disease. Outcome in 50 cases and method of management. J Cardiovasc Surg 1987;28:599-606.
15. Sato K, Fujiyoshi K, Hoshi K, Noda C, Yamaoka-Tojo M, Ako J, et al. Low stroke rate of carotid stenosis under the guideline-oriented medical treatment compared with surgical treatment. Int Heart J 2016;57:80-6.
16. Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, et al. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. Lancet 2015;385:529-38.
17. Huibers A, Calvet D, Kennedy F, Czuriga-Kovács K, Featherstone R, Moll F, et al. Mechanism of procedural stroke following carotid endarterectomy or carotid artery stenting within the International Carotid Stenting Study (ICSS) randomised trial. Eur J Vasc Endovasc Surg 2015;50:281-8.
18. Featherstone RL, Dobson J, Ederle J, Doig D, Bonati LH, Morris S, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): a randomised controlled trial with cost-effectiveness analysis. Health Technol Assess 2016;20:1-94.
19. International Carotid Stenting Study Investigators, Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. Lancet 2010;375:985-97.
20. Brooks WH, McClure RR, Jones MR, Coleman TC, Breathitt L. Carotid angioplasty and stenting versus carotid endarterectomy: randomized trial in a community hospital. J Am Coll Cardiol 2001;38:1589-95.
21. Eckstein H-H, Ringleb P, Allenberg J-R, Berger J, Fraedrich G, Hacke W, et al. Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective, randomised trial. Lancet Neurol 2008;7:893-902.
22. Ringleb PA, Kunze A, Allenberg JR, Hennerici MG, Jansen O, Maurer PC, et al. The stent-supported percutaneous angioplasty of the carotid artery vs endarterectomy trial. Cerebrovasc Dis 2004;18:66-8.
23. SPACE Collaborative Group, Ringleb PA, Allenberg J, Bruckmann H, Eckstein H-H, Fraedrich G, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. Lancet 2006;368:1239-47.
24. Ederle J, Bonati LH, Dobson J, Featherstone RL, Gaines PA, Beard JD, et al. Endovascular treatment with angioplasty or stenting versus endarterectomy in patients with carotid artery stenosis in the Carotid And Vertebral Artery Transluminal Angioplasty Study (CAVATAS): long-term follow-up of a randomised trial. Lancet Neurol 2009;8:898-907.
25. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 2001;357:1729-37.
26. Bonati LH, Ederle J, Dobson J, Engelter S, Featherstone RL, Gaines PA, et al. Length of carotid stenosis predicts peri-procedural stroke or death and restenosis in patients randomized to endovascular treatment or endarterectomy. Int J Stroke 2014;9:297-305.
27. Hoffmann A, Taschner C, Mendelowitsch A, Merlo A, Radue EW, Lyrer P, et al. Carotid artery stenting versus carotid endarterectomy - a prospective randomised controlled single-centre trial with long-term follow-up (BACASS). Swiss Arch Neurol Psychiatr 2008;159:84-9.
28. Mas J-L, Arquizan C, Calvet D, Viguier A, Albucher J-F, Piquet P, et al. Long-term follow-up study of endarterectomy versus angioplasty in patients with symptomatic severe carotid stenosis trial. Stroke 2014;7:2750-6.
29. Mas J-L, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin J-P, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med 2006;355:1660-71.
30. Mas J-L, Trinquart L, Leys D, Albucher J-F, Rousseau H, Viguier A, et al. Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial: results up to 4 years from a randomised, multicentre trial. Lancet Neurol 2008;7:885-92.
31. Naylor AR. Randomized study of carotid angioplasty and stenting versus carotid endarterectomy: a stopped trial. J Vasc Surg 1998;28:326-34.
32. Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, et al. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). Stroke 2011;42:675-80.
33. Howard VJ, Lutsep HL, Mackey A, Demaerschalk BM, Sam AD, Gonzales NR, et al. Influence of sex on outcomes of stenting versus endarterectomy: a subgroup analysis of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). Lancet Neurol 2011;10:530-7.

34. Brott TG, Hobson RW, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010;363:11-23.
35. Meschia JF, Hopkins LN, Altafullah I, Wechsler LR, Stotts G, Gonzales NR, et al. Time from symptoms to carotid endarterectomy or stenting and perioperative risk. Stroke 2015;46:3540-2.
36. Jones MR, Howard G, Roubin GS, Blackshear JL, Cohen DJ, Cutlip DE, et al. Periprocedural stroke and myocardial infarction as risks for long-term mortality in CREST. Circ Cardiovasc Qual Outcomes 2018;11:e004663.
37. Howard G, Hopkins LN, Moore WS, Katzen BT, Chakhtoura E, Morrish WF, et al. Temporal changes in periprocedural events in the carotid revascularization endarterectomy versus stenting trial. Stroke 2015;46:2183-9.
38. Timaran CH, Mantese VA, Malas M, Brown OW, Lal BK, Moore WS, et al. Differential outcomes of carotid stenting and endarterectomy performed exclusively by vascular surgeons in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). J Vasc Surg 2013;57:303-8.
39. Blackshear JL, Cutlip DE, Roubin GS, Hill MD, Leimgruber PP, Begg RJ, et al. Myocardial infarction after carotid stenting and endarterectomy: results from the Carotid Revascularization Endarterectomy Versus Stenting Trial. Circulation 2011;123:2571-8.
40. Steinbauer MGM, Pfister K, Greindl M, Schlachetzki F, Borisch I, Schuirer G, et al. Alert for increased long-term follow-up after carotid artery stenting: results of a prospective, randomized, single-center trial of carotid artery stenting vs carotid endarterectomy. J Vasc Surg 2008;48:93-8.
41. Brandl R, Brauer RB, Maurer PC. Urgent carotid endarterectomy for stroke in evolution. Vasa 2001;30:115-21.
42. Mihindu E, Mohammed A, Smith T, Brinster C, Sternbergh WC, Bazan HA. Patients with moderate to severe strokes (NIHSS score >10) undergoing urgent carotid interventions within 48 hours have worse functional outcomes. J Vasc Surg 2019;69:1471-81.
43. Welsh S, Mead G, Chant H, Picton A, O'Neill PA, McCollum CN. Early carotid surgery in acute stroke: a multicentre randomised pilot study. Cerebrovasc Dis 2004;18:200-5.
44. Berens ES, Kouchoukos NT, Murphy SF, Wareing TH, Louis S. Preoperative carotid artery screening in elderly patients undergoing cardiac surgery. J Vasc Surg 1992;15:313-21; discussion: 322-3.
45. Lin JC, Kabbani LS, Peterson EL, Masabni K, Morgan JA, Brooks S, et al. Clinical utility of carotid duplex ultrasound prior to cardiac surgery. J Vasc Surg 2016;63:710-4.
46. Ahn SS, Baker JD, Walden K, Moore WS. Which asymptomatic patients should undergo routine screening carotid duplex scan? Am J Surg 1991;162:180-4.
47. Aiello F, Meltzer A, Cohen B, Espiritu M, Burmeister J, Hoque R, et al. Risk factors for prevalence and progression of asymptomatic carotid disease in patients with peripheral arterial disease. J Vasc Surg 2012;55.
48. Anastasiadis K, Karamitsos TD, Velissaris I, Makrygiannakis K, Kiskinis D. Preoperative screening and management of carotid artery disease in patients undergoing cardiac surgery. Perfusion 2009;24:257-62.
49. Ascher E, Hingorani A, Yorkovich W, Ramsey PJ, Salles-Cunha S. Routine preoperative carotid duplex scanning in patients undergoing open heart surgery: is it worthwhile? Anna Vasc Surg 2001;15:669-78.
50. Bae H-J, Yoon B-W, Kang D-W, Koo J-S, Lee S-H, Kim K-B, et al. Correlation of coronary and cerebral atherosclerosis: difference between extracranial and intracranial arteries. Cerebrovasc Dis 2006;21:112-9.
51. Bishara RA, Taha W, AlFarouk MO, Milik IA, Wilson N. Screening for significant carotid artery disease among a cohort of 1,000 Egyptian patients. Vascular 2008;16:35-40.
52. Cheng SWK, Wu LLH, Lau H, Ting ACW, Wong J. Prevalence of significant carotid stenosis in Chinese patients with peripheral and coronary artery disease. Aust NZ J Surg 1999;69:44-7.
53. Cheng Y, Gao J, Wang J, Wang S, Peng J. Risk factors for carotid artery stenosis in Chinese patients undergoing coronary artery bypass graft interventions. Medicine 2015;94:e1119.
54. Choo KS. Clinical utility of preoperative carotid duplex ultrasonography prior to operation for peripheral artery disease. Ultrasound Med Biol 2017;43:S249.
55. Chun LJ, Tsai J, Tam M, Prema J, Chen LH, Patel KK. Screening carotid artery duplex in patients undergoing cardiac surgery. Ann Vasc Surg 2014;28:1178-85.
56. Cornily J-C, Le Saux D, Vinsonneau U, Bezon E, Le Ven F, Le Gal G, et al. Assessment of carotid artery stenosis before coronary artery bypass surgery. Is it always necessary? Arch Cardiovasc Dis 2011;104:77-83.
57. de Virgilio C, Toosie K, Arnell T, Lewis RJ, Donayre CE, Baker JD, et al. Asymptomatic carotid artery stenosis screening in patients with lower extremity atherosclerosis: a prospective study. Ann Vasc Surg 1997;11:374-7.
58. Dharmasaroja PA, Piyayotai D, Hutayanon P, Buakhamsri A, Intharakham K. Extracranial carotid stenosis and peripheral arterial disease in Thai patients with coronary artery disease. Angiology 2010;61:329-32.
59. Drohomirecka A, Ł Kołtowski, Kwinecki P, Wronecki K, Cichoń R. Risk factors for carotid artery disease in patients scheduled for coronary artery bypass grafting. Kardiol Pol 2010;68:789-94.
60. Fassiadis N, Adams K, Zayed H, Goss D, Deane C, MacCarthy P, et al. Occult carotid artery disease in patients who have undergone coronary angioplasty. Interact Cardiovasc Thorac Surg 2008;7:855-7.
61. Fowl R, Marsch J, Love M, Patterson R, Shukla R, Kempczinski R. Prevalence of hemodynamically significant stenosis of the carotid artery in an asymptomatic veteran population. Surg Gynecol Obstet 1991;172:13-6.
62. Gentile AT. Prevalence of asymptomatic carotid stenosis in patients undergoing infrainguinal bypass surgery. Arch Surg 1995;130:900.
63. Helfre M, Grange C, Riche B, Maucort-Boulch D, Thivolet C, Vouillarmet J. Usefulness of a systematic screening of carotid atherosclerosis in asymptomatic people with type 2 diabetes for cardiovascular risk reclassification. Ann Endocrinol (Paris) 2017;78:14-9.
64. Hill AB, Obrand D, Steinmetz K. The utility of selective screening for carotid stenosis in cardiac surgery patients. J Cardiovasc Surg 1999;40:8.
65. House A. Asymptomatic carotid artery stenosis associated with peripheral vascular disease: a prospective study. Cardiovasc Surg 1999;7:44-9.
66. Ignat'ev IM. Asymptomatic stenoses of carotid arteries. Angiol Sosud Khir 2012;18:72-84.
67. Jackson VP, Bendick PJ. Duplex ultrasound screening for carotid arteriosclerotic disease in asymptomatic patients. J Ultrasound Med 1985;4:411-5.
68. Kaul S, Alladi S, Mridula KR, Bandaru VS, Umamashesh M, Anjanikumar D, et al. Prevalence and risk factors of asymptomatic carotid artery stenosis in Indian population: an 8-year follow-up study. Neurol India 2017;65:279.
69. Kawarada O, Yokoi Y, Morioka N, Nakata S, Higashiue S, Mori T, et al. Carotid stenosis and peripheral artery disease in Japanese patients with coronary artery disease undergoing coronary artery bypass grafting. Circ J 2003;67:1003-6.
70. Klop RBJ, Eikelboom BC, Taks ACJM. Screening of the internal carotid arteries in patients with peripheral vascular disease by colour-flow duplex scanning. Eur J Vasc Surg 1991;5:41-5.
71. Kurvers HAJM, van der Graaf Y, Blankensteijn JD, Visseren FLJ, Eikelboom BC. Screening for asymptomatic internal carotid artery stenosis and aneurysm of the abdominal aorta: comparing the yield between patients with manifest atherosclerosis and patients with risk factors for atherosclerosis only. J Vasc Surg 2003;37:1226-33.
72. Lezama L, Santiago G, Nafria G, Novel A, Garcia T, Ruiz C, et al. Stroke and mortality after cardiac surgery and its relationship to severe carotid, In: Druckerei Stückle, *European Stroke Conference. 24th Conference, Vienna, Austria, May 13-15, 2015: Abstract e-Book*, 2015, Karger; Vienna, Austria, Cerebrovascular Diseases Conference: 24th European Stroke Conference, May 13-15, 2015, Vienna, Austria. Available at: https://doi.org/10.1159/000431011. Accessed July 12, 2021.
73. Lin R, Hingorani A, Marks N, Ascher E, Jimenez R, Aboian E, et al. Screening for carotid artery stenosis and renal artery stenosis in patients undergoing tunneled cuffed hemodialysis catheter placement. Vasc Endovascular Surg 2012;46:364-8.
74. Mackaay AJC, Beks PJ, Dur AHM, Bischoff M, Scholma J, Heine RJ, et al. The distribution of peripheral vascular disease in a Dutch

Caucasian population: comparison of type II diabetic and non-diabetic subjects. Eur J Vasc Endovasc Surg 1995;9:170-5.
75. Marek J, Mills JL, Harvich J, Cui H, Fujitani RM. Utility of routine carotid duplex screening in patients who have claudication. J Vasc Surg 1996;24:572-9.
76. Miralles M, Corominas A, Cotillas J, Castro F, Clara A, Vidal-Barraquer F. Screening for carotid and renal artery stenoses in patients with aortoiliac disease. Ann Vasc Surg 1998;12:17-22.
77. Miura T, Soga Y, Doijiri T, Goya M, Yokoi H, Iwabuchi M, et al. Kokura Memorial Hospital, Kitakyushu, Japan, Prevalence of extra-coronary artery disease in patients with coronary artery disease undergoing coronary intervention. Eur Heart J 2010;31:297-587.
78. Moraca RJ, Wanamaker K, Nitzberg D, Bailey SH, Benckart D, McGregor W, et al. The role of routine carotid artery duplex in patients referred for coronary artery bypass grafting. International Stroke Conference, February 1-2, 2012, New Orleans, Louisiana. Available at: https://www.ahajournals.org/doi/abs/10.1161/str.43.suppl_1.a3878.
79. Narayan P, Khan MW, Das D, Guha Biswas R, Das M, Rupert E. Carotid artery screening at the time of coronary artery bypass - does it influence neurological outcomes? Int J Cardiol 2017;243:140-4.
80. Pilcher JM, Danaher J, Khaw K-T. The prevalence of asymptomatic carotid artery disease in patients with peripheral vascular disease. Clin Radiol 2000;55:56-61.
81. Planas-Ballvé A, Crespo AM, Aguilar LM, Hernández-Pérez M, Canento T, Dorado L, et al. The Barcelona-Asymptomatic Intracranial Atherosclerosis study: subclinical intracranial atherosclerosis as predictor of long-term vascular events. Atherosclerosis 2019;282:132-6.
82. Posacioğlu H, İlamoğlu F, Çalkavur T, Yağdi T, Atay Y, Özbaran M, et al. Predictive values of risk factors in carotid duplex scanning before peripheral vascular surgery. Int J Angiol 2001;10:250-3.
83. Rockman CB, Jacobowitz GR, Gagne PJ, Adelman MA, Lamparello PJ, Landis R, et al. Focused screening for occult carotid artery disease: patients with known heart disease are at high risk. J Vasc Surg 2004;39:44-50.
84. Sayed A, Ahmed S, Abdelalim A, Nagah M, Khairy H. Is peripheral arterial disease associated with carotid artery disease in Egyptians? A pilot study. Egypt J Neurol Psychiatr Neurosurg 2016;53:12.
85. Stephens J, Abdel-Aziz K. Are asymptomatic Hollenhorst plaques a reliable predictor of ipsilateral carotid stenosis and medium term stroke risk? Eur J Neurol 2010;17(Suppl 3):351-625.
86. Sutthapas Chumpita, Srimahachota Supot, Charnnarong Nijasri. Prevalence of extracranial internal carotid and intracranial large arteries stenosis in patients with suspected coronary artery disease who underwent coronary angiography in Chulalongkorn Hospital. In: Druckerei Stückle. Karger; 2012.
88. Valentine R. Utility of carotid duplex in young adults with lower extremity atherosclerosis: how aggressive should we be in screening young patients? Cardiovasc Surg 1997;5:408-13.
88. Wanamaker KM, Moraca RJ, Nitzberg D, Magovern GJ. Contemporary incidence and risk factors for carotid artery disease in patients referred for coronary artery bypass surgery. J Cardiothorac Surg 2012;7:78.
89. Yamamoto K, Miyata T, Nagayoshi M, Akagi D. Carotid endarterectomy may reduce the high stroke rate for patients with the disease of abdominal aorta and peripheral arteries. Int Angiol 2006;25:35.
90. Yun W-S, Rho Y-N, Park U-J, Lee K-B, Kim D-I, Kim Y-W. Prevalence of asymptomatic critical carotid artery stenosis in Korean patients with chronic atherosclerotic lower extremity ischemia: is a screening carotid duplex ultrasonography worthwhile? J Korean Med Sci 2010;25:1167.
91. Abbasi K, Araghi MF, Zafarghandi M, Karimi A, Ahmadi H, Marzban M, et al. Concomitant carotid endarterectomy and coronary artery bypass grafting versus staged carotid stenting followed by coronary artery bypass grafting. J Cardiovasc Surg (Torino) 2008;49:285-8.
92. Bernhard VM. Carotid artery stenosis: association with surgery for coronary artery disease. Arch Surg 1972;105:837.
93. Brow T, Kakkar V, Pepper J, Das S. Toward a rational management of concomitant carotid and coronary artery disease. J Cardiovasc Surg 1999;40:837.
94. Carrel T, Stillhard G, Turina M. Combined carotid and coronary artery surgery: early and late results. Cardiology 1992;80:118-25.
95. Chiappini B, Dell' Amore A, Di Marco L, Di Bartolomeo R, Marinelli G. Simultaneous carotid and coronary arteries disease: staged or combined surgical approach? J Card Surg 2005;20:234-40.
96. Faggioli GL, Curl GR, Ricotta JJ. The role of carotid screening before coronary artery bypass. J Vasc Surg 1990;12:724-31.
97. Feldman DN, Swaminathan RV, Geleris JD, Okin P, Minutello RM, Krishnan U, et al. Comparison of trends and in-hospital outcomes of concurrent carotid artery revascularization and coronary artery bypass graft surgery. JACC Cardiovasc Interv 2017;10:286-98.
98. Giangola G, Migaly J, Riles TS, Lamparello PJ, Adelman MA, Grossi E, et al. Perioperative morbidity and mortality in combined vs staged approaches to carotid and coronary revascularization. Ann Vasc Surg 1996;10:138-42.
99. Hempe S, Moza A, Goetzenich A, Tewarie L, Bleilevens C, Autschbach R, et al. Synchronous or staged carotid endarterectomy and coronary artery bypass grafting? Propensity score matched study. Heart Surg Forum 2018;21:E359-64.
100. Hertzer NR, Beven EG. Staged and combined surgical approach to simultaneous carotid and coronary vascular disease. Surgery 1978;84:803-11.
101. Hudorovic N. Reduction in hospitalisation rates following simultaneous carotid endarterectomy and coronary artery bypass grafting; experience from a single centre. Interact Cardiovasc Thorac Surg 2006;5:367-72.
102. Lyem H, Buket S. Early results of combined and staged coronary bypass and carotid endarterectomy in advanced age patients in single Centre. Open Cardiovasc Med J 2009;3:8-14.
103. Kovacevic P, Redzek A, Kovacevic-Ivanovic S, Velicki L, Ivanovic V, Kieffer E. Coronary and carotid artery occlusive disease: single center experience. Eur Rev Med Pharmacol Sci 2012;16:483-90.
104. Oz K, Aydın Ü, Kyaruzi M, Karaman Z, Göksel OS, Yeniterzi M, et al. Staged or combined approach for carotid endarterectomy in patients undergoing coronary artery bypass grafting: a 5-year long experience. Heart Surg Forum 2016;19:276.
105. Peric M, Huskic R, Nezic D, Nastasic S, Popovic Z, Bojic M. Cardiac events after combined surgery for coronary and carotid artery disease. Eur J Cardiothorac Surg 1997;11:1074-80.
106. Peric M, Huskic R, Nezic D, Gradinac S, Popovic Z, Popovic AD, et al. Combined carotid and coronary artery surgery: what have we learned after 15 years? Cardiovasc Surg 1998;6:156-65.
107. Rosenthal D, Lamis PA. Carotid and coronary arterial disease. Am Surg 1984;50:233-5.
108. Şaşkın H, Duzyol C, Ozcan KS, Aksoy R, Idiz M. Is carotid artery stenting an alternative to simultaneous carotid endarterectomy performed for carotid artery stenosis in patients undergoing isolated coronary bypass surgery? Heart Surg Forum 2015;18:211.
109. Takach TJ, Reul GJ, Cooley DA, Duncan JM, Ott DA, Livesay JJ, et al. Is an integrated approach warranted for concomitant carotid and coronary artery disease? Ann Thorac Surg 1997;64:16-22.
110. Urschel H, Razzuk M, Gardner M. Management of concomitant occlusive disease of the carotid and coronary arteries. J Thorac Cardiovasc Surg 1976;72:829-34.
111. Xiang B, Luo X, Yang Y, Qiu J, Zhang J, Li L, et al. Midterm results of coronary artery bypass graft surgery after synchronous or staged carotid revascularization. J Vasc Surg 2019;700:1942-9.
112. Ziada KM, Yadav JS, Mukherjee D, Lauer MS, Bhatt DL, Kapadia S, et al. Comparison of results of carotid stenting followed by open heart surgery versus combined carotid endarterectomy and open heart surgery (coronary bypass with or without another procedure). Am J Cardiol 2005;96:519-23.
113. Timaran CH, Rosero EB, Smith ST, Valentine RJ, Modrall JG, Clagett GP. Trends and outcomes of concurrent carotid revascularization and coronary bypass. J Vasc Surg 2008;48:355-60; discussion 360-1.