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Carotid Artery Stenting and Cardiac Surgery in Symptomatic Patients

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Objectives The purpose of this study was to evaluate the feasibility and safety of the combined outcome of carotid artery stenting (CAS) and coronary artery bypass graft (CABG) surgery in neurologically symptomatic patients.

Background The risk of perioperative stroke in patients undergoing CABG who report a prior history of transient ischemic attack or stroke has been associated with a 4-fold increased risk as compared to the risk for neurologically asymptomatic patients. It seems appropriate to offer prophylactic carotid endarterectomy to neurologically symptomatic patients who have significant carotid artery disease and are scheduled for CABG. The CAS-CABG outcome for symptomatic patients remains underreported, notwithstanding randomized data supporting CAS for high-risk patients.

Methods In a prospective, single-center study, the periprocedural and long-term outcomes of 57 consecutive patients who underwent CAS before cardiac surgery were analyzed.

Results The procedural success rate of CAS was 98%. The combined death, stroke, and myocardial infarction rate was 12.3%. The death and major stroke rate from time of CAS to 30 days after cardiac surgery was 3.5%. The myocardial infarction rate from time of CAS to 30 days after cardiac surgery was 1.5%.

Conclusions This is the first single-center study reporting the combined outcome of CAS-CABG in symptomatic patients. The periprocedural complication rate and long-term results of the CAS-CABG strategy in this high-risk population support the reliability of this approach. In such a high-risk population, this strategy might offer a valuable alternative to the combined surgical approach; however, a large randomized trial is clearly warranted. (J Am Coll Cardiol Intv 2011;4:1190–6) © 2011 by the American College of Cardiology Foundation

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Optimal treatment of patients with concurrent carotid and coronary artery disease remains debatable despite more than 100 publications during the last 30 years (1–3). Stroke is still a major noncardiac complication of coronary artery bypass graft (CABG) surgery, with an absolute incidence of 2%. Carotid artery disease has been associated with an increased risk of perioperative stroke after CABG, rising from 3% in predominantly asymptomatic patients with unilateral 50% to 99% stenosis, to 5% in those with

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bilateral 50% to 99% stenosis, and 7% to 11% in patients with carotid occlusion (1,4,5). Moreover, the risk of perioperative stroke in CABG patients who report a prior history of transient ischemic attack (TIA) or stroke has been associated with a 4-fold increased risk as compared to the risk for neurologically asymptomatic patients (8.5% [95% confidence interval (CI): 4.9 to 12.1] versus 2.2% [95% CI: 1.4 to 3.1]) (1). Therefore, it seems appropriate to offer prophylactic carotid endarterectomy (CEA) to neurologically symptomatic patients undergoing CABG who have significant carotid artery disease (2,6–8).

The findings from the SAPPHIRE (Stenting and Angioplasty With Protection in Patients at High Risk for Endarterectomy) trial, including patients with significant cardiac disease, showed that among high-risk patients with severe carotid artery stenosis and coexisting conditions, carotid artery stenting (CAS) using an emboli-protection device is not inferior to CEA (9,10). The CAS-CABG outcome for symptomatic patients remains underreported, notwithstanding these randomized data supporting CAS for high-risk patients. In the available data describing the CAS or CEA-CABG strategy, periprocedural event rates of the symptomatic and the asymptomatic patients are scarcely reported separately. We report the results of CAS and subsequent cardiac surgery in 57 patients with symptomatic carotid artery disease.

Methods

Patient population. In a prospective, nonrandomized study, we entered 57 consecutive symptomatic patients scheduled for CAS and cardiac surgery between December 1998 and January 2008.

Patients were considered symptomatic if an ipsilateral carotid territory stroke or TIA had occurred within 4 months before the procedure. A carotid artery stenosis was considered significant when a diameter reduction of at least 70% on duplex and an angiographic stenosis of more than 50% (using the quantitative coronary analysis technique) of the luminal diameter was measured in the common carotid artery, internal carotid artery, or at the bifurcation according to the NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria (11,12).

The indications for cardiac surgery were symptomatic (documented myocardial ischemia) severe coronary artery disease (including bypass failure) not eligible for percutaneous revascularization, symptomatic valve disease, and disease (aneurysm or dissection) of the ascending aorta or arch that demanded reconstructive surgery. Exclusion criteria included: severe renal impairment (serum creatinine ≥300 μmol/l), peripheral vascular disease precluding femoral artery access, major neurological deficit or any other illness impeding informed consent, severe diffuse atherosclerosis of the common carotid artery, chronic total occlusions, long pre-occlusive lesions ("string sign" lesions). All patients gave written informed consent. This registry was approved by the ethical committee of our hospital.

Endpoint definition. The primary endpoint of the present study was the combined incidence of death, all strokes, and myocardial infarction (MI) from time of CAS to 30 days after cardiac surgery. Secondary endpoints were MI rate and death and major stroke rate from time of CAS to 30 days after cardiac surgery. In the long-term outcome, cumulative event rates at 5 years are reported.

Strokes were considered disabling (major) if patients had a modified Rankin score of more than 3 at 30 days after onset of symptoms. A minor stroke was defined as a Rankin score of 3 or less that resolved completely within 30 days (13). The diagnosis of Q-wave MI, evaluated by an independent cardiologist, was based on the presence of acute chest pain, new Q waves on the electrocardiogram, and an elevated creatine kinase to at least 2× the upper limit of the normal range with an elevated level of MB isoenzyme. In the absence of pathological Q waves, the diagnosis of non–Q-wave MI was based on the increase of creatine kinase level to more than twice the upper limit of the normal range with an elevated level of MB isoenzyme. In our institution, cardiac enzymes are drawn routinely every 8 h during the first 24 h after each procedure. A 12-lead electrocardiogram was performed in all patients following CAS and cardiac surgery. The electrocardiogram was performed daily during the first 48 h following cardiac surgery and in case of unexplained chest pain during the remaining period of hospitalization. Cardio-cerebrovascular mortality was reported separately and was defined as death related to a cardiac or neurological event (14).

Abbreviations and Acronyms

CABG = coronary artery bypass graft

CAS = carotid artery stenting

CEA = carotid endarterectomy

CI = confidence interval

MI = myocardial infarction

TIA = transient ischemic attack

CAS procedure and subsequent cardiac surgery. Carotid stenting has been performed following the highest standard of care using a distal embolic protection device since 2002. Cardiac surgery (including coronary artery bypass, valve, or reconstructive surgery of the ascending aorta) was usually scheduled at least 3 weeks after CAS, unless clinical instability dictated otherwise. The approach in our institution for this staged strategy has been described earlier (14). All patients were clinically evaluated before the procedure, during the procedure, and immediately afterward by an impartial neurologist. Before and after CABG, the same neurologist examined the patients once more. In case of a major stroke, the patient was monitored afterward in the stroke unit. All patients were evaluated by this neurologist at an outpatient clinic after 1 and 3 months.

It is our practice to perform CAS (with dual antiplatelet therapy) and then to stop the clopidogrel 7 days before CABG (aspirin continued). Clopidogrel is restarted (mean time of 2 days) after recovery from surgery. In those patients requiring urgent cardiac surgery, CAS is performed using dual antiplatelet therapy, which is not stopped before the cardiac procedure.

Statistical analysis. Proportions are expressed as percentage and continuous data are expressed as mean ± SD. For right-censored data (i.e., time to event), the Kaplan-Meier method was used to compute the long-term survival, stroke, and MI outcomes with corresponding 95% CI. The log-rank test was used to compare groups. For 95% CI, exact calculations are used (no asymptotic approximations). For all computations, R software (version 2.12, the R Foundation for Statistical Computing, Vienna, Austria) was used.

Results

Patient characteristics. The baseline clinical characteristics of all patients are shown in Table 1. The median waiting time between the last neurological event and the CAS procedure was 36 days (interquartile range: 6 to 90 days).

Angiographic and stenting results. CAS was performed predominantly in the proximal internal carotid artery (n = 52), but it also included the distal (n = 3) and proximal (without involvement of the ostium) (n = 2) common carotid artery. In 2 patients, concomitant left subclavian stenosis or occlusion was treated with angioplasty and stenting. A distal cerebral protection device was used in 29 patients (50.9%) before 2002, and since 2002, in all patients.

The mean angiographic degree of stenosis was reduced from 86 ± 4% to 4 ± 9%. We used a variety of peripheral or carotid stents: 5 Carotid Wall (Boston Scientific, Natick, Massachusetts), 48 Acculink (Guidant/Abbott, Natick, Massachusetts), 3 NexStent (Boston Scientific), and 1 Omnilink (Guidant/Abbott).

Cardiac surgery results. The median time interval between CAS and cardiac surgery was 28 days (interquartile range: 12 to 58 days). In the present series, 52 patients (91.2%) underwent CABG, in whom 4 procedures (7%) were accomplished without cardiopulmonary bypass, 3 patients (5%) had valve surgery combined with CABG, and 2 (3.5%) underwent reconstructive surgery of the ascending aorta. Eight (14%) of the cardiac interventions were redo procedures (second or third). Although the latter group is exposed to a higher risk for cardiovascular complications, we included these patients because they represent a substantial group of patients treated in our daily practice. No major bleeding requiring rethoracotomy was reported in those patients on dual antiplatelet therapy versus those on acetylsalicylic acid alone during surgery.

Table 1. Baseline Clinical Patient Characteristics (N = 57)

Age, yrs	69.7 ± 8.4
Female	19 (33.3)
Hypertension	36 (62)
Diabetes mellitus	8 (14)
Hypercholesterolemia	31 (54.4)
Smoking	11 (19.3)
Previous myocardial infarction	16 (28.1)
Valvular heart disease	14 (24.6)
Congestive heart failure	3 (5.4)
Unstable angina pectoris	21 (36.8)
Previous CABG	8 (14)
Previous PCI	7 (12.3)
Previous CEA	1 (1.8)
Major stroke	3 (5.3)
Minor stroke	12 (21.1)
TIA	42 (73.7)

Values are mean ± SD or n (%).
CABG = coronary artery bypass graft; CEA = carotid endarterectomy; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

Periprocedural outcome and 30-day follow-up. Periprocedural event rates after CAS and after cardiac surgery are listed in Table 2. During the period between CAS and surgery, 1 patient suffered a MI and 4 patients had a minor stroke of which one was contralateral. Cardiac surgery was performed in 57 patients. One patient who suffered from a MI while waiting for CABG died 3 months after CABG. One patient died (cardiac-related) and 1 patient suffered a major stroke within 30 days after cardiac surgery. In the latter patient, post-procedural duplex ultrasonography was performed and showed adequate stent apposition in the treated carotid artery without hemodynamically significant restenosis or stent thrombosis. Male and female patients had similar periprocedural complication rates.

Long-term follow-up. Overall median follow-up was 50 months, with 33% of the patients being followed for ≥60 months. There were 18 deaths (31.6%): 8 (14%) were cardiac-related (2 unknown deaths were considered as cardiac); 2 (3.5%) were neurological deaths; and 8 (11.8%) died of other causes. No repeat carotid intervention for restenosis was necessary. On duplex follow-up in 50 patients (between 3 and 6 months), 4 moderate restenoses (50% to

Table 2. Periprocedural Outcome After Staged CAS and Cardiac Surgery

Event	CAS Patients (n = 57)	Cardiac Surgery Patients (n = 57)	Total (N = 57)
All deaths	0	1 (1.5)	1 (1.5)
Cardiac deaths	0	1 (1.5)	1 (1.5)
Neurological deaths	0	0	0
Nonneurological/noncardiovascular deaths	0	0	0
All strokes*	4 (7.0)	1 (1.5)	5 (8.8)
Major strokes	0	1 (1.5)	1 (1.5)
Minor strokes	4 (7.0)*	0	4 (7.0)
All MIs	1 (1.5)	0	1 (1.5)
All deaths and major strokes	0	2 (3.5)	2 (3.5)
All deaths, all strokes, and MIs	5 (8.8)	2 (3.5)	7 (12.3)

Values are n (%). *Three ipsilateral and 1 contralateral strokes.
MI = myocardial infarction.

65%) were detected. None of these patients had symptoms related to the treated hemisphere. There was 1 late minor stroke and 1 late major stroke. No MI occurred.

A univariate analysis showing the cumulative 5-year event rates is depicted in Table 3. The survival at 5 years was 63.7% (95% CI: 51.3% to 79.1%). The freedom from all deaths, all strokes, or MI is 56.7% (see Kaplan-Meier curve in Fig. 1). The all-cause mortality and the all-death, all-stroke, and MI rates were significantly higher in patients ≥75 years of age than in those <75 years of age.

Discussion

It is considered appropriate to offer prophylactic CEA to CABG patients who have unilateral or bilateral significant carotid artery stenosis if they describe a history of TIA or stroke, especially if the index event was within the preceding 6 months. D'Agostino et al. (8) reported a periprocedural stroke rate of 17.9% in patients with unilateral carotid disease and 26.3% in those with bilateral disease undergoing isolated CABG. These patients have a very high risk of stroke during CABG, and prophylactic intervention can be justified. In the present study, we report the periprocedural complication rates and long-term results of the CAS-CABG strategy in symptomatic patients.

In some systematic reviews, the 30-day stroke rates have been evaluated and varied from 2.7% after staged CEA-CABG (57% asymptomatic) to 4.2% after staged CAS-CABG (87% asymptomatic), 4.6% after synchronous CEA-CABG (59% asymptomatic) and 6.3% after reverse staged CABG-CEA (no detailed data available describing the neurological status) (2,6,7). It is difficult to compare the outcome in symptomatic patients to such data. However, Timaran et al. (15) described the outcome for the symptomatic subpopulation in a large study based on the NIS (Nationwide Inpatient Sample) databases of 27,084 patients undergoing either synchronous CEA-CABG or staged CAS-CABG in the United States between 2000 and 2004. Stratified analyses according to the symptomatic status and type of carotid

Table 3. Cumulative 5-Year Event Rates (Univariate Analysis)

	Cumulative Event Rate at 5 Years (%)	95% CI	p Value
All-cause mortality	36.3	20.9–48.7	
Cardio-cerebrovascular mortality	21.0	7.9–32.2	
MI	1.8	0.0–5.3	
Major stroke	6.1	0.0–14.5	
Minor stroke	9.0	1.1–16.2	
All-cause mortality + minor + major stroke	43.3	27.4–55.7	
Cardio-cerebrovascular mortality (unknown included) + major stroke	22.5	9.2–33.8	
All-cause mortality + all strokes + MIs			
Age <75 yrs	35.4	16.9–49.9	0.02
Age ≥75 yrs	56.9	25.0–75.3	
Symptoms ≤30 days	45.6	16.6–64.5	0.97
Symptoms >30 days	42.8	21.9–58.1	
Without distal protection device	32.6	11.2–48.9	0.12
With distal protection device	55.4	28.0–72.3	
All-cause mortality: men	37.2	18.6–51.5	0.88
All-cause mortality: women	31.6	4.2–51.1	
All-cause mortality: age <75 yrs	27.3	10.0–41.2	0.01
All-cause mortality: age ≥75 yrs	53.9	21.1–73.1	
All-cause mortality: without distal protection device	32.6	11.2–48.9	0.49
All-cause mortality: with distal protection device	39.6	14.5–57.3	

CI = confidence interval; MI = myocardial infarction.

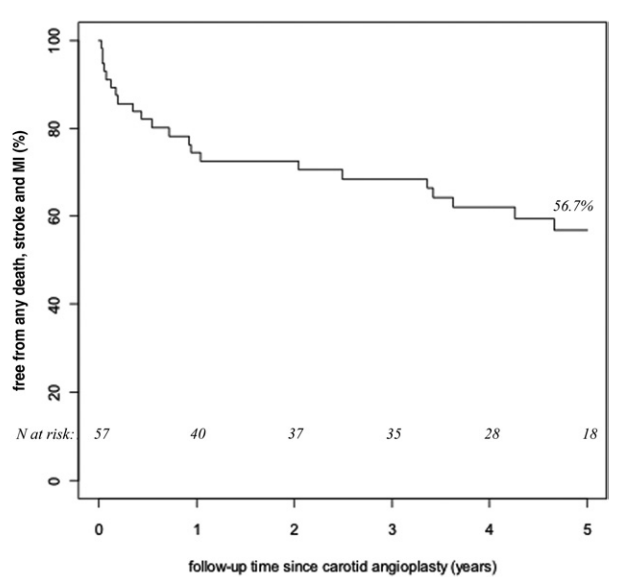

Figure 1. Kaplan-Meier Curve: 5-Year Freedom From All Deaths, All Strokes, and MIs

n indicates number at risk. Data represent Kaplan-Meier curve for patients free from any death, stroke, and myocardial infarction (MI) during follow-up. Percentage on the **right of the black line** represent the freedom from all deaths, all strokes, or MI at 5 years.

revascularization revealed that among 973 patients with symptomatic carotid stenosis, 96.4% underwent CEA-CABG, and post-operative stroke occurred in 14.2%. Only 25 patients with symptomatic carotid stenosis in this series underwent CAS-CABG, and the post-operative stroke rate was 44%. As expected, this reported event rate after CEA-CABG (14.1%) for the symptomatic subpopulation is higher than for the above-mentioned group of mainly asymptomatic patients (2,6,7). However, the 5-fold increased risk of post-operative stroke (44%) for the CAS-CABG approach compared with those undergoing CEA-CABG (odds ratio: 4.7; 95% CI: 2.1 to 10.6; p < 001) is striking. Given the small number of patients undergoing CAS-CABG, This comparison should be interpreted cautiously. In contrast to these findings, we report a favorable 30-day all-stroke rate of 8.8% and a combined risk for death, all strokes, and MI of 12.3% for the CAS-CABG approach. One possible explanation for the lower periprocedural combined risk in the present study compared with the Timaran data may be related to the fact that patients underwent cardiac surgery without discontinuation of aspirin, whereas clopidogrel was administered until 7 days before the operations. The balance between the optimal antiplatelet therapy required for CAS and not postponing CABG seems to influence this outcome favorably (16). Furthermore, the high volume of CAS procedures in our center could account for these favorable short-term results of the combined procedure. The low periprocedural MI rate of 1.5% emphasizes the reduced invasiveness of this approach, which is especially important for these high-risk patients. No statistical difference was found when these CAS results before CABG are compared with the cumulative incidence of the primary endpoint at 30 days in the SAPPHIRE trial for the symptomatic patients (8.8% vs. 2.1% SAPPHIRE CAS, p = 0.212 and 9.3% SAPPHIRE CEA, p = 0.18).

The long-term follow-up showed a survival rate of 63.7% with a significantly higher all-cause mortality rate and all-death, stroke, and MI rate for patients ≥75 years.

We report a 12.3% stroke rate at 3 years, which was not statistically different from the subgroup analyses for symptomatic patients in the SAPPHIRE study (12.3% [7 of 57 patients] vs. 6.0% [3 of 50 patients] in the SAPPHIRE CAS group (p = 0.331) and vs. 8.7% [4 of 46 patients] in the SAPPHIRE CEA group, p = 0.751), taking into account that in our study, all patients underwent CABG, whereas in the SAPPHIRE population, only a minority had coexisting severe coronary artery disease (9,10).

Whether or not the 3% rule for isolated CEA can be achieved in such a high-risk population remains uncertain. However, undertaking a CAS procedure with a ≤3% complication rate in asymptomatic patients and <6% in symptomatic patients should remain the goal of all interventionists (17,18). Patients with recent onset neurological symptoms may pose an additional problem. They face the highest risk of stroke in the first few weeks of the index event, and CAS or CEA may have to be performed with the acceptance that the procedural risk will be higher (19). Delaying the intervention might reduce the procedural risk, but it lessens the benefit of intervening because of the number of strokes that occur while waiting.

Finally, we conducted both crude and propensity score–adjusted comparisons for the periprocedural outcome between this patient group and the asymptomatic population planned for CABG in our center. When analyzing the baseline clinical patient characteristics from this study and the asymptomatic population, we found clinically comparable groups (Table 4). The periprocedural outcome for both groups is shown in Table 5. The stroke rate, as expected, is lower for the asymptomatic patients (3.1% vs. 8.8%, p = 0.05). A short-term propensity score weighting was not applicable due to a low periprocedural event rate. To adjust long-term survival for symptomatic versus asymptomatic patients for differences in baseline characteristics, we used propensity score–weighted Cox proportional hazards modeling. Long-term survival depends on being symptomatic or not. The crude hazard ratio for death is 1.62 (95% CI: 0.94 to 2.77) on average for the first 5 years after CABG for symptomatic patients versus asymptomatic patients. After propensity score–weighting (accounting for sex, age, hypertension, diabetes, smoking, hypercholesterolemia, prior valve disease, prior MI, prior congestive heart failure, and prior CEA), the adjusted hazard ratio is 1.65 (95% CI: 1.17 to 2.33). Therefore, symptomatic patients have worse long-term survival with a hazard ratio of 1.65, which cannot be explained by difference in baseline characteristics.

Study limitations. Only 4 patients underwent off-pump CABG. Therefore, a meaningful comparison with on-pump CABG or CEA–off-pump CABG could not be made (20).

Analyzing the latest natural history data, it becomes clear that about 40% of all strokes occur within the first 24 h after the index event. Therefore, a much earlier carotid intervention should be planned after symptoms (21). Current guideline documents from the American Heart Association/American Stroke Association recommend surgery within 2 weeks of symptom onset (22). These assumptions were not taken into account in our institution until recently. It might also be expected that the periprocedural CAS complication rates will rise when intervening in an earlier phase.

When interpreting the data from Timaran et al. (15), one should take into account the ascertainment bias in the NIS database for strokes after CAS. In the United States, reimbursement for CAS depends on being enrolled in a study. Therefore, all patients are carefully examined before and after therapy by a neurologist. Very few CEA patients are examined by an independent neurologist. Thus, the reporting may not be equal and could make CAS look worse than CEA.

Table 4. Single-Center Baseline Clinical Patient Characteristics for Symptomatic and Asymptomatic Patients Planned for CAS-CABG

	Asymptomatic Patients (n = 356)	Symptomatic Patients (n = 57)	p Value
Age, yrs	72.9 ± 7.7	69.7 ± 8.4	0.01
Female	104 (28.6)	19 (33.3)	0.53
Hypertension	164 (45.1)	36 (62)	0.02
Diabetes mellitus	81 (22.2)	8 (14)	0.17
Hypercholesterolemia	157 (43.1)	31 (54.4)	0.15
Smoking	72 (19.8)	11 (19.3)	0.99
History of neurological symptoms	58 (15.9)		
Previous MI	117 (32.1)	16 (28.1)	0.54
Valvular heart disease	88 (24.2)	14 (24.6)	0.99
Congestive heart failure	46 (12.6)	3 (5.4)	0.12
Unstable angina pectoris	141 (38.8)	21 (36.8)	0.77
Previous CABG	47 (12.9)	8 (14)	0.83
Previous PTCA	47 (12.9)	7 (12.3)	0.99
Previous carotid angioplasty	7 (1.9)		
Previous CEA	16 (4.4)	1 (1.8)	0.49

Values are mean ± SD or n (%).
CAS = carotid artery stenting; PTCA = percutaneous transluminal coronary angioplasty; other abbreviations as in Tables 1 and 2.

Table 5. Comparison of 30-Day Outcome Between Symptomatic and Asymptomatic Patients Undergoing CAS and CABG at St-Antonius Hospital

	Asymptomatic CAS-CABG (n = 356)	Symptomatic CAS-CABG (n = 57)	p Value
Death	13 (3.6)	1 (1.7)	0.70
Stroke	11 (3.1)	5 (8.8)	0.05
MI	7 (2)	1 (1.7)	0.99

Values are n (%).
Abbreviations as in Tables 1, 2, and 4.

Conclusions

We report the outcome of CAS-CABG in symptomatic patients. The periprocedural complication rate and long-term results of the CAS-CABG strategy in this high-risk population support the reliability of this approach. In such a high-risk population, this strategy might offer a valuable alternative to the combined surgical approach; however, a large randomized trial is clearly warranted.

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REFERENCES

1. Naylor AR, Mehta Z, Rothwell PM, Bell PR. Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature. Eur J Vasc Endovasc Surg 2002;23:283–94.
2. Naylor AR, Cuffe RL, Rothwell PM, Bell PR. A systematic review of outcomes following staged and synchronous carotid endarterectomy and coronary artery bypass. Eur J Vasc Endovasc Surg 2003;25:380–9.
3. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA guidelines for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery). J Am Coll Cardiol 1999;34:1262–347.
4. Ricotta JJ, Char DJ, Cuadra SA, et al. Modeling stroke risk after coronary artery bypass and combined coronary artery bypass and carotid endarterectomy. Stroke 2003;5:1212–7.
5. Brown KR, Kresowik TF, Chin MH, Kresowik RA, Grund SL, Hendel ME. Multistate population-based outcomes of combined carotid endarterectomy and coronary artery bypass. J Vasc Surg 2003;1:32–9.
6. Naylor AR, Cuffe RL, Rothwell PM, Bell PRF, Bell PR. A systematic review of outcomes following synchronous carotid endarterectomy and coronary artery bypass: influence of patient and surgical variables. Eur J Vasc Endovasc Surg 2003;26:230–41.
7. Naylor AR, Mehta Z, Rothwell PM. A systematic review and meta-analysis of 30-day outcomes following staged carotid artery stenting and coronary bypass. Eur J Vasc Endovasc Surg 2009;37:379–87.
8. D'Agostino RS, Svensson LG, Neumann DJ, Balkhy HH, Williamson WA, Shahian DM. Screening carotid ultrasonography and risk factors for stroke in coronary artery surgery patients. Ann Thorac Surg 1996;62:1714–23.
9. Yadav JS, Wholey MH, Kuntz RE, et al., for the SAPPHIRE Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004;351:1493–501.

10. Gurm HS, Yadav JS, Fayad P, et al., for the SAPPHIRE Investigators. Long-term results of carotid stenting versus endarterectomy in high-risk patients. N Engl J Med 2008;358:1572–9.
11. NASCET Steering Committee. North American Symptomatic Carotid Endarterectomy Trial. Methods, patient characteristics and progress. Stroke 1991;22;711–20.
12. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325; 445–53.
13. Rankin J. Cerebral vascular accidents in patients over the age of 60. II. Prognosis. Scott Med J 1957;2:200–15.
14. Van der Heyden J, Suttorp MJ, Bal ET, et al. Staged carotid angioplasty and stenting followed by cardiac surgery in patients with severe asymptomatic carotid artery stenosis: early and long-term results. Circulation 2007;116:2036–42.
15. 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.
16. Randall MS, McKevitt FM, Cleveland TJ, Gaines PA, Venables GS. Is there any benefit from staged carotid and coronary revascularization using carotid stents? A single-center experience highlights the need for a randomized controlled trial. Stroke 2006;37:435–9.
17. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421–8.
18. Biller J, Feinberg WM, Castaldo JE, et al. Guidelines for carotid endarterectomy: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke 1998;29:554–62.
19. Naylor AR. Time is brain! Surgeon 2007;5:23–30.
20. Fareed KR, Rothwell PM, Mehta Z, Naylor AR. Synchronous carotid endarterectomy and off-pump coronary bypass: an updated, systematic review of early outcomes. Eur J Vasc Endovasc Surg 2009;37:375–8.
21. Chandratheva A, Mehta Z, Geraghty OC, et al., for the Oxford Vascular Study. Population-based study of risk and predictors of stroke in the first few hours after a TIA. Neurology 2009;72:1941–7.
22. Sacco RL, Adams R, Albers G, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. Stroke 2006;37:577–617.

Key Words: cardiac surgery ■ carotid artery stenting ■ stroke.