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Clinical Research

Combined Carotid and Cardiac Surgery: Improving the Results

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Background: Aim of this study was to analyze our experience in the last 5 years of combined carotid and cardiac surgery.

Methods: During a 5-year period (January 2002-December 2006), 111 patients underwent combined carotid endarterectomy (CEA) and coronary artery bypass grafting (CABG) (group 1), while 1,446 patients underwent isolated CEA (group 2). Perioperative outcomes in the two groups were compared using χ^2 and Fisher's exact tests to analyze neurological deficits, cardiac events, and death at 30 days. Results during follow-up were analyzed using Kaplan−Meier survival curves, and both groups were compared using the log-rank test.

Results: Immediate postoperative neurological deficits occurred more frequently in group 1 patients (2.5 vs. 0.4%, $p = 0.002$), with a higher incidence of transient ischemic attacks in group 1; however, there was no difference in the incidence of stroke (1% group 1 vs. 0.6% group 2, $p =$ n.s.). Mortality rate was increased in the combined surgery group (3.5 vs. 0.5%, $p < 0.001$). Combined stroke/myocardial infarction/death rate at 30 days was 6.3% in group 1 compared with 1.4% in group 2, $p = 0.001$. Perioperative stroke/myocardial infarction/death rate was much improved in the 55% (61/111) of patients undergoing CABG off-pump (3.3 vs. 10%, $p = 0.001$). Mean follow-up was 18.7 months (range, 1-60). Survival at 24 months was significantly higher in patients of group 2 compared with group 1 (99.4 vs. 91.3% respectively, $p < 0.001$). At 24 months, there was no significant difference between the two groups in the risk of developing ipsilateral or contralateral neurologic events (3.1% group 1 vs. 1.7% group 2).

Conclusion: In our experience, combined CEA and cardiac surgery carries a higher risk of perioperative mortality than patients undergoing isolated CEA. Whenever possible, CEA combined with off-pump CABG seems to be the therapeutic strategy of choice.

INTRODUCTION

The association between carotid artery stenosis and cardiac disease is commonly encountered in clinical practice. Patients undergoing either carotid endarterectomy (CEA) or coronary artery bypass grafting (CABG) frequently have systemic atherosclerotic disease. Approximately 28% of patients who are candidates for CEA have significant correctable coronary artery disease; 12% of patients undergoing myocardial revascularization are noted to have carotid artery stenosis of more than 80%, and 22% of patients undergoing CABG have > 50% carotid stenosis.[1-3]

In addition, coronary artery disease contributes in large part to the perioperative and long-term mortality of patients undergoing CEA. Even in patients in whom CEA is not indicated, atherosclerosis is considered an important marker of coronary sclerosis.[4] In asymptomatic patients with carotid stenosis, the annual risk of myocardial infarction is

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between 5 and 9%, or higher than the annual risk of ipsilateral stroke. In contrast, the percentage of perioperative neurological events occurring during CABG varies between 1 and 5.2%.[5] Various mechanisms have been proposed for these events: atherosclerotic plaques of the ascending aorta, intraventricular thrombus, gaseous microembolizations, lipidic particles, thrombus forming during CABG surgery, carotid thromboembolic events, and cerebral hypoperfusion.[6,7]

Because of the multifactorial nature of these neurological events, the management of carotid arterial stenosis in patients who are candidates for CABG remains controversial. Proposed therapeutic strategies have included simultaneous CEA-CABG, staged or reverse staged procedures, performing only CABG, carotid artery stenting (CAS) before CABG, and the use of off-pump CABG.[8-10] However, despite multiple studies, there remain no generally accepted guidelines for the optimal therapeutic approach to adopt in this subgroup of patients.

The purpose of this study was to analyze our experience in the last 5 years of combined CEA and cardiac surgery, with the aim of highlighting short and mid-term results, possible risk factors, and comparing outcome to a control group of patients undergoing isolated CEA during the same period.

MATERIALS AND METHODS

Study Group

Over a 5-year period (January 2002-December 2006), 1,557 consecutive CEA procedures were performed by the Department of Vascular Surgery of the University of Florence. In 111 of these cases, CEA and cardiac surgery were performed simultaneously (group 1), while the remaining 1,446 patients underwent isolated CEA (group 2). All data regarding the operations performed were prospectively entered into a database, including preoperative assessment, surgical techniques and intraoperative neurologic monitoring, immediate and 30-day perioperative outcomes, and mid-term follow-up.

Preoperative Evaluation

All patients preoperatively underwent clinical history and physical examination; a two-view chest X-ray; laboratory tests, including complete blood count, coagulative parameters, and blood chemistries; an electrocardiogram; an echocardiography; a cardiac consultation; and a Duplex ultrasound scanning of extra-cranial vessels. Coronary angiography was performed in all group 1 patients.

Furthermore, all patients underwent preoperative computerized tomography angiography or magnetic resonance imaging/angiography with evaluation of the aortic arch and carotid arteries, the cerebral circulation and parenchyma.

Indications for carotid surgery were carotid stenosis $\geq$70% in asymptomatic patients and $\geq$ 50% in symptomatic ones; the degree of carotid stenosis was determined on the basis of NASCET criteria. Our indications did not differ whether the patient underwent combined carotid and cardiac surgery.

Patients were considered to be asymptomatic in the absence of neurological symptoms (transient ischemic attacks [TIA] or stroke) within 6 months from the intervention.

Surgical Strategy

Surgery for group 1 patients was carried out in collaboration with the Department of Cardiac Surgery of the Careggi Hospital in Florence. In all cases of combined surgery, the cardiosurgical operation always followed the CEA carried out under general anesthesia.

Before clamping the carotid artery, the patient was administered 30 IU/kg bolus heparin. Stump pressures were not measured. Cerebral function was monitored with somatosensory evoked potentials (SEPs) with selective use of a carotid shunt in cases of critical reduction (>50%) in SEPs. After CEA completion, cardiac surgery was performed with heparin supplemented to reach an ACT of greater than 500 seconds. In cases of surgery under cardiac arrest, the aorta was connected to the right atrium with a ‘‘two stage’’ cannula and initiation of cardiopulmonary bypass.

Isolated CEA surgery was executed using the same surgical strategy and anesthesia described in previous articles from our center, which involve extensive use of locoregional anesthesia with clinical monitoring of cerebral function, routine use of preliminary clamping of the internal carotid artery, reconstruction with patch angioplasty in most cases, intraoperative quality control with duplex and in some cases with angiography.[11]

Postoperative Management and Follow-up

Group 1 patients were typically hospitalized in the cardiac surgery ward 2 days before surgery, and transferred to the intensive care unit at the completion of surgery, then moved to a subintensive therapy unit and wards equipped to carry out cardiac rehabilitation which lasted for approximately 10 days. Patients in group 2, at the end of surgery, were transferred to a general hospital ward or, in some cases, to intensive or subintensive therapy units for monitoring.

Neurological outcomes during hospital stay were assessed by a vascular surgeon. Neurological evaluation at 30 days was independently performed in all patients by an experienced neurologist to evaluate the presence of any differences respect to the preoperative period about the neurological status.

Moreover, follow-up was performed at 1, 6, 12 months, and yearly thereafter by carotid Duplex scanning. All studies were performed using an Acuson Sequoia 512 Ultrasound System (Acuson Corporation, Mountain View, CA).

Statistical Analysis

Perioperative results in the two groups were compared using the χ^2 test and Fisher's exact test to analyze neurological deficits, cardiac events, and death at 30 days. The results during follow-up were analyzed using Kaplan–Meier survival curves, and outcomes of both groups were compared using the log-rank test. Statistical analysis was carried out using the SPSS 15.0 for Windows software (SPSS Inc., Chicago, IL).

RESULTS

Anatomical-Clinical Characteristics

Patient demographics of the two groups are shown in Table I. There were significantly higher rates of diabetes, peripheral artery disease, and ischemic heart disease in group 1 patients. The majority of patients in both groups were asymptomatic from a neurologic standpoint, but especially in group 1 (95 vs. 66%, $p < 0.001$). Carotid artery stenosis in group 1 was often incidentally found as a result of a routine preoperative cardiosurgical screening program. Among the symptomatic patients, the most frequently encountered clinical presentation was TIA in both groups. In group 2, 39 patients were treated acutely or 6% of the total patients (Table II).

The anatomical and morphological characteristics of the carotid lesions in the two groups of patients are shown in Table III. There were no differences in the two groups regarding type of carotid pathology (primary or recurrent stenosis), incidence of contralateral carotid occlusion, or prior contralateral CEA.

Table I. Demographic characteristics and comorbidities

Characteristics	Group 1	Group 2	p
Age	73.2	72.3	0.02
Male sex	82 (74%)	1,017 (70%)	NS
Hypertriglyceridemia	37 (33%)	431 (30%)	NS
Hypercholesterolemia	47 (42%)	655 (45%)	NS
Hypertension	78 (70%)	1,059 (73%)	NS
Diabetes	34 (30%)	281 (19%)	0.01
Smoker	13 (11%)	241 (16%)	NS
Ex-smoker	56 (50%)	739 (51%)	NS
PAOD	46 (41%)	387 (26%)	0.001
Ischemic cardiopathy	111 (100%)	249 (17%)	< 0.001

Table II. Clinical characteristics of patients

Characteristics	Group 1	Group 2	p
Asymptomatic	105 (95%)	965 (66%)	< 0.001
TIA	5 (4%)	265 (18%)	< 0.001
Minor stroke	1 (1%)	55 (4%)	0.001
Major stroke	0	14 (1%)	NS
Vertebrobasilar	0	108 (8%)	< 0.001
Acute	0	39 (3%)	NS

Table III. Anatomical and morphological characteristics

Characteristics	Group 1	Group 2	p
Degree of stenosis 60–79%	41 (37%)	627 (43%)	NS
Degree of stenosis 80–99%	69 (62%)	753 (52%)	NS
Pseudo-occlusion	1 (1%)	55 (4%)	NS
Aneurysm/ pseudoaneurysm	0	11 (1%)	NS
Contralateral occlusion	6 (5%)	78 (5%)	NS
Primary lesion	101 (91%)	1,207 (83%)	NS
Restenosis	1 (1%)	57 (5%)	NS
Prior contralateral CEA	9 (8%)	182 (12%)	NS

Intraoperative Characteristics

The 111 patients who underwent combined surgery were administered general anesthesia and intraoperative cerebral monitoring was based on the use of SEPs with selective use of a carotid shunt on the basis of wave modifications N20/P25.[11] In contrast, in group 2 it was possible to use local anesthesia in almost half of the patients, with direct neurological monitoring of the cooperative patient. Selective use of a carotid shunt was seen mainly in group 2 rather than group 1 (9 vs. 3%, $p = 0.02$); however, routine shunt rates were similar (Table IV). CEA was performed with application of a patch in the majority of cases, and carotid clamp times were similar in both groups (Table V).

Cardiac surgery consisted of myocardial revascularization in all cases. Cardiac surgery was carried out using cardiopulmonary bypass in 50 cases (45%) and was associated with other types of operations in 24 cases, as indicated in Table VI. Off-pump CABG was performed in 61 cases (55%).

The medium left ventricular ejection fraction in patients of group 1 was 47% (range, 30-60%). The mean number of bypasses performed was 2.6 ± 1.1 (range, 1-5), whereas the mean duration of cardiopulmonary bypass was 79.9 ± 31 min (range, 35-215).

Group 1 patients were hospitalized after surgery for a mean of 3.3 ± 6.6 days in the intensive care unit (range, 1-53). Total preoperative and postoperative hospitalization was on average 11.1 ± 5.4 days (range, 4—29).

Short-Term Results

We observed a higher incidence of immediate postoperative neurological deficit in group 1 patients, 2.5 versus 0.4% ($p = 0.002$), but this was mostly attributable to a higher incidence of TIA in this group. There was no difference in the incidence of stroke between the two groups at 30 days (1% group 1 vs. 0.6% group 2, $p =$ n.s.).

As expected, there was a higher perioperative mortality rate in the cardiac surgery group, 3.5 versus 0.5% ($p < 0.001$), linked primarily to cardiac complications (Table VII). At 30 days postsurgery, four patients of group 1 had died: one due to myocardial infarction, two due to multiorgan failure, and one due to complications of aspiration pneumonia. Three of four cases had undergone CABG using cardiopulmonary bypass. The single minor stroke that occurred in group 1 was also in a patient undergoing CABG with cardiopulmonary bypass. Perioperative stroke/myocardial infarction/death rate was much improved in the 55% (61/111) of patients undergoing CABG off-pump (3.3 vs. 10%, $p = 0.001$).

Long-Term Results

Mean follow-up was 18.7 months (range, 1-60). Estimated survival at 24 months was significantly higher in group 2 compared with group 1 (99.4 vs. 91.3% respectively, $p < 0.001$) (Fig. 1). The primary cause of death during follow-up in both groups was cardiac disease. At 24 months, there was no significant difference in the risk of subsequent neurologic events between the two groups (3.1 and 1.7%, $p =$ n.s., respectively), and the incidence of significant carotid restenosis (>70%) was 8% in group 1 and 11% in group 2 ($p =$ n.s.).

Table IV. Type of anesthesia and intraoperative cerebral protection

Method	Group 1	Group 2	*p*
General anesthesia	111 (100%)	730 (51%)	< 0.001
Local anesthesia	0	716 (49%)	< 0.001
Shunt for SEPs reduction or clinical alterations	3 (3%)	128 (9%)	0.02
Routine shunt use	4 (4%)	27 (2%)	NS

Table V. Type of carotid reconstruction

Technique	Group 1	Group 2	*p*
Direct suturing	3 (3%)	137 (9%)	NS
Patch	104 (87%)	1,258 (93%)	NS
Bypass/graft	3 (3%)	17 (1%)	NS
Eversion	1 (1%)	34 (2%)	NS
Carotid clamp time (min)	31	30	NS

Table VI. Cardiosurgery associated with CABG

Associated valvular	21	19%
Septum myomectomy	1	0.9%
Ventriculoplasty	2	1.8%

DISCUSSION

The incidence of neurological complications after coronary artery bypass has remained essentially unchanged over the past three decades with a 2% incidence of stroke.[12,13] Stroke is certainly one of the most feared complications following CABG, with a 24.8% mortality and mean hospital stay for survivors of 28 days.[5-7] Multiple risk factors for stroke in patients undergoing CABG have been identified, including age, preoperative neurologic symptoms, aortic arch disease, carotid bruit, diabetes, and degree of carotid stenosis. The heterogeneity of these factors suggests that the etiology of post-CABG stroke is certainly multifactorial and interlinked. In the high-risk subgroup of patients noted to have coexistent carotid disease; it has been estimated that 40-50% of post-CABG strokes

Table VII. Thirty-day outcomes

Event	Group 1	Group 2	*p*
Immediate neurological deficit	3 (2.5%)	6 (0.4%)	0.002
TIA	3 (2.5%)	1 (0.1%)	< 0.001
Minor stroke	1 (1%)	7 (0.5%)	NS
Major stroke	0	1 (0.1%)	NS
Myocardial infarction (MI)	2 (1.8%)	8 (0.5%)	0.05
Mortality	4 (3.5%)	7 (0.5%)	< 0.001
Total stroke/MI/death	7 (6.3%)	21 (1.4%)	0.001

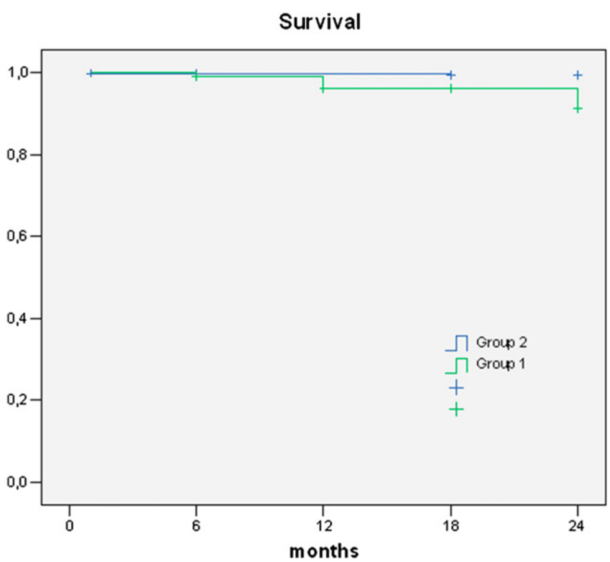

Fig. 1. Estimated 24-month survival (Kaplan–Meier curve).

may be attributed to carotid disease; however, the optimal strategy in these patients remains controversial.[12,13]

Proposed therapeutic strategies to decrease the risk of post-CABG stroke in patients with coexistent carotid disease have included simultaneous CEA-CABG, staged or reverse staged procedures, performing only CABG, CAS before CABG, and the use of off-pump CABG. However, despite multiple studies there remain no generally accepted guidelines for the optimal therapeutic approach to adopt in this subgroup of patients, and no randomized prospective studies have been performed.

Naylor et al. have published several thorough reviews of the literature concerning patients presenting with concomitant carotid and coronary disease.[13-16] In an initial review of 59 studies, they noted that 91% of screened CABG patients had no significant carotid disease and stroke risk in these patients was less than 2%. Stroke risk increased to 3% in predominantly asymptomatic patients with unilateral 50-99% carotid stenosis, 5% in those with bilateral 50-99% carotid disease, and 7-11% in patients with carotid occlusion.[13]

In a subsequent review of 97 published studies following 8,972 staged or combined procedures, Naylor et al. noted the highest operative mortality occurring in patients undergoing CEA and CABG simultaneously (4.6%, 95% C.I.), whereas the reverse staged treatment (CABG followed by CEA) carried the highest risk of ipsilateral stroke (5.8%, 95% C.I.) and stroke in general (6.3%, 95% C.I.). Myocardial infarction had the lowest perioperative risk in patients operated with the reverse staged procedure (0.9%, 95% C.I.) and the highest in patients undergoing the combination surgery (CEA-CABG) (6.5%, 95% C.I.). The risk of death/myocardial infarction/stroke was 11.5% (95% C.I.) following simultaneous surgery compared with 10.2% (95% C.I.) in staged procedures (CEA, CABG). Overall, they concluded there were no statistically significant differences between the two strategies.[14]

High-risk subgroups of patients for post-CABG stroke include not only patients with carotid disease, but also neurologically symptomatic patients, and patients with aortic arch disease. In a review of 9,939 patients in 8 published series, patients with a previous TIA or stroke had an 8.5% risk of perioperative stroke compared with 2.2% stroke risk in those patients who are neurologically asymptomatic.[13] In a review of 10 studies for a total of 111 patients suffering stroke after CABG, 48% of these patients did not have particularly significant disease in either carotid (<50% stenosis), 20% had 50-99% unilateral stenosis, 20% had 50–99% bilateral stenosis, 7% carotid occlusion with <50% contralateral stenosis, and 4% an occlusion with >50% contralateral stenosis and 1% bilateral occlusion. These data, together with those from CT scans and autopsies (frequent multifocality of the stroke), suggest that only 50% of strokes in CABG patients may be attributed to carotid artery disease. It is therefore important to understand the state of the aorta, the choice of site and aortic clamping technique, and to use the off-pump surgical method, with the aim of limiting noncarotid adverse neurological events.[12] Observational studies have reported significant reductions in the risk of post-CABG stroke using off-pump CABG; however, most of these studies did not analyze the high-risk subgroup of patient presenting with combined carotid and coronary disease. However, in a review of 12 studies including 324 synchronous CEA plus off-pump CABG procedures, the operative mortality was only 1.5% and the risk of death or any stroke significantly reduced at 2.2%.[15]

CAS before cardiosurgical revascularization has also been proposed as an alternative to combined CEA-CABG. The theoretical advantages of carotid stenting are linked to its lower invasivity and avoidance of general anesthesia, which may reduce cardiac risks.[12] However, a recent review of 11 published studies demonstrated in 760 CAS plus CABG procedures indicated an overall mortality of 5.5% and a 30 day risk of death/any stroke of 9.1%. The majority of patients (87%) were neurologically asymptomatic questioning the prophylactic value of this strategy in post-CABG stroke prevention.[16]

In our experience, combined surgery with CEA and cardiac surgery (revascularization with or without valve substitution) carried a risk of mortality at 30 days postsurgery, which is significantly higher in comparison with those patients undergoing isolated CEA. In reality, the increased risk is mainly correlated with increased cardiovascular mortality, whereas neurological complications of the combined surgery remained extremely low and similar to those obtained with isolated CEA. Similar to other series of combined CEA and off-pump CABG, we noted a marked reduction in perioperative stroke/myocardial infarction/death rates in patients undergoing CEA with off-pump CABG (3.3 vs. 10%, $p = 0.001$).

Clearly the patient who presents with significant carotid and coronary disease is almost always an individual in compromised clinical condition, which is manifested in the increase in perioperative risk and reduction in survival during follow-up. Our study at 24 months showed a decreased survival in patients requiring combined CEA-CABG versus isolated CEA (85 vs. 98.8%). However, freedom from subsequent stroke at 24 months (3.1 vs. 1.7%) and freedom from significant carotid restenosis (8 vs. 11%) were comparable in both groups.

In our opinion, the elevated incidence of perioperative neurological events in patients undergoing cardiac surgery who present with carotid disease, even if asymptomatic, warrants an aggressive prophylactic approach if results document minimal perioperative mortality and protection from subsequent neurological events in the short and long term. Our results would also suggest significantly improved results in patients undergoing combined CEA with off-pump CABG.

CONCLUSIONS

In our experience, combined CEA and cardiac surgery carries a higher risk of perioperative mortality than patients undergoing isolated CEA; however, this increased risk was mainly related to cardiovascular mortality. Neurologic outcomes of the combined surgery remained extremely low with perioperative and mid-term stroke rates similar to CEA alone. Whenever possible, CEA combined with off-pump CABG seems to be the therapeutic strategy of choice.

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