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# Same-Day Carotid Artery Stenting and Coronary Artery Bypass Surgery

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## Abstract

**Background:** The optimal treatment strategy for patients with severe carotid artery disease undergoing coronary artery bypass grafting is still problematic. The important question is whether it is necessary to treat significant carotid disease in patients who have undergone coronary artery bypass grafting. This study analyzed short- and midterm results after same-day carotid artery stenting and coronary artery bypass grafting.

**Methods:** From 2013 to 2020, a total of 69 patients were enrolled in the study. Same-day carotid artery stenting and coronary artery bypass grafting were performed in all patients. The study's primary end points were the evaluation rate of stroke, myocardial infarction, and death within short- and midterm periods after the procedures.

**Results:** The 30-day mortality was 0%. The occurrences of perioperative adverse events, namely stroke, myocardial infarction, and transient ischemic attack, were 1 (1.4%), 1 (1.4%), and 4 (5.8%), respectively. Mean (IQR) follow-up time was 28 (IQR, 17-43) months. Six (8.8%) patients died during this period. Fatal stroke was registered in 2 cases, and 1 patient experienced a disabling stroke with a fatal outcome. The other 3 patients died because of chronic renal disease, a traffic accident, and for an unknown reason, respectively. Midterm survival in the group was 91.2%.

**Conclusion:** The study showed that same-day carotid artery stenting and coronary artery bypass grafting for concomitant carotid and coronary disease treatment could be a promising and feasible therapeutic strategy.

**Keywords:** Coronary disease; carotid disease; coronary artery bypass grafting surgery; carotid artery stenting; Lyme carditis; complete heart block; right bundle branch block

## Introduction

Coronary artery disease (CAD) and carotid disease (CD) represent roughly 75% of all cardiovascular diseases. Approximately 10% (range, 4%-20%) of patients with proven CAD have significant CD, whereas 30% to 50% of patients with proven CD have significant CAD.[1]

Transient ischemic attack (TIA), reversible ischemic neurological deficit, and/or cerebrovascular insult represent some of the most frequent and most severe complications that occur during coronary artery bypass grafting surgery (CABG).[2] It is reported in 0% to 2% of cases (average, 1.7%). However, the incidence of cerebral adverse events is much higher in the presence of carotid artery (CA) disease (2%-4%) if one CA is stenotic, 4% to 8% for both carotids, and even 18% if 1 carotid is occluded and the other is stenotic.[2,3]

The etiology of perioperative stroke is multifactorial. Cerebrovascular events were caused by subsequent hypoperfusion resulting from embolic particles from the ascending aorta, CA, and bubbles of gaseous or cerebral hypoperfu-

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sion during and after the cardiac procedure.[4,5] Patients with substantial CA disease are at high risk for periprocedural cerebral events.[6] Transient ischemic attack and the preoperative history of stroke have been associated with a 4-fold increased risk of postoperative events.[3,7] Even if CA disease is present but asymptomatic, patients had a high risk of perioperative stroke after CABG.[8] During the last nearly 50 years, 2 main surgical options have been used in patients with these challenging conditions: a single-stage procedure or a double-stage procedure (either CABG followed by carotid endarterectomy [CEA], or vice versa).[9-11] Optimal management has been discussed in many studies, but the best strategy is still problematic. The better outcome was evident in the surgical revascularization in both symptomatic and asymptomatic CA disease compared with medical treatment.[12] Carotid intervention in asymptomatic patients with CA disease and concomitant coronary disease has been the most controversial issue over the past few years because the management strategy guidelines for this group of patients are still problematic.[13] The data on the efficacy of CA stenting (CAS) in treating asymptomatic CA disease are limited.[14]

This study analyzed the risk of major adverse events (TIA, stroke, myocardial infarction [MI], and death) during the early and midterm follow-up periods after same-day CAS and CABG procedures in patients with significant coronary disease and concomitant CA disease.

### Abbreviations and Acronyms

| | |
|---|---|
| ACT | activated clotting time |
| CA | carotid artery |
| CABG | coronary artery bypass grafting |
| CAD | coronary artery disease |
| CAS | carotid artery stenting |
| CCA | common carotid artery |
| CD | carotid disease |
| CEA | carotid endarterectomy |
| CT | computed tomography |
| ICA | internal carotid artery |
| MI | myocardial infarction |
| NASCET | North American Symptomatic Carotid Endarterectomy Trial |
| TIA | transient ischemic attack. |

## Patients and Methods

### Study Design

This is a prospective nonrandomized longitudinal single-center study conducted from January 2013 to December 2020. The local institutional ethics committee approved the study protocol, and all patients signed the informed consent form. The study included 69 consecutive patients who underwent same-day CABG and CAS procedures.

Inclusion criteria for the study were substantial multivessel CAD that indicated CABG, as well as concomitant severe CA stenosis suitable for carotid stenting procedures. Exclusion criteria for the study were significant heart valve disease, calcification of femoral or iliac arteries, redo procedures, and unfavorable angiographic lesion characteristics for CAS.

### Preoperative Diagnostic Procedures

The heart team (cardiologist, cardiac and vascular surgeons, and radiologist) evaluated all study participants. A preoperative physical exam was performed on all patients. CA disease was determined by a history of cerebrovascular events or carotid bruit on the auscultatory exam. Patients were considered asymptomatic if they had no history of TIA or stroke 120 days before the procedure.

The angiologist performed a preoperative color duplex scan to evaluate CA stenoses, plaque characteristics, and carotid blood flow velocity.

According to the "2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery,"[15] computed tomography (CT) angiography offers excellent sensitivity and specificity for detecting carotid stenosis. The CT angiography scans of all patients confirmed the degree of CA stenosis, characteristics of the carotid plaque, and anatomy of cerebral circulation. Stenoses were measured using the NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria.

The indication for carotid revascularization was a reduction of the artery diameter by more than 80% in asymptomatic patients or by more than 50% in symptomatic patients according to the NASCET criteria. In patients with bilateral CA disease, the severity and morphology of the plaque were used to choose which artery to treat. The radiologists gave final approval regarding the anatomical suitability for carotid stenting.

Unfavorable angiographic lesion characteristics for CAS were recorded and subdivided into "Access," "Arch," or "Target Vessel" groups. Unfavorable access characteristics were low bifurcation/short common carotid artery (CCA), tortuous CCA, diseased CCA, and diseased/occluded external CA.

Arch characteristics included severe arch calcification, significant disease at the origin of the great vessels, type III arch, and bovine arch (conjoint origin of left CCA and brachiocephalic trunk).

Target vessel diseases included pinhole stenosis, circumferential calcification of CA (more than two-thirds of the circumference of the vessel at the lesion site), angulated internal CA (ICA) origin, and angulated distal ICA.

Indication for the CABG procedure was conducted by coronary angiography examination. Significant coronary stenosis was defined as a 50% reduction lumen of the coronary artery or functional flow reserved test value less than 0.75 for borderline stenosis.

Echocardiography was performed in all patients to evaluate heart function (ejection fraction and myocardial contractility), heart valve function, and morphology of the heart and great vessels.

## Interventions

**CAS Procedure Protocol.** Carotid artery stenting was performed in the catheterization laboratory under local anesthesia before cardiac procedures. Pre- and postprocedure neurological status was evaluated, with the aim to detect old and newly created cerebrovascular disturbances. All patients received 100 mg of aspirin starting 2 days before the procedure. The percutaneous transfemoral approach was used in the stenting procedure. Heparin was administered at a dose of 200 IU/kg. All patients used a distal cerebral protection device (Emboshield; Abbott Vascular). Stenoses were dilated before placement and final stent expansion. Xact (Abbott Vascular), Cristallo Ideale (Invatec), and Carotid WALLSTENT (Boston Scientific) balloon-expandable stents were deployed into CCAs. Carotid artery stenting procedures were considered successful if residual stenoses were 20% or less and if complications such as stroke or TIA did not occur. Patients were transferred to the cardiac surgery operating theatre within 1 hour of the stenting procedure's completion. During that period, patients received intravenous heparin via infusion pump according to the activated clotting time (ACT) value, which was measured hourly. The aim was to maintain ACT for around 200 seconds.

**CABG Procedure Protocol.** The CABG procedures were performed using the standard on-pump technique. The surgery was done under general heparinization 400 IU/kg (target ACT >480 seconds). The graft of choice was the internal mammary artery for left anterior decedent artery bypass, and great saphenous vein grafts were used for other coronary target arteries. Standard ascending aorta cannulation and venous cannulation were performed, and cardiopulmonary bypass was performed with a standard nonpulsatile technique. A crystalloid or cold blood cardioplegia was used. After the intervention was complete and patients were weaned from the cardiopulmonary bypass, a complete heparin reversal was conducted by infusing a full dose of protamine and antifibrinolytic agent (tranexamic acid).

**Periprocedural Pharmacological Protocol.** Dual antiplatelet therapy was administered soon after the procedure, provided chest tube bleeding was less than 50 mL for 3 consecutive hours. Six hours after the cardiac procedure, 300 mg of clopidogrel was given as a loading dose in the intensive care unit via nasogastric tube, followed by 75 mg/day for 1 year postoperatively. In the patients with increased chest tube drainage, the clopidogrel loading dose was postponed to 10 hours after the surgical procedure. A 100-mg/day dose of aspirin was started the first morning after the procedure and continued for the remainder of the patient's life.

## End Points

The end points of this study were the evaluation of major adverse events (TIA, stroke, MI, and death) in the early and midterm after the CAS and CABG procedures. A TIA was confirmed if the duration of symptoms (numbness, confusion, trouble seeing, severe headache) lasted fewer than 24 hours. A neurologist evaluated all patients in the early postoperative period. In addition, neurological symptomatology was evaluated using a CA doppler or CT brain examination. If the neurological deficit entirely subsided within 24 hours, a CT scan was not performed. The stroke was defined as a new focal neurologic deficit that persisted longer than 24 hours, with acute or subacute ischemic brain lesions confirmed by CT examination.

Strokes were classified according to their location (ipsilateral or contralateral) and their consequences (fatal, disabling, and nondisabling). A stroke was considered fatal when it caused patient death. The primary characteristic of a disabling stroke was disability 6 months after hospital discharge (at least moderate disability, with the need for some help in daily affairs). A nondisabling stroke was characterized by, after 6 months, patients who, at most, had only slight disability that did not require them to seek assistance with daily affairs.

An MI diagnosis was based on electrocardiogram changes, now regional wall motion abnormality detected by transthoracic ultrasonography, and elevation of the cardio-specific enzymes (CK-MB that was 5 times the 99th percentile of the normal reference range and high-sensitivity troponin I level).

## Follow-Up

Follow-up was performed by telephone interview. All patients were contacted.

### Statistical Analysis

Basic (descriptive) statistics included mean values, SDs, medians, and interquartile ranges of the monitored parameters. The difference in the distribution of specific characteristics among the groups was discovered using the $\chi^2$ or Fisher exact test. The normality of the distribution of numerical variables was examined by applying the Shapiro-Wilk and Kolmogorov-Smirnov tests. The comparison between the groups was made using the Student *t* test and Mann-Whitney test. Binominal logistic regression analysis was used to define the relationship between the dependent binary variable and independent variables. All statistical methods were significant if the *P* value was .05 or less. Statistical software SPSS 25.0 (IBM) for Windows 10 was used to process the data.

**TABLE I. Preoperative Characteristics of Patients[a]**

| Characteristic | No. (N = 69) | % |
|---|---|---|
| Male sex | 49 | 71 |
| Family history of CVD | 43 | 62.3 |
| Hypertension | 67 | 97.1 |
| Hypercholesterolemia | 55 | 79.7 |
| Renal insufficiency | 2 | 2.9 |
| History of TIA | 3 | 4.3 |
| History of stroke | 7 | 10.3 |
| Peripheral vascular disease | 10 | 14.5 |
| COPD | 9 | 13 |
| History of MI | 33 | 47.8 |
| STEMI | 8 | 11.6 |
| Diabetes mellitus | 31 | 44.9 |
| NYHA classification | | |
| Class I | 6 | 8.7 |
| Class II | 50 | 72.5 |
| Class III | 13 | 18.8 |
| Ejection fraction, % | | |
| <30 | 9 | 13 |
| 30-50 | 36 | 52.2 |
| >50 | 24 | 34.8 |

COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; MI, myocardial infarction; NYHA, New York Heart Association; STEMI, ST-segment elevation myocardial infarction; TIA, transient ischemic attack.

[a] Mean (SD) data are for continuous variables with normal distribution; median value and IQRs are for continuous variables with nonnormal distribution.

## Results

The study included 69 patients (49 male, 20 female) with an average (SD) age of 65.3 (7.4) years. Preoperative cerebrovascular adverse events occurred in 14.6% of patients. The preoperative mean EuroSCORE II was 2.1 (IQR, 1.7-2.6). Other preoperative characteristics of the patients are reported in Table I. In 39.1% of patients, diffuse coronary disease was registered. The mean (SD) value of treated carotid stenosis was 84.4% (9.9%), and that of contralateral stenosis was 45.9% (25.3%). The internal CA peak systolic velocity was 320 (IQR, 270-440) cm/s, and the ICA end-diastolic velocity was 145 (IQR, 110-200) cm/s by Doppler velocity measurement. Additional diagnostic characteristics are presented in Table II. No postoperative revision was conducted because of bleeding. Intraoperative and perioperative characteristics are presented in Table III.

### End Points

The 30-day rate of death was 0%. In 1 patient with severe bilateral asymptomatic CA disease, periprocedural ipsilateral stroke was registered. The reason for stroke was acute in-stent thrombosis, as revealed by CT and color duplex scan. In the same patient, because of perioperative MI and ventricular fibrillation, cardiopulmonary resuscitation was performed. This patient was

**TABLE II. Diagnostic Characteristics of Patients**

| | No. | % |
|---|---|---|
| Coronary artery angiography | | |
| Three-vessel coronary disease | 60 | 87 |
| Left main disease | 17 | 24.6 |
| Diffuse coronary disease | 27 | 39.1 |
| CA disease | | |
| Degree of stenosis on treated CA (CT angiography), % | | |
| <60 | 0 | 0 |
| 60-69 | 2 | 2.9 |
| 70-79 | 13 | 18.8 |
| 80-89 | 30 | 43.5 |
| 90-99 | 24 | 34.8 |
| Degree of stenosis on untreated CA (CT angiography), % | | |
| <50 | 36 | 52.2 |
| 50-70 | 22 | 31.9 |
| 70-99 | 6 | 8.7 |
| 100 | 5 | 7.2 |

CA, carotid artery; CT, computed tomography.

discharged from the hospital after the recovery period. The rate of procedural TIA was 5.8%. In these patients, statistical analyses did not show a significant difference in the preoperative characteristics in compared groups. Patients with postoperative TIA were older than were the patients without TIA, at near statistical significance ($P$ = .07). The cardiac procedure in patients with TIA was postponed for 30 days. The clinical outcomes within 30 days after revascularization are presented in Table IV.

### Follow-Up

The mean (IQR) follow-up period was 28 (17-43) months. Six (8.8%) patients died during the follow-up period (Fig. 1). Two patients had a mortality stroke, and one had a massive disabling stroke with fatal complications. All patients who had a stroke had stenosis of 80% to 90%. The reasons for mortality in the other 3 cases were renal failure, a traffic accident, and an unknown cause. Hospitalization resulting from heart failure was registered in 1 case. The patients who died had a significantly lower ejection fraction than the rest of the group (32.5% [12.1%] vs 48.2% [10.17%]) ($P$ = .03). Patient sex had no influence on the in-hospital and midterm mortality rate ($P$ = .999) (Fig. 2), nor did it influence the occurrence of major events ($P$ = .999).

**TABLE III. Intraoperative and Perioperative Characteristics of Patients[a]**

| Characteristic | Value (N = 69) |
|---|---|
| CPB time, mean (SD), min | 76.9 (25.9) |
| Cross-clamp time, mean (SD), min | 53.7 (18.3) |
| No. of bypasses, median (IQR) | 2 (2-4) |
| Inotropic agents, No. (%) | 31 (44.9) |
| Chest tube drainage in 6 h, median (IQR), mL | 200 (100-300) |
| Chest tube drainage in 24 h, median (IQR), mL | 400 (300-575) |
| Ventilation time, mean (SD), h | 12.7 (3.9) |
| Revision because of bleeding, No. (%) | 3 (4.3) |
| Mental confusion, No. (%) | 8 (11.6) |
| Pleural effusion, No. (%) | 3 (4.3) |
| Atrial fibrillation, No. (%) | 19 (27.5) |
| Wound infection, No. (%) | 5 (7.2) |
| Mediastinitis, No. (%) | 0 (0) |
| ICU stay, median (IQR), d | 2 (1-3) |
| In-hospital stay, median (IQR), d | 7 (6-10) |

CPB, cardiopulmonary bypass; ICU, intensive care unit; IQR, interquartile range.

[a] Mean (SD) data are for continuous variables with normal distribution; median value and IQRs are for continuous variables with nonnormal distribution.

## Discussion

Perioperative stroke increased mortality in the open heart surgery population. This condition is multifactorial, caused by atheroembolic dislodgment from the ascending aorta during cannulation, debridement of calcified heart valves, aortic cross-clamping, and proximal anastomosis construction.[8] The rate of perioperative stroke was about 2% in most patients who underwent CABG, but this rate reached 11% in high-risk patients with significant bilateral disease or contralateral occlusion of the carotid artery.[3,16] Patients with asymptomatic severe CA disease had a 3% rate of periprocedural stroke, and stroke increased the mortality rate to 21%.[4,17] Surgical coronary artery revascularization had better clinical results than medical treatment.[12] The 2 most common revascularization strategies are (1) CEA performed at the same time as CABG (simultaneous) or before the CABG procedure (staged) or (2) CAS performed simultaneously (hybrid) or staged with the CABG procedure.[9,10]

The primary goal of this study was to explore the safety of the same-day strategy—CAS followed by CABG—in terms of (1) adverse neurological and/or cardiac events during CAS, (2) adverse neurological and/or cardiac events during CABG, (3) tendency for increased bleeding during CABG, and (4) 30-day rate of major cardiac and/or neurological events.

It was found that this strategy (same-day procedure, sequential CAS followed by CABG) is an acceptable alternative for the 1-stage procedure in a select group of patients.

More than 85% of patients undergo surgical revascularization in Western countries because of asymptomatic CA disease. In the study by Feldman et al,[12] which included 22,501 procedures, more than 96% of patients in the cohort underwent CEA and CABG for asymptomatic disease.

Current guidelines do not recommend routine preoperative screening for CD in those who have undergone cardiac surgery procedures.[18]

**TABLE IV. Clinical Outcomes Within 30 Days of Hybrid Revascularization**

| Major events | No. (N = 69) | % |
|---|---|---|
| Stroke | 1 | 1.4 |
| Transient ischemic attack | 4 | 5.8 |
| Myocardial infarction | 1 | 1.4 |
| Death | 0 | 0 |
| Death/stroke/myocardial infarction | 2 | 2.8 |

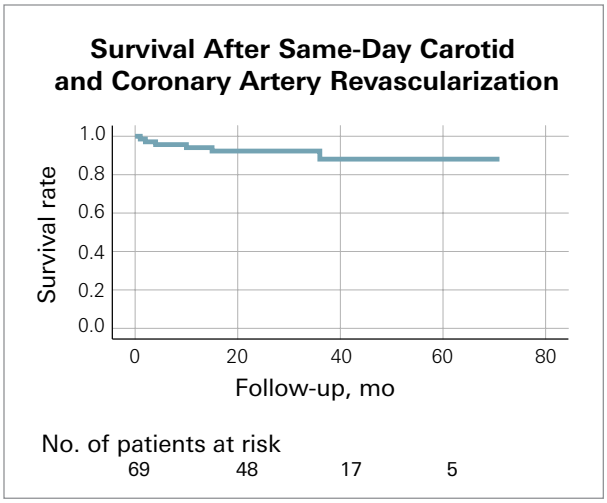


**Fig. 1** Kaplan-Meier survival curve in patients who underwent same-day carotid artery stenting and coronary artery bypass surgery showed an 8.8% mortality rate during the follow-up period ($P < .05$).

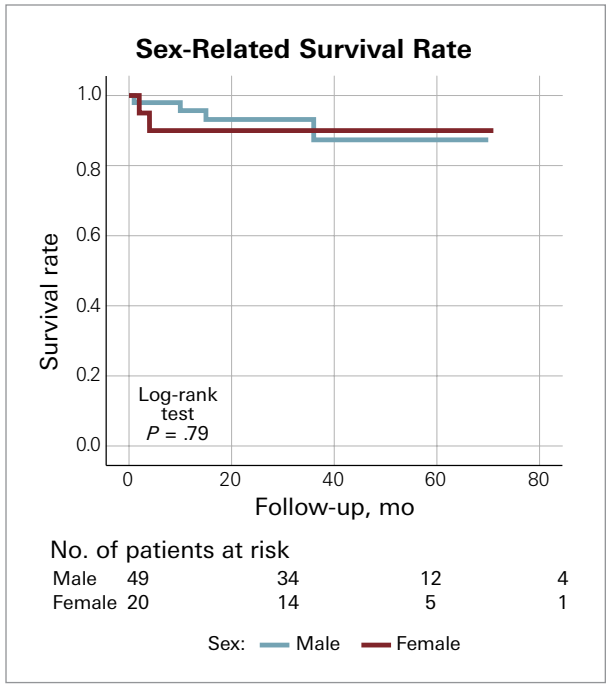


**Fig. 2** Kaplan-Meier survival curves for male and female patients who underwent same-day carotid artery stenting ($P < .05$).

The optimal treatment of combined carotid and heart disease remains controversial, especially in patients with asymptomatic CA disease.[19] The decision to treat asymptomatic disease in the setting of the cardiac procedure was complex because cardiac intervention may be complicated by disease in other vascular beds, but there is no clear evidence of benefits for the treatment of asymptomatic carotid disease simultaneously with cardiac surgery.[20] Santarpino et al[21] showed a low prevalence of perioperative stroke in patients with significant asymptomatic CA disease. Several studies presented a 2% to 4% perioperative stroke rate in a population of patients with untreated 50% to 99% unilateral and bilateral carotid stenosis.[16,19,22] Naylor et al[23] claim that untreated unilateral carotid stenoses of 70% to 99% in populations who undergo open heart surgery did not increase the incidence of perioperative stroke (2%). A prospective multicentric observational study revealed a significant risk of perioperative stroke in patients with CA stenosis of more than 90%.[21] The meta-analysis and systematic review analyzed the 30-day results of different revascularization strategies. In the synchronous CEA and CABG group, cumulative death rates and stroke were 8.2%, and composite outcomes (death, stroke, and MI) were 11.5%. This group had the highest rate of postoperative adverse events. The staged CEA and CABG showed better results than simultaneous surgery (6.1% and 10.2%, respectively).[18] In the CAS and CABG group, rates of adverse outcomes reached 7.5% for death and stroke and 9.4% for composite outcomes.[23] These results show that staged procedures are generally associated with lower stroke and death rates than simultaneous ones.[18,23] Van der Heyden et al[24] described a satisfactory rate of combined death, stroke, and MI (6.7%) in the population of patients with asymptomatic CA disease who underwent staged CAS and CABG. Feldman et al[12] demonstrated that staged CAS and CABG were associated with a low risk of mortality; they claim that this approach could be a viable alternative to the surgical approach (CEA and CABG).[25]

The first multicentric study (101 patients) published by Versaci et al[10] presented 30-day clinical outcomes after the hybrid procedure (CAS and CABG); the rate of major postoperative adverse events was 4%. In this study, the rate of adverse composite outcomes was 2.8% in the 30 postoperative days. The aggregate efficacy/safety outcomes of adverse events during the postoperative period did not differ significantly between CAS and CEA procedures.[16] A meta-analysis by Sardar et al[14] revealed a higher incidence of minor (nondisabling) stroke in the CAS group than the CEA group, where MI was more common. The single-center study by Shishehbor et al[26] suggested that more interstage MI exists in the staged CEA and CABG group. The simultaneous revascularization using CAS and CABG is a feasible and promising therapeutic strategy, a statement confirmed by Versaci et al.[10] Their claim was supported by Brott et al[27] in the guidelines on the management of patients with extracranial carotid and vertebral disease.

The literature described a minimal number of studies that presented results about patients with significant

carotid and coronary disease treated on the same day with simultaneous CAS and CABG.

This study evaluated this new strategy after collecting a reasonable number of patients over an acceptably long period. The reason why the number of patients indicated for this particular strategy was limited (69 patients) was because the decisive factor for indicating this approach was "durability of the carotid lesion," a final decision that was made by the interventional radiologist. Many patients were selected to undergo either single- or double-stage surgical revascularization procedures during the same period. However, these "groups" are impossible to compare owing to the bias inherent in the decision-making process from the beginning. Because of this, randomized and prospective studies might be pretty problematic, even impossible, to design because of the following reasons: (1) institutions are rarely able to recruit enough patients over a reasonably short period, (2) criteria for randomization could be challenging to define, and (3) inconsistency might be a problem owing to the possibility of long-lasting studies.

The only realistic option for exploring this particular surgical strategy is to retrospectively analyze obtained results and eventually compare them with the results obtained at the same institution using another surgical strategy.

### Study Limitations

The small sample size and single-center study were major limitations of this study. Future multicenter prospective randomized studies with a large number of participants are needed to confirm the benefit of this approach.

## Conclusion

The results of this study confirmed the possibility of CAS being a safe and effective option for treating patients with concomitant carotid and coronary disease. Carotid artery stenting and CEA procedures should be complementary rather than competitive strategies that are used based on the individual characteristics of patients with concomitant disease. In these patients, a complex procedure that takes more time and is more logistically demanding should be replaced with a less-complicated one. The future prospective randomized study should additionally confirm this constatation.

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