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A Modified Combined Approach to Operative Carotid and Coronary Artery Disease: 82 Cases in 8 Years

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ABSTRACT

Background: A significant number of patients undergoing coronary artery surgery have severe carotid artery disease. It is also true that up to half of the patients undergoing carotid endarterectomy (CEA) have severe treatable coronary lesions. This study aims to review data regarding 82 patients of combined approach in 8 years; the second half consists of 44 patients whose CEA was performed under local anesthesia. It compares results of the conventional and the modified approaches to simultaneous surgery.

Methods: All 82 patients who planned to have a concomitant procedure were recorded prospectively between 1995 and 2003. From 1998, the surgical technique has been modified to switch to local anesthesia for CEA, rather than perform under a single general anesthetic period. All pre- and perioperative data as well as in-hospital and outpatient control (mid- to long-term) data were recorded. A *P*-value of less than .05 was considered as significant. Analysis of survival was performed by using the Kaplan–Meier method and the log-rank test.

Results: The 30-day follow-up was 100% complete for all patients. All patients were followed for 59.59 ± 29.68 (range 8 to 114 months) months postoperatively. Three patients (6.8%) in the modified and 2 (5.2%) in the standard group had intraluminal shunting ($P > .05$). In the standard group, 3 patients expired and 3 had perioperative stroke; only 1 patient had a stroke in the modified group and two expired ($P > .05$). Mean survival time according to Kaplan–Meier test was 109.97, SE 2.84, 95% CI (104.41-115.52) months for the former group, whereas it was 62.79, SE 1.20, 95% CI (60.45-65.13) months for the latter. Actuarial estimates of survival during ten-year follow up were 94.44% SE 3.83 in ten-year follow-ups and 97.67% SE 2.30 in 5-year follow-ups for the modified group ($P > .05$).

Conclusions: Avoidance from extended periods of general anesthesia and cardiopulmonary bypass periods as well as immediate recognition of impaired cerebral flow during CEA and the time it provides to take preventive measures are the most important benefits of the modified technique without significantly changing hospital and long-term mortality and stroke. It may also reduce the cost and the waiting period for the suffering patient.

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INTRODUCTION

The current indications for carotid endarterectomy for either symptomatic or asymptomatic patients have been well described [Executive Committee for the Asymptomatic Carotid Atherosclerosis Study 1995, Hertzer 1986, North American Symptomatic Carotid Endarterectomy Trial Collaborators 1991]. Coronary artery bypass grafting (CABG) is also a well-defined area in the modern era of cardiac surgery [CASS Principal Investigators and Their Associates 1983]. However, there are conflicting results regarding the cases with concomitant carotid and coronary artery disease. The facts that 40% to 50% of patients undergoing carotid endarterectomy (CEA) have significant coronary artery disease [Cinar 2004, Executive Committee for the Asymptomatic Carotid Atherosclerosis Study 1995] and that 8% to 17% of CABG patients have severe carotid artery disease [Berens 1992, Fagglioli 1990] make the situation more significant for the surgeon. It is important to mention that the major cause of mortality for CEA patients is myocardial infarction.

The current options for the surgeons are threesome: a combined approach and a staged approach, which may be a CABG following CEA or vice versa (the reverse-staged procedure). The latter option is universally less preferable as the literature suggests a significantly higher incidence of stroke with this approach [Hertzer 1989]. However, it should be noted that technical aspects of CEA used in conjunction with CABG might play a critical role in the postoperative outcome. Tolerability of carotid clamping by the patient, intracerebral collateralization, and the need for shunt insertion should all be considered for the interpretation of the results. It is also noteworthy that complications due to carotid shunt insertion may cause tragic results. Most of the studies, including the two large meta-analyses in the literature, comment on a combined approach with a single general anesthesia and many do not even comment on the aforementioned issues regarding the safety of CEA. Our surgical team was using the conventional single-anesthesia technique for combined procedures until 1998 when the authors modified the technique to use local anesthesia for CEA and then to proceed with general anesthesia for CABG. The aim of this study is to review our 8-year experience with combined procedures and to compare the results of either technique.

MATERIALS AND METHODS

Patient Selection and CEA

Institutional approach for concomitant carotid and coronary artery disease has been a staged procedure unless indicated otherwise. All CABG patients above 65 years of age or those with severe (>70%) left main coronary disease, severe peripheral occlusive arterial disease or a history of a cerebrovascular event, and those with an audible carotid bruit were candidates for carotid investigation for a possible stenosis. Patients with left main coronary artery disease or with multivessel disease, NYHA class III-IV and left ventricular dysfunction or unstable patients due to a cardiac aspect were deemed for a combined approach if they had asymptomatic or symptomatic uni- or bilateral carotid artery stenosis of more than 70% or if they had symptomatic, but less severely occluded carotid arteries. All patients undergoing either procedure gave their informed consent for the procedures and the study. Local institutional scientific committee approval was also obtained before the conduct of the study. All pre- and perioperative cardiac and neurological data were prospectively recorded in institutional CEA & CABG database between June 1995 and August 2003. Until 1998, all combined procedures were conducted with the conventional single general anesthesia technique (38 patients- the standard approach) and the authors used local anesthesia for all CEA procedures, including the combined CEA and CABG procedures since then (the modified approach- 44 patients).

Local and General Anesthesia

All patients had standard opiate and hypnotic-induced general anesthesia, which was maintained with propofol and short-acting muscle-relaxing agents. During CEA under general anesthesia, stump pressure measurements were taken. Intraluminal carotid shunting was applied for all patients with severe bilateral carotid disease or if the stump pressure was lower than 50 mm Hg. For local anesthesia technique from 1998, standard superficial and deep blockade with 0.25% Bupivacaine were applied with an additional 2% lidocaine locally into the surgical field when necessary. Premedicated with 0.5 mg/kg of diazepam to relieve anxiety, all patients received nasal oxygen to provide optimal saturations. Extra sedative agents were not needed in any of the patients except that some patients received intravenous fentanyl bolus injections in analgesic doses. All patients were intensively followed for their neurological status all through the operation by verbal communication and applying neurological examinations. A positive cross-clamp test (any sign of neurological deficit, worsening state of cooperative skills/consciousness within 3 minutes of CCA and ICA clamping) was thought to be adequate as an indication of shunting. Anesthesiologists were encouraged to provoke temporary mild hypertension all through the procedure with volume replacement (or rarely with dopamine or dobutamine infusion) when appropriate, until the patient was given general anesthesia for intubation and CABG surgery. In all patients, CEA was conducted with low-dose heparinization (1 mg/kg) and another dose of heparin (total- 3 mg/kg) was given prior to onset of cardiopulmonary bypass (CPB) to achieve activated clotting times of 750 seconds.

Postoperatively, any signs of neurological deficit were also analyzed by a clinical neurologist and a plain cranial CAT scan was taken if indicated and/or the patient was hemodynamically stable. Such a CAT scan in the early postoperative period was aimed at looking for early focal hypodensity and/or initial mass effect defined as mild to severe compression of the ventricles. Neurological states, persisting for less than 48 hours, were accepted as transient deficits. Nonlateralizing deficits, as cranial nerve involvement or dysarthria and lacunar states, were accepted as minor neurological sequeleae with favorable prognosis if the Rankin score for the patient was 2 or less. Motor hemiparesia/hemiplegia states, sensorimotor stroke states and hemispheric syndromes with a Rankin score of 3 or higher were all included in the definition of stroke with a worse prognosis. These patients were evaluated and followed using National Institutes of Health Stroke Scale (NIHSS) and the Rankin Scale by the same neurologist. Perioperative myocardial infarction (MI) was considered if any two of the following were observed: new Q waves longer than 0.04 seconds on ECG and/or a decrease in the R-wave amplitude, more than 25% in two or more derivations; perioperative myocardial band levels of creatine kinase enzyme more than 100 IU/L or more than 5 times of preoperative level; previously nonexistent left ventricular wall segmental movement defect or troponin I levels more than 3.7 μg/L at peak level or more than 3.1 μg/L and 2.5 μg/L at 12th and 24th hours, respectively.

Coronary Artery Bypass Surgery

For all patients following midline sternotomy, CABG was proceeded with CPB at 28-30°C with standard aortic and single, two-staged venous cannulation using intermittent cold blood cardioplegia in an antegrade fashion from the aorta with topical cardiac cooling. After a single arresting dose, cardioplegia was repeated every 20 minutes in the aforementioned fashion. All distal anatomoses were made during a single cross-clamp period and proximal anastomoses were made using side-biting aortic clamp during rewarming. In all patients, bypass perfusion was maintained at 70 mm Hg or higher to enhance cerebral perfusion and after the closure of the sternotomy, a second look to carotid incision was applied for closure, which also enabled the surgeons to detect any complications as dissection, plaque rupture, and occlusion as well as hemorrhage in the carotid region.

Statistical Analysis

Statistical analyses were done by using SPSS 10.0 (SPSS Inc, Chicago, Ill). Data are expressed as mean ± standard deviation. A *P*-value of less than .05 was considered to indicate statistical significance. 'Fischer's Exact test', 'Levene's *f*-test', 'Independent-Samples *T*-test', 'Wilcoxon (Gehan) statistics' and 'Kaplan–Meier method' were used for the statistical evaluation of data.

Table 1. Preoperative Characteristics of the Patients*

Preoperative Characteristics	The Standard Group	The Modified Group	P†
Age (years)	67.55 ± 5.2	67.7 ± 4.46	.890‡
Preoperative MI, n	4	1	.699§
Preoperative stroke, n	14	12	.353‖
SAP, n	8	4	.126‖
USAP, n	16	19	.922‖
LMCA lesion >50% Stenosis, n	10	18	.165‖
TIA, n	34	30	.020‖
Neurologically asymptomatic, n	2	3	>.999§
HT, n	24	30	.632‖
COPD, n	8	9	.947‖
Hyperlipidemia, n	22	20	.261‖
Preoperative renal failure, n	2	1	.594§
POAD, n	4	6	.745§
DM, n	12	15	.809‖

*MI indicates myocardial infarction; SAP, stable angina pectoris; USAP, unstable angina pectoris; LMCA, left main coronary artery; TIA, transient ischemic attack; HT, hypertension; COPD, chronic obstructive lung disease; POAD, peripheral obstructing arterial disease; DM, diabetes mellitus.

†$P < .05$ indicates significance.

‡Independent T Test.

§Fisher's Exact Test.

‖ Pearson's Chi-Square Test.

Table 2. Operative Data of 82 Patients*

Preoperative Characteristics	The Modified Group	The Standard Group	P†
XCL duration, min	43.79 ± 12.92	42.26 ± 13.74	.604 ‡
CPB duration, min	53.34 ± 14.81	50.53 ± 14.29	.386 ‡
CEA primary closure, n	33	28	.890§
CEA saphenous patch-closure, n	11	10	.520§
Intraluminal Shunting, n	3	2	> .999‖
Perioperative inotropic need, n	4	8	.328§

*XCL indicates cross-clamp; CPB, cardiopulmonary bypass; CEA, carotid endarterectomy.

†$P < .05$ indicates significance.

‡Independent T test.

§Pearson's Chi-Square Test.

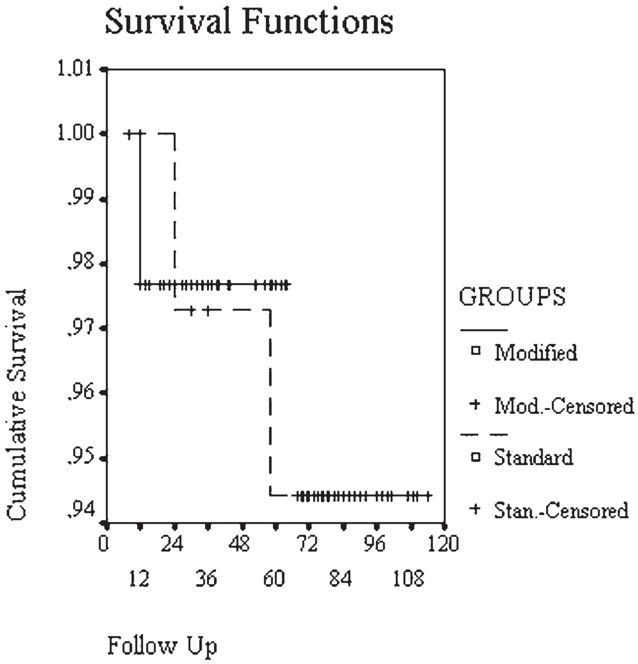
‖Fisher's Exact Test.

Demographic and baseline variables were analyzed by using the Student *t*-test for continuous variables and the Pearson Chi-Square, Fisher's Exact test for qualitative variables. Wilcoxon (Gehan) statistics were used for the comparison of survival experience.

Analysis of survival was performed by using the Kaplan–Meier method. Statistical differences in Kaplan–Meier survival estimates were determined by using the log-rank test.

RESULTS

The 30-day follow-up was 100% complete for all patients. All patients were followed up for 59.59 ± 29.68 (range 8 to 114 months) months postoperatively. Preoperative data for both groups are summarized in Table I. Indications for CABG in majority of the patients in both the groups were unstable angina or left main lesion with more than 50% stenosis (the standard group; 16 patients, 42% and 10 patients, 26% vs. the modified group; 19 patients, 43% and 18 patients, 40%, respectively). Table 1 also depicts the indications for CEA. Two patients in the standard and 3 in the modified group were operated although they were neurologically asymptomatic and had a normal neurological history. It may be noted that, 10 of 14 (71%) patients with a history of stroke in the standard group had a radiologically detectable infarcted area whereas only 2 out of 12 (16%) patients had such a lesion as detected on a cerebral computerized tomography ($P < .05$). Three patients (6.8%) in the modified and 2 (5.2%) in the standard group had intraluminal shunting. Two of the patients in the former group had severe bilateral carotid artery stenosis and the stump pressure was lower than 50 mm Hg in the other. Primary suture was the technique of preference, when feasible in 30 patients (75%). One of those patients in the modified group required shunting due to development of dysarthria upon carotid clamping. He recovered full neurological function upon constitution of cerebral flow with a shunt. He, however, had a perioperative MI and low output state requiring inotropes. He woke up with mild ipsilateral hemiparesia, which totally disappeared on day 2. The second patient in the modified group was noted to have had an ulcerative plaque causing transient neurological states on multiple occasions. She had a shunt insertion upon blurring of vision upon clamping, but otherwise had an uneventful hospital stay. Similar frequencies of carotid arteriotomy closure techniques were observed in either group (saphenous patch-closure, 10 patients, 26% vs. 11 patients, 25%, $P > .05$). Also, the mean aortic clamping time and mean cardiopulmonary bypass durations were similar (Table 2). In all patients but one in the standard group, CEA was conducted before the onset of cardiopulmonary bypass. This particular patient had to undergo CEA with cardiopulmonary bypass, systemic heparinization, and cooling due to hemodynamic and cardiac instability. He also required shunt insertion and a saphenous patch for closure of the arteriotomy during CEA and received inotropic support in the postoperative period for 8 hours. His postoperative period was otherwise uneventful. Table 2. shows the operative data regarding the standard and the modified groups. Three patients expired in the standard group; one had perioperative MI and developed a low-output state without any signs of perioperative neurological dysfunction. The other two, however, woke up with severe ipsilateral hemiplegia in the postoperative period and lost consciousness with eventual death on days 12 and 20, respectively. Another patient with a perioperative MI and low cardiac output woke up with contralateral lower extremity paralysis. He quickly recovered from a low-output state with inotropes, and his arm and forearm movements began on day 2 resulting in discharge to the ward on day 3. He was discharged from the hospital with residual monoparesia to be followed by the neurology outpatient clinic. In the modified group, we observed that a single patient expired secondary to a stroke involving



Kaplan-Meier survival curves for the standard and modified groups. Mean survival time in the standard and the modified groups were 109.97 ± 2.84 (95% CI; 104.41-115.52) and 62.79 ± 1.2 (95% CI; 60.45-65.13) months, respectively (*P* = .779).

ipsilateral MCA area. He unfortunately never developed consciousness, postoperatively and was lost on day 2 due to hemodynamic compromise. This particular patient was one of the four patients observed in this group, having received a moderate-high dose inotropic support. Another was a 65-year-old lady operated on an urgent basis and she unfortunately had perioperative MI and a low-output state. She was successfully discharged from the hospital on day 12 without further complications. Although not statistically significant, the standard group had a higher mortality and stroke than the modified group (3 patients expired and a total of 3 patients had stroke in the former, only one mortality and stroke was observed in the latter). Patients in the standard and the modified groups received 2.375 ± 0.8 and 2.49 ± 0.79 coronary bypass grafts per patient ($P > .05$). It is important to note that all 82 patients in the study received in situ left internal mammary artery graft to LAD.

Only two patients, both in the standard group, were lost from the mid- to long-term follow-ups due to patient-related reasons (12th and 72nd months, respectively). Three patients were observed to have neurological adverse events, one of which was a fatal stroke due to contralateral carotid artery in time. All were noted to have a normal or insignificant carotid lesion at the time of the initial operation. And, one patient expired due to metastatic lung cancer, 36 months after the combined procedure. Only one patient was noted to develop a restenosis 24 months after the initial procedure, which was managed successfully with stenting. In the modified group, three neurological adverse events were noted, one of which was a fatal stroke. All of them were related to the non-operated side. One patient in the standard group had a fatal ipsilateral stroke. One patient in this latter group was observed to have dialysis-dependent renal failure and he unfortunately succumbed 23 months after his surgery.

Kaplan–Meier survival analysis was applied to all the 82 patients to determine mid- and long-term effects of such a modification of the standard technique, and we have found no survival differences between the two groups (Figure 1.). The mean survival time according to Kaplan–Meier test was 109.97, SE 2.84, 95% CI (104.41-115.52) months for the standard group, whereas it was 62.79, SE 1.20, 95% CI (60.45-65.13) months for the modified group. Actuarial estimates of survival during ten-year follow-up were 94.44% SE 3.83 in ten-year follow-ups and 97.67% SE 2.30 in 5-year follow-ups for the modified group. There was no statistically significant difference between the two groups in terms of survival probabilities according to the Log-rank test, and in terms of the mean survival time according to the Kaplan–Meier test.

DISCUSSION

The fact that intraluminal shunting was needed in more patients from the modified group despite similar patient characteristics in both groups was attributed to a direct assessment of the neurological status of the patients and thus, a better analysis of the need for an intraluminal shunt. Stump pressure measurements, electroencephalographic monitoring, and the actual need for carotid shunting may not be parallel, and routine shunting, even in high-risk CEA patients, may not be necessary [Cinar 2004]. The modified approach with an awake patient during CEA allows the surgeon to monitor the patient's neurological status directly; thus it may affect the need for insertion of intraluminal shunts based on classic methods as stump pressure measurement. This difference in shunting, although not reaching statistical significance (5.2% vs. 6.8%, NS), may be a result of such a selective approach. It is noteworthy that a radiologically detectable infarcted area on plain and contrast-enhanced tomography was present in a significantly higher proportion of patients with a stroke history in the standard approach group (71% vs. 16%, $P < .05$). It is arguable that the lower incidence of radiological lesions in the modified group may be attributed to less severe intracranial atherosclerotic disease, but the difference in the rate of shunting, despite a similar contralateral carotid disease distribution, does not support it. Although not detected in this series, neurological insults due to mechanical trauma by the carotid shunt (eg., thromboembolic or atheroembolic events, intimal flap elevation or dissection) may thereby be minimized too. It may be suggested that such a modified approach to concomitant procedures may be beneficial in the detection of shunt-related complications and in relieving them by re-exploration of the carotid artery, if possible [Cinar 2004].

It is debatable that a secondary benefit of the modified technique may be a gross estimation of the timing of a neurological event during a concomitant CEA-CABG procedure. Sensitivity and specificity of CEA with local anesthesia has been well established by previous studies[Gurer 2003, McCarthy 2002, McCarthy 2004]. Thus, a smooth CEA operation without any neurological dysfunction may be an indicator of a CABG-related neurological injury (embolic or hemorrhagic). An additional benefit of full-dose systemic heparinization for CPB after the CEA procedure may exist to overcome the hypercoagubility state seen after any surgical procedure. Relief of an obstruction in the carotid artery may even be beneficial in the setting of a CABG-related neurological complication by attenuation of the ischemic insult. Bonacchi M et al reported a randomized study on the use of CPB during a combined procedure. They presented similar hospital mortality and perioperative stroke rates for patients who had CEA with or without CPB. It is to be noted, that CEA was performed under general anesthesia in all cases. In our study, we observed 4 cases of mortality from either group (4.8%). They reported a comparably higher mortality of 6%. They also reported that the use of CPB during CEA did not affect long-term survival [Bonacchi 2002].

Many authors recognize older age as the single independent risk factor for stroke after CABG procedures [Gardner 1986, Tuman 1992]. It is not only recognized as a risk for extracranial carotid and aortic atherosclerotic disease, but it may also increase the incidence or severity of intracranial or aortic atherosclerosis, thus an increased risk for perioperative stroke during CPB. Both groups in our study consisted of patients of similar age group, possibly due to the intrinsic nature of the atherosclerotic process. Other risk factors, such as CPB duration and possible causes of thromboembolic phenomena, were noted in the charts of our patients. Both the standard and the modified group had similar CPB times ($P > .05$). Since CEA was not performed in any, but one, of the patients during CPB, extracorporeal perfusion periods were notably shorter. Likosky DS et al presented a recent data on the prediction of perioperative stroke after coronary artery surgery, indicating a significant risk increment after 90 minutes upon analysis of 11,825 consecutive coronary patients [Likosky 2003].

Additionally, it should be mentioned that the grade of atherosclerosis/calcification of the ascending aorta, an intraoperative finding, was not noted in any of the patients. This is arguably one of the weaknesses of this review. Nevertheless, it should be added that the least "calcified" regions of the aorta are chosen for cannulation as a general approach and we recognized no "porcelain aorta" notes in any of the patient charts, nor did we notice a conversion from CPB to beating heart surgery due to a diffusely atherosclerotic aorta.

Some may argue that the operative stress of a conscious patient may be detrimental by exacerbating the ischemic insult from the cardiac point of view; nevertheless, it is notable that the perioperative MI rate in the modified group was lower. Additionally, in-hospital mortality was lower in the same group due to lower perioperative stroke and MI rates. So, the modified method is a reliable operative technique from the points of both cardiac and carotid artery surgery. A survival analysis of two groups supports this argument as no difference was found between the standard and the modified groups ($P > .05$). In support of this argument, McCarthy R et al commented that CEA with local anesthesia is not associated with any increased anxiety or discomfort [McCarthy 2002].

Our results may also be compared to staged-procedures. Antunes PE et al reported, in their similar series, stroke rates of 2.4% from isolated CEA and 3.9% from CABG procedures (1). A total of 5 patients with stroke in 77 patients and 83 CEA (6.3%) is comparable to our 4 cases with stroke (4.8%) in 82 cases and one patient (2%) in the modified group. Our perioperative MI rate is also lower (3 patients, 3.6%) than that Antunes PE et al reported (6.3%). Our mortality rate seems to be higher than that was reported in their study (4.8% vs. 1.3), which can be attributed to many factors, such as the number of cases with contralateral carotid occlusion (6 patients in their series vs. 12 patients in ours) or preoperative cardiac status of the patients. In our patient group, a total of 12 patients required inotropic support. Although not statistically significant, a need for pharmacological inotropic support was higher in the standard group (8 vs. 4 patients).

Avoidance from extended periods of general anesthesia and cardiopulmonary bypass periods are the most important benefits of the modified technique. It may be more important in elderly patients with co-morbidities, such as renal or pulmonary compromise. Secondary advantages are immediate recognition of impaired cerebral flow during CEA and that the surgeon may apply the necessary measures of cerebral protection such as shunt insertion. Also, shunt-related complications may be noticed earlier and a carotid re-arteriotomy may be applied to terminate an obstruction surgically. Other less pronounced, but equally important aspects of simultaneous, also of our modified technique include reduction of procedural/therapeutic cost and the reduction of waiting period for the suffering patient in comparison to the staged approach.

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