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Staged or Combined Approach for Carotid Endarterectomy in Patients Undergoing Coronary Artery Bypass Grafting: A 5-Year-Long Experience

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ABSTRACT

Background: Optimal surgical approach for patients with hemodynamically significant carotid and coronary disease remains controversial. We analyzed our 5-year experience and compared early and long-term outcome following staged and combined carotid and coronary artery bypass.

Methods: 312 consecutive patients undergoing carotid endarterectomy and coronary artery bypass between 2008 and 2013 were prospectively enrolled in the study. Patients were scheduled for a staged (carotid endarterectomy followed by coronary artery bypass within 1 week) procedure (Group S) unless they were unstable in terms of cardiac status (were deemed to a combined procedure; Group C). All patient data including demographics, risk factors, immediate perioperative events, 30-day, and long-term outcome were prospectively recorded and then analyzed. Groups S and C were compared for pre- and perioperative data as well as immediate, 30-day, and long-term survival. A P value less than .05 was considered significant. Survival analysis was made using Kaplan-Meier method and log-rank test.

Results: Group S included 204 patients and Group C included 108 patients. Preoperative demographics and clinical data were similar in the two groups except that preoperative cerebrovascular events were more common in Group C (31.7% versus 22.22%, $P = .036$) and bilateral carotid disease was more common in Group S. The EuroSCORE was higher in Group C (2.91 versus 2.65, $P = .013$). Carotid surgery techniques were similar; intraluminal shunting was more frequent in group C than group S (33.33% versus 9.88%, $P = .001$). Additional cardiac procedures in addition to coronary surgery was predominant in Group C. 30-day neurological adverse event rates, ICU, and hospital stay were significantly higher in Group C. The 30-day mortality was also sigficantly higher in Group C (1.96% versus 4.62%, $P = .001$).

Conclusion: Staged and combined surgical approaches yield comparable outcomes. A staged approach may provide a more favorable neurological outcome with significantly reduced need for intraluminal shunting. Long-term outcome is, however, similar.

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INTRODUCTION

Stroke is one of the major complications after coronary artery bypass grafting (CABG), with a reported incidence of 2.1-5.2% and related mortality of 0-38% [D'Ancona 2003; McKhann 1997]. Significant carotid artery stenosis (CAS) is one of the predisposing factors for stroke among patients undergoing open heart surgery. CAS is detected incidentally in 8-14% of patients undergoing CABG. Carotid endarterectomy (CEA) reduces the risk of recurrent stroke in patients with severe CAS [North American Symptomatic Carotid Endarterectomy Trial Collaborators 1991]. Coronary artery disease (CAD) is presented in 40-50% of patients undergoing CEA [Ogutu 2014]. CEA in patients with untreated CAD has a 17% risk of perioperative myocardial infarction and about a 20% risk of perioperative death. Similarly, those with untreated CAS also carry a risk of stroke after CABG [Lutz 2008]. Although developments in percutanous techniques have presented an alternative for only a subset of patients, none of the randomized trials could demonstrate any significant benefit of stenting over surgery; thus CEA remains the therapy of choice in most patients [Biller 1998; Steinbach 2002].

There has been much controversy about the optimum treatment with combined carotid and coronary disese. To date, no Level I evidence exists. We published our initial results earlier [Cinar 2005]; however, we have observed improving outcomes with evolving technical trends over time. Therefore, we investigated our early and late outcome following our current staged and concomitant CEA and CABG practice to identify a stepwise approach and risk groups after our initial study.

PATIENTS AND METHODS

312 consecutive patients scheduled for CEA and CABG (either staged or concomitant) between 2008 and 2013 were included in the study and all patient data were prospectively recorded for variables such as demographics, preoperative risk factors, perioperative and postoperative complications, all early (within 30 days of operation) and late adverse

neurologic events, as well as mortality. Institutional review board approval for the study and informed consent for the study and procedures were obtained from all patients.

Patient Selection

Group S (staged approach; n = 204) included patients with stable cardiac disease (i.e., NYHA class II or less stable angina pectoris) and symptomatic cerebrovascular disease attributible to moderate to severe carotid artery stenosis on intention-to-treat basis. Unless contraindicated by specific conditions or complications, CEA was followed by CABG within one week. Group C (concomitant approach; n = 108) included unstable cardiac patients (i.e., NYHA class III and IV, left main coronary artery stenosis, post-infarction angina, multivessel disease with severe left ventricular dysfunction) with symptomatic moderate to severe carotid stenosis or asymptomatic severe carotid stenosis as widely suggested [Ferguson 1999]. Operative and anesthetic techniques used for CEA and CABG were described in detail in earlier studies [Cinar 2005; Cinar 2004]. In group C patients, cervical incision was closed with a sterile gauze until systemic protamine was given and then the cervical incision was closed. Patients that are candidates for emergency or off-pump CABG and one patient with paraganglioma in addition to carotid stenosis were excluded.

Group S patients were operated using local anesthesia as described in earlier published series [Cinar 2004]. Group C patients underwent concomitant surgery under a single-stage general anesthesia as described before [Cinar 2005]. Any impact of anesthetic techniques on the outcome were considered insignificant with regard to GALA Trial [GALA Trial Collaborative Group 2008]. Continous cerebral monitorization with near infrared response specrophotometry (NIRS) and carotid stump pressure monitorization were applied during general anesthesia. A carotid shunt was applied if the carotid stump pressure was less than 50 mmHg or if a relative decrease in rSO_2 of greater than 20% before clamping value occured.

Early Postoperative Period

All patients were followed in the postoperative intensive care unit until hemodynamically stable. Any signs of neurological deficit were assessed by the same clinical neurologist and a plain cranial computerized tomography was taken whenever indicated. Neurological states persisting for less than 48 hours were defined as transient deficits. Nonlateralizing deficits, lacunar states, and sensorimotor stroke states were minor neurological squeleae with favorable prognosis if Rankin score for the patient was 2 or less. Motor hemiparesia/hemiplegia, sensorimotor stroke states, and hemispheric states with Rankin score 3 or more were all included in the definition of stroke with a worse prognosis. These patients

Table 1. Preoperative Demographic Parameters*

	Group S (n = 204)	Group C (n = 108)	*P*
Age	63.8 ± 9.4 (42-86)	63.7 ± 8.7 (48-84)	.710
Female, n (%)	60 (29.41)	33 (30.55)	.911
Male, n (%)	144 (70.58)	75 (69.44)	.858
Hypertention, n (%)	180 (88.23)	94 (87.03)	.92
DM, n (%)	48 (23.52)	27 (25)	.831
Renal dysfunction, n (%)	38 (18.62)	15 (13.88)	.652
COPD, n (%)	70 (34.31)	42 (38.88)	.782
PAD, n (%)	44 (21.56)	14 (19.44)	.667
LVEF <40%, n (%)	28 (13.72)	12 (11.11)	.856
EuroSCORE	2.65 ± 1.02	2.91 ± 1.14	.013
Contralateral carotid disease, n (%)	36 (17.64)	15 (13.88)	.002
Neurological status, n (%)			
Symptomatic			
TIA	64 (31.37)	24 (22.22)	.036
Stroke	12 (5.88)	7 (6.48)	.932
Asymptomatic	140 (68.62)	82 (75.92)	.032

*Continous data are presented as mean ± standard deviation. Bold values indicate statistical significance. DM indicates diabetes mellitus; COPD, chronic obstructive pulmonary disease; PAD, periferic arterial disease; LVEF, left ventricle ejection fraction; TIA, transientischemic attack.

Table 2. Perioperative and Postoperative Findings*

	Group S (n = 204) n (%)	Group C (n = 108) n (%)	*P*
Carotid shunt, n (%)	20 (9.8)	36 (33.33)	.001
Carotid clamping, time/min	23.95 ± 15.6	32.36 ± 17.0	.241
Carotid closure technique, n (%)			
Direct suture, n (%)	35 (17.15)	18 (16.6)	.882
Patchplasty	164 (80.39)	86 (79.62)	.783
Eversion	5 (2.45)	4 (3.70)	.954
CEA operation side			
Left	72 (35.29)	33 (30.55)	.851
Bilateral	32 (15.68)	11 (10.18)	.045
Grafts number of patient	3.05 ± 0.35	3.04 ± 0.38	.15
Aortic cross clamp time, min	55 ± 18	68 ± 22	.062
CPB, min	82.65 ± 16	102.28 ± 26	.034
IABP, n (%)	5 (2.45)	3 (2.77)	.966
Intensive care unit stay, day	1.84 ± 1.20	2.42 ± 1.68	.025
Hospital stay, day	4.72 ± 2.64	7.36 ± 2.46	.033

*Continous data are presented as mean ± standard deviation. Bold values indicate statistical significance. CPB indicates cardiopulmonary bypass; IABP, intraaortic ballon pump counterpulsation.

were evaluated using National Institutes of Health Stroke Scale (NIHSS) and the Rankin scale. Perioperative myocardial infarction (MI) was considered if any of the following were observed: new Q waves longer than 0.04 seconds on ECG and/or a decrease in R-wave amplitudes more than 25% in two or more derivations; perioperative myocardial band levels of creatinine kinase more than 100 IU/L or more than 5 times of preoperative level; previously non-existent left ventricular wall segmental movement defect or troponin I levels more than 3.7µg/L and 2.5 µg/L at postoperative 12th and 24th hours, respectively.

Midterm to Late Follow-Up

Patients were examined by the surgical and cardiology teams and the same neurologist on postoperative days 7 and 30, and then every 6th month. The median time of follow-up was 52 months (IQR 12-65 months). A carotid artery doppler ultrasound was requested at 6th month control.

Statistical Analysis

The Shapiro-Wilk test was used in evaluating the normality of the distribution of the continuous variables and Levene's test was used in evaluating the homogeneity of variance

Table 3. Logistic Regression for Peroperative Morbidity in the First Month and Mortality during the Early- and Late-Term

	Group S (n = 204) n (%)	Group C (n = 108) n (%)	OR	95% CI	*P*
Postoperative morbidity					
Neurological events	2 0.98	5 4.62	0.22	0.1-0.75	.015
Cardiac events†	6 2.94	4 3.70	0.96	0.66-1.67	.784
Pulmonary complications	3 1.47	9 8.33	0.23	0.12-0.97	.001
Others (hemorrhage, hematoma, cranial nevre palsy)	6 2.94	3 2.77	1.13	0.9-1.9	.961
Carotid restenosis (>50% of diameter)	4 1.96	3 2.77	0.85	0.8-2.26	.665
Postoperative mortality					
Early	4 1.96	5 4.62	0.22	0.15- 0.84	.001
Late	2 0.98	3 2.77	0.43	0.24- 1.68	.67
Risk adjusted mortality‡					
Early	2 0.98	3 2.77	0.35	0.24-6.56	.078
Late	2 0.98	2 1.85	0.49	0.41 -1.15	.85

OR indicates odds ratio; CI, confident interval. Bold values indicate statistical significance.
†New onset cardiac event during postoperative period.
‡Mortality after equation of the risks among groups.

Table 4. Logistic-Regression Analysis with Variables in the Equation

						95 % CI	
Step Ia	β ± SEb	Waldc	df	Sig	Odds Ratio	Lower	Upper
Groups	2.678 ± 1.215	4.217	1	.024	1.524	1.134	1.966
CPB (hour)	0.078 ± 0.026	7.245	1	.003	1.087	1.026	1.845
EF	-0.003 ± 0.045	0.002	1	.035	0.985	0.886	1.125

CPB indicates cardioplumonary bypass; ACO, additional cardiac operations; EF, ejection fraction; CI, confidence interval; SE, standard error.
aVariables entered on step I are Groups, CPB, ACO, and EF.
bCoefficients and the SE for each predictor variable in the model. The negative coefficient for EF indicates the odds of stroke and death decline with increasing EF.
cWald statistic and associated P values indicates how useful each predictor variable is. Odds ratio less than 1 indicates that an increase in the value of the predictor variable is associated with a decrease in the odds of the event (stroke and death). The 95% CI indicates the magnitude of the association (SPSS 2.0 software; SPSS, Chicago, IL).

in the groups. The outcomes of the homogeneity and normality tests were used to determine the statistical methods to be applied in comparing the study groups. The data was presented as percentages or mean ± standard deviation (SD). Univariate comparisons were computed using the Pearson chi-square test or Fisher exact test for categorical variables and independent sample t test or Mann-Whitney U test for continuous variables. Any factor with a P value of <.1 on the univariate analysis was then entered into a multiple logistic regression analysis. The statistical analysis was performed using the SPSS version 20.0 software (SPSS, Chicago, IL, USA). A *P* value of <.05 was considered significant. Survival analysis was made using Kaplan-Meier method and log-rank test.

RESULTS

Between 2008 and 2013, 312 consecutive patients undergoing CEA and CABG procedures were enrolled in the study. Group S included 204 patients that underwent CEA with local anesthesia one week before cardiac surgery and Group C included 108 patients that underwent concomitant CEA with cardiac surgery under single-stage general anesthesia.

Early Results (30 Days)

The 30-day follow-up was 100% in both groups. Groups S and C were similar in regard to age, sex, renal dysfunction, smoking, diabetes, hypertension, peripheral occlusive arterial disease, ejection fraction, and preoperative neurological status (Table 1). 31.7% of patients in Group S had preoperative history of a transient cerebrovascular adverse event in contrast to 22.22% in Group C (*P* = .036). Preoperative stroke rates were, however, similar. Contralateral carotid artery stenosis was more common in Group S (17.64% versus 13.88 %, *P* = .002). As a result, bilateral CEA in a staged fashion was more frequent in Group S than in Group C (33.33% versus 9.88%, *P* = .001, respectively). The two groups were similar for carotid artery closure techniques (80.39% versus 79.62%, *P* = .783) and clamp durations (Table 2). Shunt insertion was more frequent in group C than in Group S (33.33% versus 9.88%, *P* = .001, respectively).

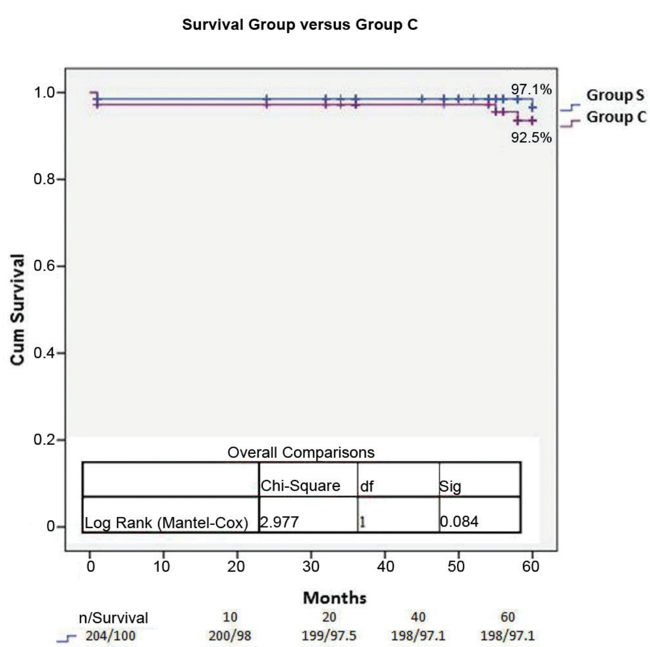
With regard to cardiac operations, combined cardiac procedures in addition to sole CABG were more frequent in group C as a whole (Table 3), except that additional aortic valve replacement was more common in Group S (7.84% versus 4.62%, *P* = .04). Expectedly, the mean EuroSCORE was higher in Group C than Group S (2.91 versus 2.65, *P* = .013). Early cardiac morbidity rates were similar in the two groups (perioperative cardiac events: low cardiac output states, perioperative arrhythmia, MI; 2.94% versus 3.70%; *P* = .78; OR = 0.96; 95% CI = 0.66-1.67).

Early postoperative pulmonary complications were lower in Group S (1.47% versus 8.33%, *P* = .001). Perioperative transient neurological adverse events were more common in Group C (0.98% versus 4.62%, *P* = .015). Both ICU and hospital stay in Group C were longer than in Group S (Table 2).

Early mortality was also higher in Group C than in Group S (4 versus 5 patients; 1.96% versus 4.62%, *P* = .001). Early mortality was, however, similar in both groups if only isolated CABG patients were included in the analysis (0.98% versus 0.35%, *P* = .078). The logistic regression model identified concomitant surgery (being in Group C), longer aortic clamp time, and cardiopulmonary bypass periods as predictors of early stroke/death.

Late Results

The 36-month follow-up was 100% in both groups. The median time of follow-up was 44.5 months (IQR 12-65 months). Late mortality was similar in both groups (Table 4). Death/stroke-free survival was similar in both groups (97.1% versus 92.5%; *P* = .084 (Figure). Early and late mortality was also similar in both groups when patients with concomitant cardiac procedures were excluded in regard to standardized EuroSCORE risk analysis. In one Group S patient, an acute ICA occlusion was detected before leaving the operation room and the carotid artery was reopened leading to thrombectomy from the distal suture margin and patch closure. Unfortunately, he expired due to respiratory failure and pneumonia in spite of total neurological recovery. Carotid restenosis rates were similar in both groups (*P* = .665). Notably, all restenosis cases were asymptomatic at the time of diagnosis after 24th-month follow-up (5 women, 2 men) and all had direct suture closure at the time of initial carotid surgery.



Kaplan-Meier analysis for long-term death/stroke-free survival in Groups S and C (*P* = .084). Numbers of patients at risk are listed by months of follow-up.

DISCUSSION

Systematic reviews of the current medical data have suggested that the risk of stroke after isolated coronary bypass grafting (CABG) is less than 2% in patients with no significant carotid disease; and between 3-5% in patients with asymptomatic carotid disease with more than 50% stenosis [Naylor 2002; Naylor 2003]. While approximately 91% of the 4674 screened patients undergoing CABG had no significant carotid disease, operative stroke rate increased from 1.8% to 5.2% in patients with bilateral carotid disease (50-99% stenosis). Of note, most of the patients found to have a carotid lesion upon screening were asymptomatic [GALA Trial Collaborative Group 2008]. Combination of aortic arch atherosclerosis and the presence of carotid stenosis has even a more dramatic impact by increasing perioperative stroke rates following CABG as high as 14% [Goto 2000]. In spite of three decades of reported data, combining CEA and CABG remains controversial, mostly due to heterogeneity of patient groups, surgeons' preferences, and data presentation [Naylor 2003; Bryne 2006]. Since Brener's initial review including 35 studies and 2928 patients in 1998 [Brener 1996], there has been a favorable trend of 1-2% in all endpoints following both staged and combined procedures. Naylor et al reported in their review that operative mortality in staged procedures has fallen to 3.9% or even as low as 3.3% in published series since the millenium [Naylor 2003]. We have observed a 30-day mortality of 1.96% for staged procedures in this prospective series. Mortality was significantly higher in the combined group, comparable to published data [Naylor 2002]. Perioperative stroke rate in our current series was even less than 1% with a staged approach in contrast to 4.6% for patients in the combined group. This finding is consistent with Dr. Naylor's review of 7753 patients and our earlier experience [Cinar 2005; Naylor 2002; Naylor 2003].

Perioperative myocardial infarction has been notoriously one reason for proponents of combined CEA and CABG with the risk increasing from 0.9% up to 6.5% with the staged procedures [Naylor 2003]. In our current prospective series, cumulative rate of perioperative cardiac events (MI, low cardiac output states, perioperative arrhythmia) was similar in both groups (2.94% versus 3.7%), although it was slightly higher in combined procedures. This difference between our favorable results and the published data may be due to a strictly one-week maximum policy in our approach, in contrast to longer intervals between CEA and CABG in staged procedures (average 6 months) in most series [Naylor 2003]. Of note, patients requiring emergency CABG were excluded from the study.

In the current era of evidence-based medicine, most issues related to mortality and stroke may be adressed with randomized trials; however, implementation and planning of such trials would confront many medical, ethical, and rational questions. As in our series, most surgeons prefer a combined approach, a longer and more complex procedure in sicker patients in terms of cardiac status. Group C patients in our cohort have apparently undergone more complex procedures to support this argument. Increased cerebrovascular adverse event rates following a combined procedure is therefore hardly attributible to carotid disease or this surgical approach; ascending aortic or intracardiac procedures with longer cardiopulmonary periods obviously carry their own risks of hypoperfusion states and atheroembolic or air macro/microemboli [Naylor 2003; Goto 2000; Borger 2005].

The prospective nature and long-term follow-up are particular strengths of this study. The major limitation is the non-randomized nature of the study; however, this appears to be non-practical due to aforementioned reasons. Our results have demonstrated that a staged approach may be favorable whenever possible. Nevertheless, longer cardiopulmonary periods and additional cardiac procedures were significant predictors of mortality/stroke. The latter may be the explanation for the higher early mortality rates with combined procedures; long-term mortality/stroke rates were similar.

Another significant finding was a higher tendency for intraluminal shunting during CEA in Group C patients. This is highly consistent with our earlier published data and the results of the GALA trial [Cinar 2004; GALA Trial Collaborative Group 2008]. We have found this current analysis of a 5-year-long experience very useful in appreciation of regional anesthesia for CEA. As the results of the GALA trial have indicated, the one major advantage of local anesthesia is avoidance from unnecessary shunting and its probably rare but catastrophic complications [Cinar 2004].

Conclusion

Until parallel data is available, staged and combined surgical approaches yield comparable outcomes. A staged approach may provide a more favorable neurological outcome with a significantly reduced need for intraluminal shunting. Long-term outcome is, however, similar.

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