



Simultaneous Hybrid Revascularization by Carotid Stenting and Coronary Artery Bypass Grafting

The SHARP Study

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Objectives In an attempt to reduce post-operative events we investigated a new therapeutic strategy consisting of a simultaneous hybrid revascularization by carotid artery stenting (CAS), immediately followed by an on-pump coronary artery bypass graft (CABG).

Background Preventing stroke and cardiovascular events after coronary artery revascularization in patients with elevated surgical risk is a complex and multifaceted problem.

Methods One hundred-one consecutive patients with severe carotid and coronary artery disease and a standard EuroSCORE ≥ 5 were included in this multicenter study. Immediately after CAS, patients underwent CABG. The primary end point was the incidence of stroke, acute myocardial infarction (AMI), or death at 30 days. Secondary outcomes were transient ischemic attacks; major local complications; bleeding and systemic complications within 30 days after treatment; and any stroke, AMI, or death occurring from the 31st day to the end of the 12-month follow-up. All clinical outcomes were assessed by an independent monitoring board.

Results The rate of procedural success was 98%. The 30-day cumulative incidence of disabling stroke, AMI, or death was 4%: 2 patients died (2%) in the post-operative period, and 2 patients (2%) had a stroke immediately after CAS and before CABG. Three patients died from the 31st day to the 12th month after the procedure.

Conclusions Our findings indicate that in high-risk patients with coronary artery disease suitable for CABG and carotid artery disease, the hybrid revascularization by CAS immediately followed by CABG is a promising and feasible therapeutic strategy. (J Am Coll Cardiol Intv 2009;2:393–401) © 2009 by the American College of Cardiology Foundation

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The optimal management of patients with concomitant coronary and carotid artery disease is not known (1-4). The importance of this clinical problem is accentuated by the finding that patients frequently present atherosclerosis of both arterial systems: 8% to 14% of coronary artery bypass graft (CABG) patients have significant carotid artery stenosis (5), and 40% to 50% of carotid endarterectomy (CEA) patients have coronary artery disease (CAD) (6,7).

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Among patients undergoing CEA in the Veterans Affairs Cooperative Study (8) and the ACAS study (Asymptomatic Carotid Atherosclerosis Study) (4), 20% and 49% of deaths, respectively, were due to cardiac causes. Similarly, the incidence of perioperative stroke in patients undergoing CABG is elevated in those with concomitant severe carotid artery stenosis (4).

Abbreviations and Acronyms

AMI = acute myocardial infarction

CABG = coronary artery bypass graft

CAD = coronary artery disease

CAS = carotid artery stenting

CEA = carotid endarterectomy

CT = computed tomography

EuroSCORE = European system for cardiac operative risk evaluation

TIA = transient ischemic attack

The combined surgical approach is associated with an increased risk of mortality and morbidity (5,9-11). In the staged surgical approach that addresses the carotid artery lesion with CEA first, followed within several days to several weeks by CABG, the incidence of perioperative stroke during CABG is reduced. However, the risk of acute myocardial infarction (AMI) during CEA and in the period preceding CABG is rather high (5,9,10). Carotid artery stenting (CAS) with cerebral protection devices is rapidly

evolving as an alternative to CEA (12), mainly for patients with severe carotid artery stenosis at high surgical risk, such as patients with CAD (13). A staged CAS-CABG approach has been recently proposed, but the need for a dual antiplatelet aggregation therapy lasting 3 to 4 weeks after stenting might represent a limitation for CABG (14).

We recently proposed a new therapeutic strategy consisting of a simultaneous hybrid complete revascularization by CAS, immediately followed by on-pump CABG. Such an approach has the potential to minimize the incidence of cardiac events in patients at high surgical risk (15). In a subsequent larger study we demonstrated the feasibility of this therapeutic option (16). We carried out the prospective SHARP (Simultaneous Hybrid Revascularization by Carotid Artery Stenting and Coronary Artery Bypass Grafting) study to demonstrate the poten-

tial clinical applicability of this approach as an alternative to the combined or staged strategies currently adopted.

Methods

The study was conducted in 4 high-volume centers: Tor Vergata University Hospital, Rome, Italy (coordinating center); Ospedale Civile di Mirano, Venice, Italy; Heart Center, Hamburg, Germany; and Clinica San Rocco di Franciacorta, Ome, Italy. Only experienced cardiac surgeons (more than 300 CABG procedures performed/year) and interventional cardiologists or radiologist (more than 150 CAS procedures performed as primary operator and more than 50 CAS in the last 2 years) were involved in the study. The protocol was approved by the local institutional ethics committee, and all the patients provided written informed consent.

A team of physicians composed of neurologist, anesthesiologists, cardiac surgeons, and interventional physicians was assembled. The neurologist was responsible for the initial evaluation and neurological follow-up of the patients. An independent data and safety monitoring board of each center, not affiliated with the study investigators, reviewed clinical data to identify safety concerns. The monitoring board in each center was also responsible for selecting all patients with eligible criteria to be included in the registry. **Patients.** Patients were eligible if they were 18 years of age or older, had concomitant critical carotid and coronary disease with coronary arteries impossible to revascularize percutaneously, and were suitable for CABG. All patients had a surgical risk expressed as Standard European system for cardiac operative risk evaluation score (EuroSCORE) ≥ 5 (17,18), a carotid artery stenosis $\geq 50\%$ in the symptomatic disease or $\geq 80\%$ in asymptomatic disease, as determined by the NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria (19). The presence of carotid artery stenosis was evidenced by echocardiography duplex scanning, then confirmed by catheter angiography and either magnetic resonance angiography or computed tomography (CT) scan angiography. A CT scan with or without angiographic dye, depending on preprocedural serum levels of creatinine, was performed in all patients to provide the maximum information regarding the aortic arch, the extent of aortic disease, and the brain (Fig. 1). In case of bilateral carotid artery stenosis, the choice of the carotid artery to treat was made according to clinical criteria or to the severity and morphology of plaque in case of asymptomatic patients.

Exclusion criteria were: coagulopathy; intolerance to heparin, aspirin, ticlopidine, or clopidogrel; ischemic stroke within the previous 6 weeks; presence of intraluminal carotid artery thrombus; peripheral vascular disease precluding use of catheter-based techniques; intracranial aneurism more than 9 mm in diameter; concomitant aortic and valve

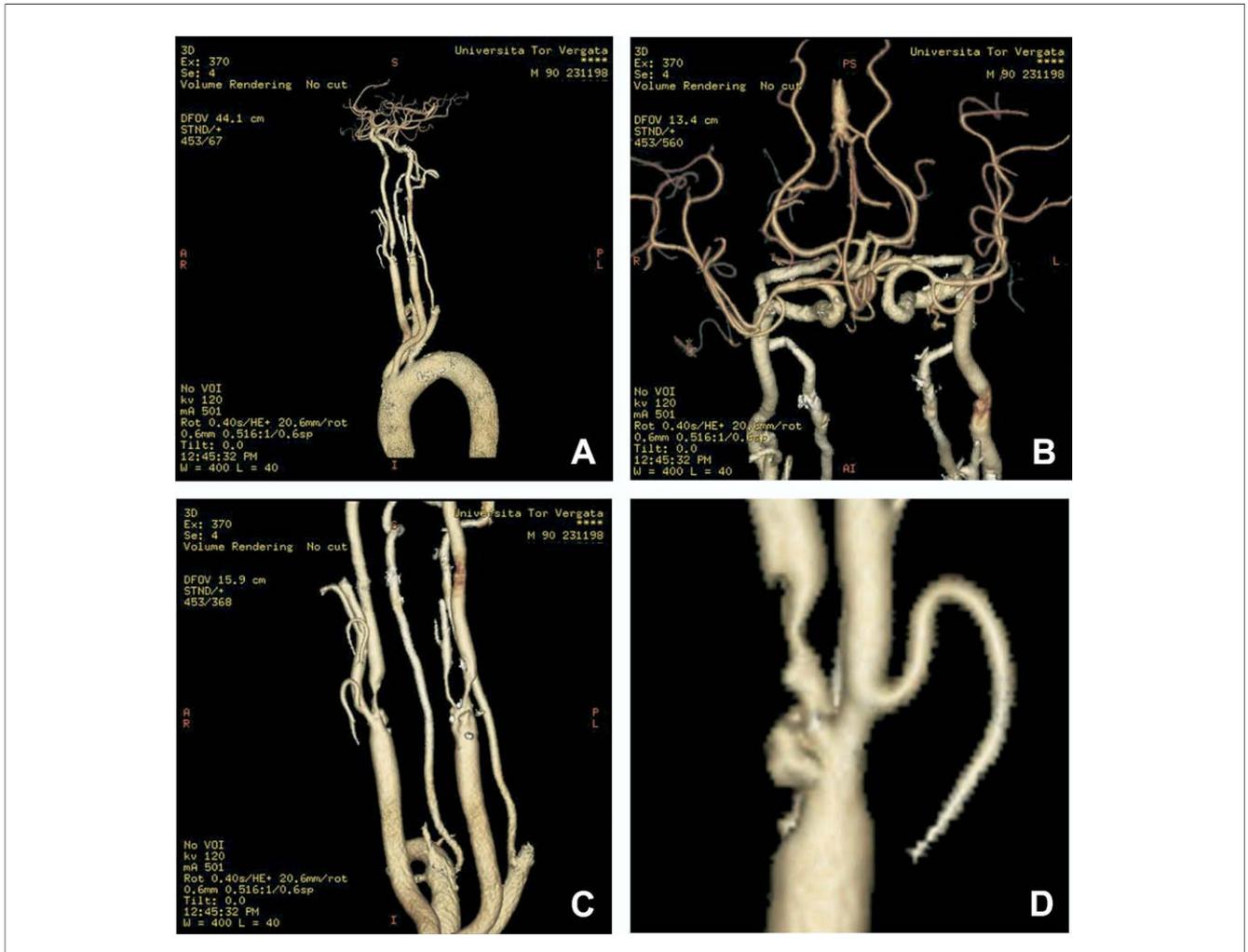


Figure 1. Multidetector CT Scan of Epiaortic Vessels

An electrocardiographic, gated, 64-multidetector computed tomography (CT) scan is performed to provide the maximum anatomical information regarding the aortic arch, the amount of calcium, epiaortic vessels, and intracranial circulation. (A) A CT volume rendering shows a type III aortic arch. (B) Anatomical intracranial circulation. (C, D) Both carotid arteries are involved in critical ulcerated stenosis.

disease or hemodynamically significant valvular heart disease; life expectancy of <1 year; or pregnancy.

Clinical evaluation. Exertional angina was classified according to the Canadian Cardiovascular Society classification (20). Patients were classified as having unstable angina according to Braunwald's criteria (21). Patients were classified as having had an AMI if they had definite electrocardiographic changes and documentation of abnormal cardiac enzyme levels (22). Patients were classified as having had a stroke according to the World Health Organization Task Force on Stroke and other Cerebrovascular Disorders (23).

CAS and CABG. The CAS procedures were performed under local anesthesia through a percutaneous transfemoral access with the use of stents and protection devices approved by the Accreditation Committee. An introducer sheath was positioned in the femoral artery, and heparin (1 mg/kg) was

administered intra-arterially as a bolus. Then a guiding catheter was placed in the common carotid artery, proximally to the bifurcation. A distal filter protection was used in all patients. If needed, the lesion was pre-dilated after the placement of the protection device. After deployment, stents were post-dilated to achieve a residual stenosis $\leq 30\%$. During and after CAS pressure monitoring was obtained to prevent hyperperfusion syndrome. At the end of the procedure, patients were transferred directly to the operating room for CABG. Surgeons performed CABG procedure according to standard practice. All CABG were performed on normothermic cardiopulmonary bypass with warm blood cardioplegia as myocardial cardioplegic protection.

Periprocedural pharmacological protocol. Aspirin 100 mg once daily was started at least 3 days before CAS and daily after combined procedure was performed. As previously

mentioned, heparin was administered 1 mg/kg as a bolus intra-arterially immediately before the stent implantation procedure and in the operating room before the cardiopulmonary bypass 2 mg/kg as a bolus. Activated clotting time (ACT) was checked every 30 min and was constantly maintained ≥ 250 s until the CABG procedure and ≥ 480 s until the end of the cardiopulmonary bypass. Tranexamic acid (TXA) 2 g in bolus was administered as an antifibrinolytic agent over 20 min before sternotomy and then as endovenous infusion (0.5 g/h) until the patient was admitted to the post-operative intensive care unit. Clopidogrel, 300 mg as a loading dose, followed by 75 mg/day for 1 month was started in the intensive care unit via a nasogastric tube 6 h after the end of CABG surgery, providing that surgical bleeding from the thoracic drains had either definitely stopped, or when it was < 50 ml/h for 3 consecutive hours from the sixth post-operative hour on.

Follow-up and end points. Neurological evaluation, including assessment according to the National Institutes of Health Stroke Scale, the Barthel Index of functional levels in activities of daily living, the Rankin scale of functional disability and monitoring for adverse clinical events, was performed within 24 h after the procedures, daily thereafter until hospital discharge, and at 6- and 12-month follow-up visits by a neurologist (24–26).

A computerized tomographic brain scan was performed before discharge from the hospital and compared with the pre-operative CT scan. Color duplex ultrasonography evaluation was repeated before hospital discharge and at the 6- and 12-month follow-up.

The primary end point was the combined incidence of stroke, AMI, or death within 30 days after the treatment. Secondary outcomes were the incidence AMI, TIA, major local complications, bleeding and systemic complications within 30 days after the treatment and the combined incidence of stroke, AMI, or death from the 31st day to 12 months of the follow-up. The occurrence of stroke, AMI, death, and other clinical events was assessed by an independent safety monitoring board that reviewed the data periodically.

Data collection and statistical analysis. Clinical and procedural data were updated on a specific website to be analyzed by the data coordinating center (Division of Cardiac Surgery, Tor Vergata University of Rome). The investigators had full access to all data. Carotid and intracranial arteries angiography was performed before CAS, and the results were analyzed with the use of a computerized system. The study design, all analysis, and the decision to publish were determined solely by the principal investigator and the study investigators. The analysis of immediate, 30-day, and 12-month outcomes was possible for all the patients included in the registry. Continuous variables were tested for normal distribution with the Kolmogorov-Smirnov 1-sample test. Those variables with a normal distribution were expressed as mean \pm SD. Variables with a skewed distribution were logarithmically transformed

for statistical analysis and were expressed as medians and interquartile range. Categorical variables were expressed as proportion and percentages. Statistical analysis was performed according to “intention to treat” analysis. Kaplan-Meier survival analysis was used to analyze event-free survival.

The SAS software (version 8.2, SAS Institute, Inc., Cary, North Carolina) was used for all the analyses. The authors vouch for the completeness and veracity of data and data analyses.

Results

Patients and treatment. Between February 2006 and March 2007, 101 high-risk consecutive patients with severe carotid artery disease and CAD were enrolled in the study. At the time the procedures were performed, 26 patients (26%) had unstable angina, 41 (41%) had exertional angina class III/IV, and 16 (16%) had had a previous cerebrovascular accident. Fifty-six patients (55%) had significant bilateral carotid artery stenosis, 79 (78%) had 3-vessel CAD, and 41 (41%) had left main stem involvement. The mean Standard EuroSCORE was 8.6 ± 2.5 . Other baseline clinical characteristics of the patients are reported in Table 1.

Table 1. Baseline Characteristics of the Patients (n = 101)

Age, yrs	69.2 \pm 8.1
Male sex	86 (85)
Exertional angina class III/IV*	41 (41)
Unstable angina	26 (26)
Diabetes	51 (50)
Chronic renal failure†	15 (15)
Bilateral carotid stenosis	56 (55)
Patients with symptomatic carotid stenosis	15 (15)
Percent carotid stenosis in symptomatic patients	79.4 \pm 9.1
Percent carotid stenosis in asymptomatic patients	80.5 \pm 8.2
Bilateral carotid stenosis	56 (55)
Type III aortic arch‡	8 (8)
CT Agatston score§, median (range)	205 (80–325)
3-vessel disease	79 (78)
Left main involvement	41 (41)
Previous AMI	5 (5)
LVEF	51.7 \pm 11.2
Surgical risk	8.6 \pm 2.5

Values are expressed as mean n (%) or mean \pm SD except where indicated otherwise. *According to the classification system of the Canadian Cardiovascular Society (CCS). †Serum creatinine concentration exceeding 2 mg/dl and creatinine clearance rate of < 50 ml/min. ‡According to the classification of aortic arches for carotid access (reprinted, with permission, from Myla S. Carotid techniques: an algorithmic approach. In: Henry M, Ohki T, Polydorou A, Strigaris K, Kiskinis D, editors. Angioplasty and Stenting of the Carotid and Supra-aortic Trunks. United Kingdom: Taylor & Francis Group, 2004:291–300). §Atherosclerotic burden measurement (reprinted, with permission, from Agatston AS, Janowitz WR, Holdner FJ, Zusmer NR, Viamonte M Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990;15:827–32). ||Surgical risk expressed as EuroSCORE (Eur J Cardiothor Surg 1999;15:816–23). AMI = acute myocardial infarction; CT = computed tomography; LVEF = left ventricular ejection fraction.

Table 2. Characteristics of Treatment and In-Hospital Stay (n = 101)

Stenting	
Mean length of lesion (mm)	15.2 ± 6.4
Predilation of stenosis	25 (25)
Duration of procedure (min)	
Median	27
Interquartile range	14-92
Volume of angiographic dye administered (ml)	42 ± 19
Type of stent used	
Carotid Wallstent (Boston Scientific)	62 (61)
Acculink (Abbott)	17 (17)
X-ACT(Abbott)	12 (12)
Vivexx (Bard Peripheral Vascular)	6 (6)
Cristallo (Invatec)	4 (4)
Cerebral protection used	
FilterWire EZ (Boston Scientific)	39 (39)
Spider (ev3)	5 (5)
EPI FilterWire (Boston Scientific)	46 (46)
AccUNET (Abbott)	11 (11)
CABG intervention	
Duration of extracorporeal circulation (min)	
Median	78
Interquartile range	66-103
Clamping time (min)	
Median	47
Interquartile range	35.5-59.8
Number of graft	3.0 ± 0.7
LIMA + RIMA	18 (18)
Ventilation time (h)	
Median	12
Interquartile range	7.2-13.8
Transfusions (U)	
Median	0
Interquartile range	0-2
Number of red blood cell transfused patients	18 (18)
Number of patients who received more than 2 blood units	1 (1)
Tube drainage	
At 24 h	
Median	310
Interquartile range	60-1,000
Total	
Median	450
Interquartile range	100-1,150
Intensive care stay (days)	
Median	2
Interquartile range	2-3
Post-operative length of stay (days)	
Median	9
Interquartile range	7-14
Values are expressed as mean n (%) or mean ± SD except where indicated otherwise. CABG = coronary artery bypass graft; LIMA = left internal mammary artery; RIMA = right internal mammary artery.	

Table 3. Clinical Outcomes Within 30 Days After Hybrid Revascularization (n = 101)

Nonfatal stroke	2 (2)
TIA	1 (1)
Death	2 (2)
Fatal stroke	0
AMI*	0
Other cause	0
Any stroke, AMI*, or death	4 (4)
Major local complications	
Hematoma	0
Femoral pseudoaneurysm at puncture site	1 (1)
Thrombosis at puncture site	1 (1)
Major bleeding	4 (4)
Renal failure†	1 (1)
Values are expressed as mean n (%). *Acute myocardial infarction (AMI) defined by at least 2 of the following criteria: typical chest pain lasting 20 min or more; serum levels of creatine kinase, creatine kinase-MB, or troponin at least twice the upper limit of the normal range; and new Q-wave on at least 2 adjacent derivations. †Acute renal failure after intervention (serum creatinine >1.5 mg/dl) or impairment of pre-existing chronic renal failure (basal value of serum creatinine + 0.5 mg/dl for 2 consecutive days). TIA = transient ischemic attack.	

In 77 of the 101 patients (76%), the loading dose of clopidogrel was administered 6 h after the end of CABG and, in the remaining 24 patients (24%), 10 h after CABG. Procedural data are reported in Table 2.

End points. The rate of procedural success was 98%, and the 30-day cumulative incidence of disabling stroke, AMI, or death was 4%. Two patients (2%) with severe bilateral carotid artery disease had a stroke immediately after carotid artery stent implantation, with a transient aphasia associated with mild hemiparesis in 1 patient and with paralysis of the left arm in the other patient. In these cases the cardiac surgical procedure was delayed for 2 months, after a partial functional neurological recovery was achieved. One other patient had a brief and transient post-stenting cerebral ischemia that was completely resolved by the end of the stenting procedure. This patient underwent neurological evaluation and CT scan to rule out hemorrhage before inducing general anesthesia for the planned surgical procedure.

Two patients (2%) with a standard EuroSCORE >8 died of multiple-organ failure approximately 30 days after CABG (Table 3).

The 12-month cumulative incidence of stroke, AMI, or death was 7% (95% confidence interval: 0.91 to 0.99) (Fig. 2). Secondary outcomes are reported in Table 3. In particular, 3 patients had post-operative bleeding requiring re-intervention, and 1 patient had pericardial tamponade requiring pericardial drainage 4 days after CABG. Three patients died from the 31st day to 12 months after the procedures.

The median duration of post-operative hospital stay was 9 days (interquartile range, 7 to 14 days). The median

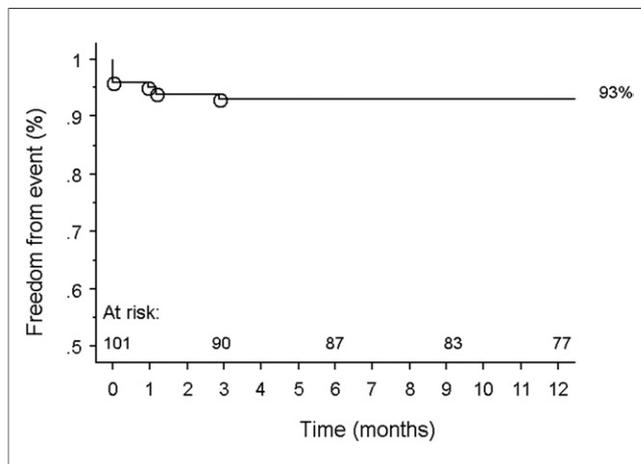


Figure 2. Actuarial Event-Free Survival at 12 Months

Kaplan-Meier event-free survival in patients that underwent simultaneous hybrid revascularization by carotid artery stenting and coronary artery bypass graft surgery. The 12-month cumulative incidence of disabling stroke, acute myocardial infarction, or death was 7%. Three patients died between the 31st day and 12 months after intervention.

duration of intensive care unit stay was 2 days (interquartile range, 2 to 3 days), and the median ventilation time was 12 h (interquartile range, 7.3 to 13.8 h). The incidence of primary outcome events at 12 months is summarized in Table 4.

Discussion

Neurological complications of varying severity unfortunately are relatively common after CABG, in particular in a certain high-risk group of patients. Extracranial carotid artery disease is significantly associated with a type I adverse neurological outcome (i.e., death due to stroke or hypoxic encephalopathy, nonfatal stroke, TIA, stupor, or coma at the time of discharge) (27). Hemodynamically significant carotid artery stenoses are associated with as many as 30% of early post-operative CABG strokes (28). These complications can have important clinical and psychological effects on the affected patients. Roach et al. (27) showed that adverse neurological events occurred in 6.1% of patients, nearly one-half of whom (3.1%) had severe complications including stroke and coma. In those who had complication after CABG, the mortality rate was very high (21%). Preventing stroke and cardiovascular events after CABG is an important and complex problem. The trend to perform coronary surgery in an increasingly elderly population underscores the importance of the issue (29,30). Concomitant carotid artery disease might be a major factor contributing to the occurrence of post-operative stroke (31,32). Other factors, however, might be equally important. Carotid artery disease might be a marker of diffuse atherosclerosis, affecting also aortic arch, arch vessels, and intracranial vessels.

The presence of generalized atherosclerosis might increase the occurrence of hemorrhage, watershed ischemia, or emboli, all of which might result in a stroke. Otherwise, concomitant significant CAD increases the mortality among patients undergoing CEA (2,3). In patients with such a disease, a simplified operative management like hybrid revascularization by CAS and CABG can minimize the negative impact of diffuse atherosclerotic disease. In fact, our findings indicate that, in symptomatic patients with combined carotid artery disease and CAD at high surgical risk, the approach that we proposed is a feasible therapeutic option with good immediate and mid-term clinical results.

Recently, a series published by a single institution in the last 7 years has shown that in 1,769 patients undergoing combined procedures the incidence of stroke and TIA averages 3.8%, AMI averages 3.1%, and mortality averages 4.5% (11). Recently, Hertze and Mascha (33) confirmed these results, reporting a post-operative stroke and operative mortality rate of 10.3% for simultaneous CEA and CABG surgical interventions. According to these results, in a previous series of 180 consecutive patients undergoing combined surgical revascularization at the Tor Vergata University of Rome between 1991 and 2002, the 30-day mortality and stroke rate was 10% and 1.1%, respectively (34), with a mortality rate of 14.5% when the standard EuroSCORE was 6 or more and 3.4% when it was lower than 5. These high-risk patients could be treated by an alternative strategy such as the hybrid approach proposed in this study.

In fact, in a recent study, we demonstrated a reduction of the mortality rate to 5.4% when the hybrid approach was used in high-risk patients (16). Remarkably, 14% of these patients treated with CAS and CABG also underwent valve surgery repair.

As compared with combined surgical revascularization, the hybrid strategy requires a shorter surgical time and less extensive surgical trauma, thus reducing cofactors known to increase morbidity and mortality. A recent meta-analysis demonstrated a superiority of CEA as compared with CAS regarding the evaluation of death and stroke at 30 days (35).

Table 4. Incidence of Clinical Events at 12 Months (n = 101)

Any stroke, AMI, or death at 30 days*	4 (4)
Any stroke, AMI, or death between 31 days and 12 months	3 (3)
Stroke	0
Death	3 (3)
AMI	0
Any stroke, AMI, or death within 12 months	7 (7)

Values are expressed as mean n (%). *Any stroke or death included a stroke in 2 patients immediately after carotid artery stenting implantation, the planned coronary artery bypass grafting was delayed 2 months later after neurological recovery.

AMI = acute myocardial infarction.

However, this superiority is not evident if combined hard end point analysis such as death, stroke, and myocardial infarction are considered (34). As compared with CEA, CAS has uncertain efficacy and safety in patients at risk for stroke for atherosclerotic stenosis of the internal carotid artery (36). In particular in high-risk patients for CEA, mainly due to severe CAD, the SAPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) trial showed that CAS was safer than CEA, because it had a lower postprocedure risk of AMI at 30 days as compared with surgery (13). This is likely to be the case mainly in patients with elevated surgical risk, such as the patients involved in the SHARP (Study of Heart and Renal Protection) study. In fact, according to our inclusion criteria, we enrolled only patients with a standard EuroSCORE equal to or above 5, with an elevated surgical mortality. In particular, when the standard EuroSCORE is 8, as it is in our study, the surgical mortality rate might be as high as 14.5% (18,37,38). In this high-risk subset of patients, specific surgical complications are also elevated: Fukuda et al. (37) reported a morbidity rate of 56.5%. In particular, when both internal carotid arteries have significant stenosis, the risk of stroke after cardiac surgery is particularly high: 25%, as reported by Tunio et al. (38). On the contrary, with the percutaneous hybrid approach as in our study, the stroke rate was only 2% (2 patients), considering that 55% of our patients had bilateral internal carotid artery disease. Such results might also be due to the fact that our study involved only high-volume centers and all the procedures were performed by experienced operators.

In particular, the invasive cardiologist or radiologist involved in the study performed more than 150 CAS as primary operator, according to the consensus document on carotid stenting procedures (39).

Another potential advantage of the simultaneous hybrid approach as compared with a combined surgical approach is that during the CAS procedure the patient is awake and the neurological outcome will be known instantly rather than after the patient emerges from general anesthesia. However, our strategy might have some additional advantages as compared with staged CEA- or CAS-CABG, because it seems to reduce the risk of AMI during CEA (13) or in the time elapsing between the 2 procedures, because this interval is virtually eliminated (40). In fact, the AMI rate in the time the patient is waiting for CABG after carotid artery procedure was 4.4% and 5.8%, respectively, when CEA- and CAS-CABG was performed (11,38). Finally, we reported the same intensive care and hospital stay, compared with our low-risk patients, despite the elevated risk of morbidity of patients enrolled. This fact is very important also for economic reasons, because costs are reduced in the high-risk subset of patients, as in those with high EuroSCORE (41).

Normothermic cardiopulmonary bypass has been used in our patients. Although hypothermia might be safer from a neurological point of view (42), it carries a higher risk of bleeding, due to platelet dysfunction, in patients that should undergo aggressive antiplatelet aggregation treatment after CAS (43).

It is likely that off-pump techniques might further reduce the overall stroke risk, especially in patients with aortic wall disease.

Nonetheless, our study also demonstrated safety of the periprocedural pharmacological protocol and the timing of antiplatelet administration proposed: in fact, the bleeding rate after surgical intervention was low. Only 1 patient had pericardial tamponade requiring pericardiocentesis, and 3 patients had bleeding after surgery requiring reintervention. In all patients the need for post-operative blood transfusions was not different from those who underwent conventional treatment where antiplatelet aggregation therapy was stopped before CABG (44).

Moreover, no cardiovascular event, stroke, or TIA occurred from hospital discharge to the first 30-days of the follow-up.

Therefore, in patients with combined carotid artery disease and CAD at high surgical risk, the proposed hybrid approach seems to be a possible alternative therapeutic strategy.

Study limitations. This study has a certain number of limitations. It was not a randomized trial comparing hybrid approach (CAS and CABG) versus an all surgical approach (CEA and CABG). The patient population is not very large, although composed of carefully selected individuals coming from 4 high-volume centers. Indeed, at the present time a larger number of patients with multivessel CAD are treated percutaneously, with drug-eluting stents in particular, when at high surgical risk.

The use of angiographic dye during the CAS procedure might be the major drawback of this approach, in particular in high-risk patients with chronic renal failure. In our study only 1 patient with chronic renal failure had transient renal impairment after the procedure. Particular attention was made to reduce the amount of angiographic dye (i.e., a "road-mapping" X-ray acquisition was used during the stent implantation, and in patients with chronic renal failure, a pre-treatment with fluid administration and acetylcysteine was made) (45).

Conclusions

Even if a randomized clinical study is needed to verify our clinical approach, our findings indicate that, in high-risk patients with CAD suitable for CABG and carotid artery disease, hybrid revascularization by CAS immediately followed by CABG is a feasible and promising therapeutic strategy.

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REFERENCES

- Mackey WC, O'Donnell T, Callow AD. Cardiac risk in patients undergoing carotid endarterectomy: impact on perioperative and long-term mortality. *J Vasc Surg* 1990;11:226-33.
- North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade of carotid stenosis. *N Engl J Med* 1991;325:445-53.
- European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Surgical Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. *Lancet* 1991;337:1235-43.
- Executive committee for the asymptomatic carotid atherosclerosis study: Endarterectomy for Asymptomatic Carotid Atherosclerosis Study. *JAMA* 1995;273:1421-8.
- Borger MA, Fremes SE, Weisel RD, et al. Coronary bypass and carotid endarterectomy: does a combined approach increase risk? A meta-analysis. *Ann Thorac Surg* 1999;68:14-20.
- Cishek MB, Gershony G. Role of percutaneous transluminal coronary angioplasty and bypass graft surgery for the treatment of coronary artery disease. *Am Heart J* 1996;131:1012-7.
- Salasidis GC, Latter DA, Streinmetz OK, et al. Carotid artery duplex scanning in preoperative assessment for coronary artery revascularization: the association between peripheral vascular disease, carotid artery stenosis, and stroke. *J Vasc Surg* 1995;21:154-62.
- Hobson RW II, Weiss DG, Fields WS, et al. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. *N Engl J Med* 1993;328:221-7.
- 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.
- Das SK, Brow TD, Pepper J. Continuing controversy in the management of concomitant coronary and carotid disease: an overview. *Int J Cardiol* 2000;74:47-65.
- Huh J, Wall M Jr., Soltero E. Treatment of combined coronary and carotid artery disease. *Cur Opin Cardiol* 2003;18:447-53.
- Mathias KD. Angioplasty and stenting for carotid lesions: an argument for carotid lesions. *Adv Surg* 1999;32:225-43.
- Yadav JS, Wholey MH, Kuntz RE, et al. Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493-501.
- Lopes DK, Mericle RA, Lanzino G, Wakhloo AK, Guterman LR, Hopkins LN. Stent placement for the treatment of occlusive atherosclerotic carotid artery disease in patients with concomitant coronary artery disease. *J Neurosurg* 2002;96:490-6.
- Chiariello L, Tomai F, Zeitani J, Versaci F. Simultaneous hybrid revascularization by carotid stenting and coronary artery bypass grafting. *Ann Thorac Surg* 2006;81:1833-5.
- Versaci F, Del Giudice C, Scafari A, et al. Sequential hybrid carotid and coronary artery revascularization: immediate and midterm results. *Ann Thorac Surg* 2007;84:1508-13, discussion 1513-4.
- Roques F, Nashef SA, Michel P, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. *Eur J Cardiothorac Surg* 1999;15:816-22.
- Toumpoulis IK, Anagnostopoulos CE, Swistel DG, DeRose JJ Jr. Does EuroSCORE predict length of stay and specific postoperative complications after cardiac surgery? *Eur J Cardiothorac Surg* 2005;27:128-33.
- North American Symptomatic Carotid Endarterectomy Trial: methods, patient characteristics, and progress. *Stroke* 1991;22:711-20.
- Campeau L. Grading of angina pectoris. *Circulation* 1976;54:522-3.
- Braunwald E. Unstable angina: a classification. *Circulation* 1989;80:410-4.
- Anderson JL, Adams CD, Antman EM, MD, et al. Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction). *J Am Coll Cardiol* 2007;50:1-157.
- Goldstein M, Barnett HJM, Orgogozo JM, et al. Recommendations on stroke prevention, diagnosis, and therapy. Report of the WHO Task Force on Stroke and other Cerebrovascular Disorders. *Stroke* 1989;20:1407-31.
- Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. *Md State Med J* 1965;14:61-5.
- Rankin J. Cerebral vascular accidents in patients over the age of 60. II. Prognosis. *Scott Med J* 1957;2:200-15.
- Brott T, Marler JR, Olinger CP, et al. Measurements of acute cerebral infarction: a clinical examination scale. *Stroke* 1989;20:864-70.
- Roach GW, Kanchuger M, Mangano CM, et al. Adverse cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. *N Engl J Med* 1996;335:1857-63.
- D'Agostino RS, Svensson LG, Neuman 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.
- 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.
- Prati P, Vanuzzo D, Casaroli M, et al. Prevalence and determinants of carotid atherosclerosis in a general population. *Stroke* 1992;23:1705-11.
- Faggioli GL, Curl GR, Ricotta JJ. The role of carotid screening before coronary artery bypass. *J Vasc Surg* 1990;12:724-9.
- Schwartz LB, Bridgman AH, Kieffer RW, et al. Asymptomatic carotid artery stenosis and the stroke in patients undergoing cardiopulmonary bypass. *J Vasc Surg* 1995;21:146-53.
- Hertze NR, Mascha EJ. A personal experience with coronary artery bypass grafting, carotid patching, and other factors influencing the outcome of carotid endarterectomy. *J Vasc Surg* 2006;43:959-68.
- Borioni R, Nardi P, Garofalo M, et al. Eventi cardiologici a lungo termine dopo endarteriectomia carotidea. *Ital Heart J Suppl* 2004;5:534-8.
- Ederle J, Featherstone RL, Brown MM. Percutaneous Angioplasty and Stenting for Carotid Artery Stenosis. The Cochrane Collaboration. Issue 1. Hoboken, NJ: John Wiley and Sons, 2008.
- Mas JL, Chatellier G, Beysen B, et al., EVA-3S Investigators. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. *N Engl J Med* 2006;355:1660-71.
- Fukuda M, Takagi Y. Application of preoperative risk severity evaluation system (EuroSCORE=European system for cardiac operative risk evaluation) for cardiac operative patients. *Masui* 2004;53:1149-54.
- Tunio AM, Hingorami A, Ascher E. The impact of an occluded internal carotid artery on the mortality and morbidity of patients undergoing coronary artery bypass grafting. *Am J Surg* 1999;178:201-5.
- Cremonesi A, Setacci C, Bignamini A, et al. Carotid artery stenting. First consensus document of the ICCS-SPREAD Joint Committee. *Stroke* 2006;37:2400-9.
- Randall MS, McKewitt 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.
- Pinna Pintor P, Bobbio M, Colangelo S, Veglia F, Marras R, Diena M. Can EuroSCORE predict direct costs of cardiac surgery? *Eur J Cardiothorac Surg* 2003;23:595-8.

42. Rees K, Beranek-Stanley M, Burke M, Ebrahim S. Hypothermia to reduce neurological damage following coronary artery bypass surgery. *Cochrane Database Syst Rev* 2001;1:CD002138.
43. Boldt J, Knothe C, Welters I, Dapper FL, Hempelmann G. Normothermic versus hypothermic cardiopulmonary bypass: do changes in coagulation differ? *Ann Thorac Surg* 1996;62:130-5.
44. Levi M, Cromheecke ME, de Jonge E, et al. Pharmacological strategies to decrease excessive blood loss in cardiac surgery: a meta-analysis of clinically relevant endpoints. *Lancet* 1999;354:1940-7.
45. Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000;343:180-4.

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