META-ANALYSIS

Carotid artery stenting versus carotid endarterectomy in the treatment of symptomatic and asymptomatic carotid stenosis: a systematic review and meta-analysis

Xuefeng Kan¹, Yong Wang¹, Bin Xiong¹, Bin Liang¹, Guofeng Zhou¹, Huimin Liang¹, Chuansheng Zheng¹

ABSTRACT

Purpose: To evaluate the short-term and intermediate-to-long-term efficacy and safety of carotid artery stenting (CAS) compared with carotid endarterectomy (CEA).

Materials and Methods: The published literature was electronically searched for randomized controlled trials (RCTs) between CAS and CEA for the treatment of carotid stenosis performed from January 2000 to January 2017. The short-term and intermediate-to-long-term outcomes were evaluated.

Results: We identified 10 RCTs including 7,183 participants with symptomatic or asymptomatic carotid stenosis. Our meta-analysis found different results between the patients with and those without symptoms. In patients with symptomatic carotid stenosis, the total stroke incidence in the CAS group was significantly higher than that in the CEA group within the 30-day periprocedural period (p<0.001); however, the myocardial infarction incidence in the CAS group was significantly lower than that in the CEA group (p<0.05). There was no significant difference between the two groups in the mortality within 30 days post-procedure, but the intermediate-to-long-term incidence of stroke or death in the CAS group was higher than that of the CEA group (p<0.05). In contrast, for asymptomatic patients, there were no significant differences between the CAS and CEA groups in the short- and intermediate-to-long-term outcomes.

Conclusion: For patients with symptomatic carotid stenosis, CEA is associated with an increased risk of myocardial infarction, whereas CAS is correlated with an increased risk of procedurally related strokes. However, for patients with asymptomatic carotid stenosis, no significant difference was found in the efficacy or safety between CAS and CEA.

Keywords: carotid artery stenting; carotid endarterectomy; carotid stenosis; meta-analysis

¹From the Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China.
Correspondence: Chuansheng Zheng, Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China. E-mail: hqzcsxh@sina.com.
Funding: This work was supported by grant from the National Science Foundation of China (No. 81371662 and No. 81601578).
Conflicts of interest: No conflict of interest exits in the submission of this manuscript. The manuscript has been read and approved by all authors. The work described was original research that has not been published previously and is not under consideration for publication elsewhere.

Journal of Interventional Medicine 2018;1(1): 42-48.
DOI:10.19779/j.cnki.2096-3602.2018.01.09

INTRODUCTION

Severe stenosis of a carotid artery is a major risk factor of ischemic stroke. It was reported that 20–25% of all strokes are caused by extracranial carotid artery stenosis (1). The main aim of carotid stenosis treatment is to reduce the risk of stroke and stroke-related death. Although carotid endarterectomy (CEA) has been recognized as the “gold standard” for the treatment of severe symptomatic carotid artery stenosis (2-4), Previous studies have indicated that carotid artery stenting (CAS) may be alternative with equivalency in preventing ipsilateral stroke (5-7). Which treatment strategy to use for treating carotid artery stenosis, CAS or CEA, has been controversial (8). Several previous studies indicated that CAS was inferior to CEA because CAS was associated with a significant increase in the rate of stroke or death at 30 days post-procedure (9-11). However, other studies have shown that CAS and CEA seem to be equivalent, especially for elderly patients who are less than 70 years old (12, 13). Notably, previous meta-analyses did not take into account the symptoms of carotid stenosis. In the current study, we systematically reviewed the available evidence comparing CEA with CAS in the treatment of symptomatic or asymptomatic carotid stenosis. The goal of this study was to provide data to guide clinicians using evidence-based medicine in appropriately choosing between these
two procedures in clinical practice.

**MATERIALS AND METHODS**

**Data sources and search strategy**

The literature in electronic databases (Cochrane Library, Medline/Pubmed, Embase database, National Research Register, China National Knowledge Infrastructure) and on the internet (Google) was searched for publications about RCTs comparing CAS and CEA in the treatment of carotid stenosis that had been conducted between January 2000 and January 2017. Additionally, we manually searched the relevant references of identified reviews and articles to find additional studies that were not included in the above search results. We used Medical Subject Heading (MeSH) terms in PubMed and MEDLINE, EMTREE terms in EMBASE, and keyword search terms for carotid stenosis, stenting, carotid, and carotid endarterectomy in the above databases. To restrict our search to RCTs, we then applied a modified version of the McMaster RCT Hedge filter to optimize the sensitivity and specificity of our PubMed, MEDLINE, and EMBASE results. We further restricted our searches in these databases to articles published in English or Chinese.

**Inclusion criteria**

Eligible trials that fulfilled the following criteria were included in this analysis: 1) RCTs of participants with symptomatic or asymptomatic carotid artery stenosis comparing CAS with CEA, with or without an embolic protection device (EPD); and 2) reporting the 30-day peri-procedural or intermediate- to long-term safety and efficacy.

**Exclusion criteria**

Non-randomized controlled trials, animal trials, studies of poor quality, and studies lacking required data that were not able to be acquired after contacting the study author were excluded.

**Data extraction**

Two investigators (X.F.K. and Y.Z.) independently extracted data using a standard form. Disagreements were resolved by consensus. Data pertaining to any stroke/death, restenosis, or TIA (Transit ischemic attack) rates were extracted and pooled for the main analysis according to the intention to treat principle.

**Quality assessment and statistical analysis**

The quality evaluation criteria recommended by the Cochrane Library systematic reviews Handbook version 4.2.2 was used to evaluate the quality of the included studies. A quality score of “A” represents the mild possibility of a corresponding bias and a score of “B” represents the moderate possibility. RevMan 5.0.25 software provided by the Cochrane Collaboration meta-analysis was used to analyze the collected data. The evaluated short-term outcomes were the incidence of stroke, death, or myocardial infarction within 30 days post-surgery, whereas the evaluated intermediate- to long-term outcomes were the incidence of stroke or death >30 days post-surgery.

First, we analyzed the heterogeneity among studies using χ² tests (α = 0.10) and the I² metric; p < 0.05 was taken to represent the existence of heterogeneity, and I² ≥ 50% was taken to represent significant heterogeneity. The fixed effects model (low heterogeneity) or random effects model (high heterogeneity) was then applied according to the results of the heterogeneity test, and pooled relative risks (RRs) and 95% confidence intervals (95% CI) were estimated. Lastly, Egger’s tests were performed to evaluate publication biases in the meta-analysis.

**RESULTS**

### Table 1 Characteristics of the included controlled randomized trials.

| Study, Year (NO. of references) | No. of patients | No. of asymptomatic patients | No. of CAS | No. of CEA | Mean age (year) | Mean follow-up (month) | Use of EPD | Quality |
|--------------------------------|----------------|------------------------------|------------|------------|----------------|------------------------|------------|---------|
| Alberts, 2001 (14)             | 219            | 0                            | 107        | 112        | 66             | 12                     | NO         | B       |
| Cavatas, 2001 (15)             | 504            | 0                            | 251        | 253        | 67             | 23.5                   | NO         | A       |
| Brooks, 2004 (7)               | 85             | 85                           | 43         | 42         | 68             | 48                     | NO         | B       |
| EVA-3S, 2008 (16)              | 527            | 0                            | 265        | 262        | 69.5           | 42                     | YES        | A       |
| SAPPHIRE, 2008 (6)             | 333            | 237                          | 167        | 166        | 72.5           | 36                     | YES        | A       |
| SPACE, 2008 (17)               | 1196           | 0                            | 607        | 589        | 68.4           | 24                     | YES        | A       |
| Steinbauer, 2008 (18)          | 87             | 0                            | 43         | 44         | 68.5           | 65                     | YES        | B       |
| BACASS, 2008 (19)              | 20             | 0                            | 10         | 10         | NR             | 24                     | YES        | A       |
| ICSS, 2010 (20)                | 1710           | 0                            | 853        | 857        | 70             | 36                     | YES        | A       |
| CREST, 2010 (21)               | 2502           | 1181                         | 1262       | 1240       | 69             | 48                     | YES        | A       |

NR, not reported; NO., number.
Study selection

Based on searches using the keywords described above, we initially identified 1,230 potentially relevant studies. After reading the title, abstract, and/or full text to determine the eligibility of the study and applying the exclusion criteria, ten RCTs (6, 7, 14-21) that compared CEA with CAS in the treatment of symptomatic and asymptomatic carotid stenosis were chosen for the meta-analysis (Fig. 1). Seven of these RCTs were determined to have a quality score of “A,” and the other three were each assigned a “B.” The meta-analysis included a total of 7,183 patients with symptomatic (5,680 patients) or asymptomatic (1,503 patients) carotid stenosis (Table 1).

Table 2 Study outcomes

| Model classification | Model for analysis | RR (95% CI) | \(P\) for heterogeneity | \(I^2\) (%) | \(P\) for Egger's test |
|----------------------|--------------------|-------------|--------------------------|-------------|-----------------------|
| Any stroke incidence in short-term in symptomatic patients | FEM | 1.57 (1.25–1.97) | 0.09 | 43 | 0.6973 |
| The mortality in short-term in symptomatic patients | FEM | 1.50 (0.83–2.74) | 0.33 | 13 | 0.1515 |
| Myocardial infarction incidence in short-term in symptomatic patients | FEM | 0.44 (0.23–0.85) | 0.98 | 0 | 0.7224 |
| Stroke or death incidence after 30 days in symptomatic patients | REM | 1.27 (1.01–1.60) | 0.04 | 50 | 0.3672 |
| The short and intermediate to long-term efficacy in asymptomatic patients | REM | 1.28 (0.75–2.16) | 0.05 | 62 | 0.5103 |

FEM, fixed effects model; REM, random effects model.

Figure 1. Flow chart of the included randomized controlled trials (RCTs).
Figure 2. The short-term and intermediate- to long-term efficacy in symptomatic patients. (A–B) Total stroke incidence (A) and mortality (B) at 30 days post-surgery in symptomatic patients. (C) Myocardial infarction incidence within 30 days post-surgery or at >30 days post-surgery in symptomatic patients. (D) Incidence of stroke or death at >30 days post-surgery in symptomatic patients.

Figure 3. The short-term and intermediate- to long-term efficacy in asymptomatic patients. Abbreviations: (a), the short-term efficacy in asymptomatic patients in this trial; (b), the intermediate- to long-term efficacy in asymptomatic patients in this trial.

Figure 4. Funnel plots of the incidence of stroke, death, or myocardial infarction. (A–B) Funnel plot of the total stroke incidence (A) or mortality (B) within 30 days post-surgery in symptomatic patients. (C) Funnel plot of myocardial infarction incidence with 30 days post-surgery or at >30 days post-surgery in symptomatic patients. (D) Funnel plot of the incidence of stroke or death at >30 days post-surgery in symptomatic patients. (E) Funnel plot of the short-term and intermediate- to long-term efficacy in asymptomatic patients.

Study outcomes
Total stroke incidence within 30 days post-surgery in symptomatic patients

The level of heterogeneity among the eight studies that compared total stroke incidence within 30 days post-surgery in symptomatic patients with carotid stenosis between those treated with CAS and those treated with CAE was determined not to be significant (p = 0.09, I² = 43 %). Therefore, a fixed effects model was used to analyze the results of these studies. The pooled results (RR: 1.57, 95% CI: 1.25–1.97, p < 0.001) show that CAS was associated with a higher risk of stroke from any cause within 30 days post-surgery compared with CEA (Fig. 2A; Table 2).

Mortality within 30 days post-surgery in symptomatic patients

The level of heterogeneity among the eight studies that compared mortality within 30 days post-surgery in symptomatic patients with carotid stenosis between
those treated with CAS and those treated with CAE was determined not to be significant ($p = 0.33, I^2 = 13\%$). Therefore, a fixed effects model was used to analyze the results of these studies. The pooled results (RR: 1.50, 95% CI: 0.83–2.74, $p = 0.18$) show that the difference in mortality between the CAS and CAE groups was not statistically significant (Fig. 2B; Table 2).

**Myocardial infarction incidence within 30 days post-surgery in symptomatic patients**

The heterogeneity among the nine studies that compared myocardial infarction incidence within 30 days post-surgery in symptomatic patients with carotid stenosis between those treated with CAS and those treated with CAE was determined not to be significant ($p = 0.98, I^2 = 0\%$). Therefore, a fixed effects model was used to analyze the results of these studies. The pooled results (RR: 0.44, 95% CI: 0.23–0.85, $p = 0.01$) show that CEA was associated with a higher risk of myocardial infarction within 30 days post-surgery compared with CAS (Fig. 2C; Table 2).

**Incidence of stroke or death at >30 days post-surgery in symptomatic patients**

The heterogeneity among the nine studies that compared the incidence of stroke or death at >30 days post-surgery in symptomatic patients with carotid stenosis between those treated with CAS and those treated with CAE was determined to be significant ($p = 0.04, I^2 = 50\%$). Therefore, a random effects model was used to analyze the results of these studies. The pooled results (RR: 1.27, 95% CI: 1.01–1.60, $p = 0.04$) show that CAS was associated with a higher risk of stroke or death compared with CEA (Fig. 2D; Table 2).

**Periprocedural and intermediate- to long-term outcomes in asymptomatic patients**

The heterogeneity among the six studies that compared both short-term and intermediate- to long-term outcomes in asymptomatic patients with carotid stenosis between those treated with CAS and those treated with CAE was determined to be significant ($p = 0.05, I^2 = 62\%$). Therefore, a random effects model was used to analyze the data from these studies. The pooled results (RR: 1.28, 95% CI: 0.75–2.16, $p = 0.36$) show that there was no significant difference between these two treatment groups (Fig. 3; Table 2).

**Publication bias**

For symptomatic patients in the CEA and CAS groups, the any stroke incidence, the mortality, the myocardial infarction in short-term, and the stroke or death incidence after 30 days was assessed by a fixed effects model. For asymptomatic patients in the two groups, the short and intermediate to long-term efficacy was assessed by a random effects model. The result was similar to the combined result. The funnel plot distributions (Fig. 4) and the result of an Egger’s test also suggest that there was no publication bias and that the results are reliable ($p > 0.05$).

**DISCUSSION**

There are many studies comparing CAS with CEA in efficacy and safety. Brott et al. (21) performed the largest RCT, which enrolled 2,502 patients with symptomatic or asymptomatic carotid stenosis and followed up on them for a median period of 2.5 years. The results showed that there was no significant difference in the estimated four-year rates of the primary end point (stroke, death, or myocardial infarction) between the CEA and CAS groups. However, previous meta-analyses reported that CAS significantly increased the risk of stroke and decreased the risk of myocardial infarction compared with CEA (22, 23). A meta-analysis by Bangalore et al. similarly found that CAS significantly elevated the risk of both periprocedural and intermediate- to long-term outcomes but declined the rate of periprocedural myocardial infarction (24). However, asymptomatic patients may well exhibit distinct rates of these events (10). Unlike the previous meta-analyses, the meta-analysis in the present study separately evaluated the efficacy of symptomatic and asymptomatic patients who underwent CEA or CAS. We found that the outcomes of asymptomatic patients were different from those of symptomatic patients. The heterogeneous patient populations, different endpoints, and different endovascular devices of the previous RCTs and meta-analyses comparing CAS with CEA all likely contributed to the somewhat conflicting results of these studies.

Ten recent RCTs comparing CEA with CAS were included in our meta-analysis. We obtained results similar to those of previous studies for patients with symptomatic carotid stenosis: CAS was associated with a reduction in the incidence of myocardial infarction but with an increased risk of stroke within the 30-day periprocedural period and an increased risk of stroke or death as intermediate- to long-term outcomes. Interestingly, for patients with asymptomatic carotid stenosis, our meta-analysis produced results that are different from those of previous meta-analyses: there were no differences between the CAS and CEA groups in the short-term and intermediate- to long-term outcomes. This difference is likely due to the symptomatic and asymptomatic populations being combined in most previous meta-analyses, rather than analyzed separately as in this study.

The results of both the former meta-analyses and the present meta-analysis indicate that CAS is superior to CEA only in the incidence of myocardial infarction in the short-term. This difference may be attributable to the respective natures of the CAS and CEA techniques. In recent years, EPDs have been widely used to reduce the risk of stroke during the CAS procedure. However, its use is not without potential complication (25), and EPDs are not effective in preventing cerebral ischemia during stenting (26). Our findings confirm the view that CAS is likely to be a better option than CEA for symptomatic patients, especially those who are at elevated risk for myocardial infarction within 30 days post-surgery.
In our study, we found no significant benefits of one procedure over the other when comparing CEA with CAS, which may challenge the traditional view of CEA as the “gold standard” treatment both for symptomatic and asymptomatic carotid stenosis. Though previous studies had recently suggested other symptoms (such as an ulceration, intraplaque hemorrhage, or microembolism) that could help identify high-risk patients with asymptomatic carotid stenosis who may benefit from these two procedures (26-28), definitive conclusions about the superiority of one interventional strategy over another still could not be reached. The inconclusive results of recent RCTs of interventional strategies (CEA vs CAS) likely stem from these studies failing to evaluate adequate numbers of patients with asymptomatic carotid stenosis and their recruitment of heterogeneous groups of patients.

Age, anatomy, treatment cost, and patient willingness are also important factors that may influence the choice of CEA or CAS in clinical practice. The result of a meta-analysis by Economopoulos et al. showed that the difference between CEA and CAS in long-term stroke rates was significant, especially in patients over 68 years old, but little difference in these rates was observed in those less than 68 years old (23). Furthermore, recent guidelines recommend that CAS rather than CEA should be used when revascularization is indicated but neck anatomy is unfavorable for arterial surgery (29). Concerning the median total hospital charges for these procedures, CAS is more expensive than CEA ($33,500 vs $21,200, respectively) (30). Lastly, some patients may choose CAS because it is minimally invasive or because they are afraid of general anesthesia, so their decisions must be respected.

Several factors present in this study may have influenced the results of the meta-analysis. Firstly, the number of included RCTs was limited, particularly RCTs including patients with asymptomatic carotid stenosis. Because there were so few asymptomatic patients included in the studies, we analyzed the combined short-term and intermediate- to long-term efficacy of CEA versus CAS in the asymptomatic patients. When the ongoing clinical trial of ACST-2 (31) is finished, it should be possible to analyze separate efficacies for these patients. Secondly, the follow-up periods in the included studies were quite different, and some of them were not long enough. Lastly, clinical heterogeneity among the studies existed, such as an inconsistency in the use of EPD or dual antiplatelet therapy or the differences among surgeon skills (32) and patient conditions. Notably, although significant heterogeneity existed among the included studies, there was no publication bias detected, and the results were reliable.

In conclusion, for patients with symptomatic carotid stenosis, CEA is associated with an increased risk of cardiac ischemia whereas CAS is correlated with an increased risk of procedurally related strokes. However, for patients with asymptomatic carotid stenosis, no significant differences were found in the efficacy and safety between CAS and CEA.

REFERENCES
1. Kazmierniak MK. [Stenosis of the carotid arteries]. Wiad Lek 2003; 56: 260-265.
2. Barnett HJM, Taylor DW, Haynes RB, et al. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991; 325: 445-453.
3. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or mild (0-29%) carotid stenosis. European Carotid Surgery Trialists' Collaborative Group. Lancet 1991; 337: 1235-1243.
4. Brown K, Itum DS, Preiss J, et al. Carotid artery stenting has increased risk of external carotid artery occlusion compared with carotid endarterectomy. J Vasc Surg 2015; 61: 119-124.
5. Brooks WH, Jones MR, Gieler P, et al. Carotid angioplasty with stenting versus endarterectomy: 10-year randomized trial in a community hospital. JACC Cardiovasc Interv 2014; 7: 163-168.
6. Gunn HS, Yadvay JS, Fyad P, et al. Long-term results of carotid stenting versus endarterectomy in high-risk patients. N Engl J Med 2008; 358: 1572-1579.
7. Brooks WH, McClure RR, Jones MR, et al. Carotid angioplasty and stenting versus carotid endarterectomy for treatment of asymptomatic carotid stenosis: a randomized trial in a community hospital. Neurosurgery 2004; 54: 318-324; discussion 324-315.
8. Zhang L, Zhao Z, Ouyang Y, et al. Systematic Review and Meta-Analysis of Carotid Artery Stenting Versus Endarterectomy for Carotid Stenosis: A Chronological and Worldwide Study. Medicine (Baltimore) 2015; 94: e1060.
9. Roffi M, Mukherjee D, Clair DG. Carotid artery stenting vs. endarterectomy. Eur Heart J 2009; 30: 2693-2704.
10. Meier P, Knapp G, Tamhane U, et al. Short term and intermediate term comparison of endarterectomy versus stenting for carotid artery stenosis: systematic review and meta-analysis of randomised controlled clinical trials. BMJ 2010; 340: c467.
11. Liu ZJ, Fu WG, Guo ZY, et al. Updated systematic review and meta-analysis of randomized clinical trials comparing carotid artery stenting and carotid endarterectomy in the treatment of carotid stenosis. Ann Vasc Surg 2012; 26: 576-590.
12. Murad MH, Flynn DN, Elamin MB, et al. Endarterectomy vs stenting for carotid artery stenosis: a systematic review and meta-analysis. J Vasc Surg 2008; 48: 487-493.
13. Bonati LH, Dobson J, Algra A, et al. Short-term outcome after stenting versus endarterectomy for symptomatic carotid stenosis: a preplanned meta-analysis of individual patient data. Lancet 2010; 376: 1062-1073.
14. Alberts MJ. Results of a multicenter prospective randomized trial of carotid artery stenting vs carotid endarterectomy. Stroke 2001; 32: 325d.
15. 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: 1729-1737.
16. Mas JL, Trinquart L, Leys D, 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 Neurology 2006; 7: 885-892.
17. Eckstein HH, Ringleb P, Allenberg JR, 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.
18. Steinbauer MG, Pfister K, Greindl M, et al. Alert for increased long-term follow-up after carotid artery stenting: results of a prospective, randomised, single-center trial of carotid artery stenting vs carotid endarterectomy. J Vasc Surg 2008; 48: 93-98.
19. Hoffmann A, Engelser T, Taschner C, et al. Carotid artery stenting versus carotid endarterectomy - A prospective randomised controlled single-centre trial with long-term follow-up (BACASS). Schweizer Archiv Für Neurologie Und Psychiatrie 2008; 159: 84-89.
20. Ederie J, Dobson J, Featherstone RL, 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; 376: 985-995.
21. Brott TG, Hobson RW, 2nd, Howard G, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 2010; 363: 11-23.
22. Murad MH, Shihhour A, Shah ND, et al. A systematic review and
meta-analysis of randomized trials of carotid endarterectomy vs stenting. J Vasc Surg 2011; 53: 792-797.
23. Economopoulos KP, Sergentanis TN, Tsivgoulis G, et al. Carotid artery stenting versus carotid endarterectomy: a comprehensive meta-analysis of short-term and long-term outcomes. Stroke 2011; 42: 687-692.
24. Bangalore S, Kumar S, Witterslev J, et al. Carotid artery stenting vs carotid endarterectomy: meta-analysis and diversity-adjusted trial sequential analysis of randomized trials. Arch Neurol 2011; 68: 172-184.
25. Cremonesi A, Manetti R, Setacci F, et al. Protected carotid stenting: clinical advantages and complication of embolic protection device in 422 consecutive patients. Stroke 2003; 34: 1936-1941.
26. Bonati LH, Jongen LM, Haller S, et al. New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). Lancet Neurol 2010; 9: 353-362.
27. Hirt LS. Progression rate and ipsilateral neurological events in asymptomatic carotid stenosis. Stroke 2014; 45: 702-706.
28. Markus HS, King A, Shipley M, et al. Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Embolisation Study (ACES): a prospective observational study. Lancet Neurol 2010; 9: 663-671.
29. Brott TG, Halperin JL, Abbara S, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of NeuroInterventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery. Circulation 2011; 124: 489-532.
30. Paraskevas KI, Moore WS, Veith FJ. Cost implications of more widespread carotid artery stenting consistent with the American College of Cardiology/American Heart Association guideline. J Vasc Surg 2012; 55: 585-587.
31. Rudarakanchana N, Dialynas M, Halliday A. Asymptomatic Carotid Surgery Trial-2 (ACST-2): rationale for a randomised clinical trial comparing carotid endarterectomy with carotid artery stenting in patients with asymptomatic carotid artery stenosis. Eur J Vasc Endovasc Surg 2009; 38: 239-242.
32. Roffi M, Sievert H, Gray WA, et al. Carotid artery stenting versus surgery: adequate comparisons? Lancet Neurol 2010; 9: 339-341; author reply 341-332.