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Original Article

Long-Term Outcomes of Synchronous Carotid Endarterectomy and Coronary Artery Bypass Grafting versus Solely Carotid Endarterectomy

Shiyan Ren, MD, PhD,[1] Peng Liu, MD, PhD,[1] Guolin Ma, MD,[2] Fei Wang, MD,[1] Songyi Qian, MD,[1] and Xueqiang Fan, MD[1]

Objective: To compare the effect of combined carotid endarterectomy (CEA) and coronary artery bypass grafting (CABG) with solely CEA.

Methods: During a five-year period ending December 2009, 25 consecutive patients received concomitant CEA and CABG, whereas, 62 consecutive patients underwent only CEA. They were followed at the median for 64.5 months. The Kaplan-Meier method was used to evaluate the survival rate of patients in both groups.

Results: There was no significant difference in terms of age, proportion of gender, risk factors of coronary artery disease and carotid artery stenosis. The degree of carotid artery stenosis was identical in both study groups. One patient in CEA/CABG group had 60% stenosis of carotid artery with ulcerative plaque. There was no early death in the short post-operative period. Restenosis was found on ultrasonography in 4 patients in the CEA/CABG group, and 12 patients in the CEA group; no statistical difference was found between both groups (P = 0.952). The intubation time, ICU stay, and hospital stay in CEA/CABG group were longer than in solely CEA group (P <0.001). The median duration of follow–up was 64.5 months (IQR 24–84 months). The survival rate was 88 %(22/25) in CEA/CABG group and 80.6 %(50/62) in CEA group, product-limit analysis showed that there was no significant difference in survival rates between two groups (P >0.05).

Conclusion: concomitant carotid endarterectomy and CABG can be safely performed, it could prevent stroke and would not increase the overall risk of surgery.

Keywords: carotid endarterectomy, coronary artery bypass grafting, carotid artery stenosis, coronary artery disease

Introduction

Stroke is the main cause of death, just behind coronary artery disease (CAD) and cancer.[1)] Carotid endarterectomy combined carotid endarterectomy (CEA) is the preferred choice for symptomatic patients with carotid artery stenosis and can prevent stroke in patients with high-grade occlusive lesions at the carotid bifurcation, and CEA has been accepted as the standard therapy for carotid artery stenosis.[2,3)]

In general, the degree of carotid artery stenosis is correlated with the severity of coronary artery stenosis.[2–5)]

[1]*Department of Cardiovascular Surgery, China-Japan Friendship Hospital, Beijing, China*
[2]*Department of Radiology, China-Japan Friendship Hospital, Beijing, China*

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Corresponding author: Peng Liu, MD, PhD. Department of Cardiovascular Surgery, China-Japan Friendship Hospital, No 2, Yinghua Yuan East Road, Chaoyang District, Beijing 100029, China
Email: Liupeng61@yahoo.com.cn

During the cardiac surgery, a severe stenotic carotid artery or embolization from an ulcerative plaque could cause hypofusion to the brain and lead to perioperative neurological events; thus the ischemic neurological injury during cardiopulmonary bypass is inevitable.

In certain cases, patients with carotid stenosis often have the severe coronary artery stenosis requiring coronary artery bypass grafting (CABG). Yet there has been no agreement that a staged or concomitant CEA and CABG (CEA/CABG) is safer in patients with carotid artery stenosis and CAD in reducing neurological morbidity during and after cardiac surgery.[4,5] For answering this question, we prospectively recorded our patients undergoing combined CEA/CABG, or solely CEA in order to compare the feasibility and outcomes of these two procedures. Treatment indications, periprocedural complications, and clinical outcomes were analyzed.

Materials and Methods

The Hospital Review Board approved the surgical protocol, presurgical informed consent was obtained from all patients. In a five-year prospective study from February 2003 to December 2009, we prospectively documented periprocedures and outcomes of our 25 consecutive patients who received concomitant CEA/ CABG and 62 consecutive patients who underwent only CEA. Data were documented to analyze the complications during and after CEA and CABG at our hospital.

Inclusion criteria in this study included stenosis of the common carotid artery, internal carotid artery or carotid bifurcation and CAD, systematic carotid stenosis >60%, and asymptomatic carotid stenosis >70%. On preoperative color duplex ultrasound scan imaging, a stenosis >70% was defined as peak systolic velocity >250 cm/s, according to North American Systematic Carotid endarterectomy methodology[2]; criteria for elective CABG included two-vessel or triple-vessel diseases with stenosis >75%, or left main trunk symptomatic CAD, or with diameter >1.5 mm in the targeted coronary artery, or the left ventricular ejection fraction >40%. Exclusion criteria included patients failure to provide consent for the treatment, ongoing or recent myocardial infarction (MI) or stroke in the previous 3 months, left ventricular ejection fraction <40% or documented heart failure, poorly controlled hypertension, or diabetes mellitus, renal insufficiency, respiratory failure, patients with steroid-dependent chronic obstructive pulmonary disease or measured forced expiratory volume in 1 second <30% of predicted or <1L/sec. Exclusion also included significant atherosclerotic disease of the ascending aorta, aortic arch, and supra-aortic trunk at computed tomography (CT) scan.

The endpoint of this study was the incidence of death and disabling stroke. Wound infection was defined as the secondary analyses. Major adverse cardiac events referred to death from any reasons within 30 days after surgery. Stroke was diagnosed if a modified Rankin score was higher than 3 at 30 days following the onset of symptoms. Transient ischemic attack (TIA) and amaurosis fugax was diagnosed if a focal cerebral dysfunction of presumed vascular origin disappeared within 24 hours. Cardiovascular death was defined as death related to a cardiac or neurological event. Perioperative MI was defined as the appearance of new Q wave with persistent ST-segment changes associated with abnormal increase of myocardial enzyme including CK-MB and troponin I. Asymptomatic was defined as no neurological symptoms such as TIA or stroke within 6 months prior to surgery.

All patients were studied with ultrasound, computed tomographic angiography (CTA), magnetic resonance angiography (MRA) or conventional digital subtraction angiography (DSA) to document the grade of carotid stenosis. Categories of stenosis with ultrasound measurement were used based on the standard ultrasound criteria: mild, less than 50%; moderate, 50%–69%; severe, 70%–99%; and occluded, 100%. A preoperative angiogram was routinely performed in all patients prior to surgery, the surgical procedure was determined based on angiographic results. Concomitant CEA/CABG would be performed if the patient had the stenosis of carotid artery and coronary artery stenosis, and had symptoms of heart diseases.

Surgical strategy

CEA procedure

Our patients underwent a unilateral CEA with artificial patches and concomitant CABG/CEA, the CEA was performed first in the concomitant procedure. During the CEA procedure, an incision was made alone the anterior border of the sternocleidomastoid muscle, after opening the carotid sheath, the common carotid artery, internal and external carotid arteries were exposed and isolated, a bolus heparin 1 mg/kg was administered before clamping the carotid artery. Transcranial Doppler (TCD) was used to monitor the cranial blood supply and cerebral function, and arterial shunt was used in all patients. However, cerebral protection devices were not used. Hyperfusion was controlled with lowering blood pressure. Blood pressure was controlled below 120/80 mmHg for patients with

hypertension, ipsilateral carotid stenosis >80% and or contralateral carotid artery stenosis. The arteriotomy was closed with polytetrafluoroethylene patch.

CABG procedure

The cardiac surgery was started after ending of CEA procedure. CABG procedure was performed through full median sternotomy. A 4.5-mm opening on the aorta was punched with a puncher, a continuous 6/0 prolene (polypropylene) was used for proximal anastomosis and a continuous 7/0 prolene was used for distal anastomosis, immobilization of targeted lesion arteries and regional myocardial control were performed with a stabilizer (Octopus, Medtronic), an intraluminal shunt and a CO_2 blower were employed during anastomosis. Bypass was performed with autologous great saphenous veins. Intubations were weaned within 24 hours postoperatively. Intra-aortic balloon pump (IABP) was removed within 6 hours postoperatively. All patients were discharged 2 to 3 weeks after operation.

Perioperative treatment protocol

All patients received statin orally prior to surgery. If the patient was scheduled for CABG, and was on aspirin and clopidogrel, they were discontinued 5 days prior to surgery and low-molecular-weight heparin for anticoagulation was used instead. Clopidogrel (75 mg/d) and aspirin 100 mg/d were administered starting 3 days after the surgical procedure, clopidogrel was continued for 3 months, whereas aspirin was continued for life. All patients received an intravenous heparin bolus (100 u/kg) to achieve systemic anticoagulation during surgery.

Follow-up

Patients were instructed to follow up at 1, 3, and 6 months after treatment, then yearly afterwards at the clinic, or via phone call if patients could not visit the clinic. Carotid duplex ultrasound with Doppler measurement of flow velocities was performed to establish the patency of the treated carotid artery. All cardiac events or neurological status were investigated.

Statistical analysis

Fisher's exact test was used for categorical variables, the student's t-test was used for normally distributed continuous variables, and the Wilcoxon rank-sum test for ordinal or skewed continuous variables. The survival, stroke and MI outcomes with corresponding 95% confidence intervals were analyzed by the Kaplan-Meier method. Computation was done with software SPSS 13.0. A $P < 0.05$ was considered statistically significant.

Results

Outcome events within 30 days after surgery

The characteristics of the patients treated with CEA/CABG are compared with those treated with solely CEA in Table 1. There was no significant difference in terms of age, proportion of gender, risk factors of CAD and carotid artery stenosis (**Table 1**). The degree of carotid artery stenosis was identical in both study groups. One patient in CEA/CABG group had 60% stenosis of carotid artery with ulcerative plaque. Of the 25 patients undergoing concomitant CEA / CABG, 5 (20%) were performed on pump-CABG. One patient had arteriosclerosis obliterans (ASO) on right leg and received femoral-popliteal bypass.

No early mortality and stroke occurred in both groups. Short-term events included deviated tongue protrusion, numbness of face and wound infection; no significant difference was observed. Tongue protrusion and numbness of face recovered within 3 weeks postoperatively. One patient in the combined group and 6 in CEA group experienced voice change, which improved completely within 6 months. One patient in the combined CEA/CABG and 7 in the CEA group had an injured marginal mandibular branch of the facial nerve, which resolved with no special treatment. In CEA group, three patients with postoperative MI were treated medically, three patients had delayed neck hematoma that was evacuated successfully. Three patients (12%) had sternal wound infection 2–3 weeks after the CABG procedure, S. aureus was cultured from the wound culture, and they were treated by wound care and systemic antibiotics (**Table 2**).

Long-term results (>30 days after surgery)

87% patients were followed up, the median duration of follow-up was 64.5 months (IQR 24–84 months). The rate of disabling stroke or death did not differ statistically between patients in CEA/CABG group and CEA group. There were 3 deaths documented in CEA/CABG group: one died of heart attack at 3 year after surgery. Another one died of sudden death with unknown reasons at 5years after CEA/CABG, this patient had untreated contralateral carotid artery stenosis and had cerebral hemorrhage. The third one died in traffic accident. In CEA group, 12 deaths were reported, the cause of death included acute MI (n = 3), sudden stroke (n = 3), multiple organ failure (n = 2), lung cancer (n = 1), secondary hepatic metastases

Table 1 Basic characteristics of patients

	CEA + CABG n	%	CEA n	%	P
No of patients	25		62		
Male	21	84.00	48	77.42	0.356
Age	70.9	283.60	69	111.29	
Risk factors					
hypertension	14	56.00	39	62.90	0.359
DM	11	44.00	32	51.61	0.343
hyperlipedemia	8	32.00	22	35.48	0.481
smoker	10	40.00	36	58.06	0.098
ex smoker	9	36.00	29	46.77	0.25
History of MI	6	24.00	14	22.58	0.546
CAD	7	28.00	38	61.29	0.005
PVD	5	20.00	13	20.97	0.585
Stroke	6	24.00	11	17.74	0.349
TIA	9	36.00	22	35.48	0.576
Blindness	3	12.00	5	8.06	0.416
Amaurosis fugax	2	8.00	6	9.68	
Contralateral lesion					
occlusion	4	16.00	9	14.52	0.548
moderate	2	8.00	7	11.29	0.492
mild	14	56.00	32	51.61	0.448
normal	5	20.00	14	22.58	0.519
CABG on pump	5	25.00	0	0	

CEA: combined carotid endarterectomy; CABG: coronary artery bypass grafting; CAD: coronary artery disease: TIA: transient ischemic attack

Table 2 Outcomes of patients undergoing combined CEA/CABG vs. CEA only

	CEA + CABG n = 25	%	CEA n = 62	%	P value
Short-term (<30d)					
Deviationoftongue	1	4	5	8.06	0.834
Numbnessofface	1	4	7	11.29	0.512
Neckhematoma	0	0	3	4.84	0.554
Voicechange	1	4	6	9.68	0.628
MI	0	0	3	4.84	0.554
Stroke	0	0	4	6.45	0.32
Woundinfection	3	12	1	1.61	0.127
Cumulativerisk	6	24	29	46.77	0.05
Long-term (<30d)					
TIA	1	4	6	9.68	0.628
Stroke	1	4	5	8.06	0.834
MI	1	4	6	9.68	0.628
Restenosis	4	16	12	19.35	0.952
Mortality	3	12	12	19.35	0.611
Cumulativerisk	10	40	41	66.13	0.025
Intubationtime (h)	15.16 ± 3.48		4.65 ± 3.86		0.000
ICUstay (h)	24.92 ± 11.94		11 ± 6.3		0.000
Hospitalstay (day)	17.04 ± 4.73		9.42 ± 2.14		0.000

CEA: combined carotid endarterectomy; CABG: coronary artery bypass grafting; TIA: transient ischemic attack

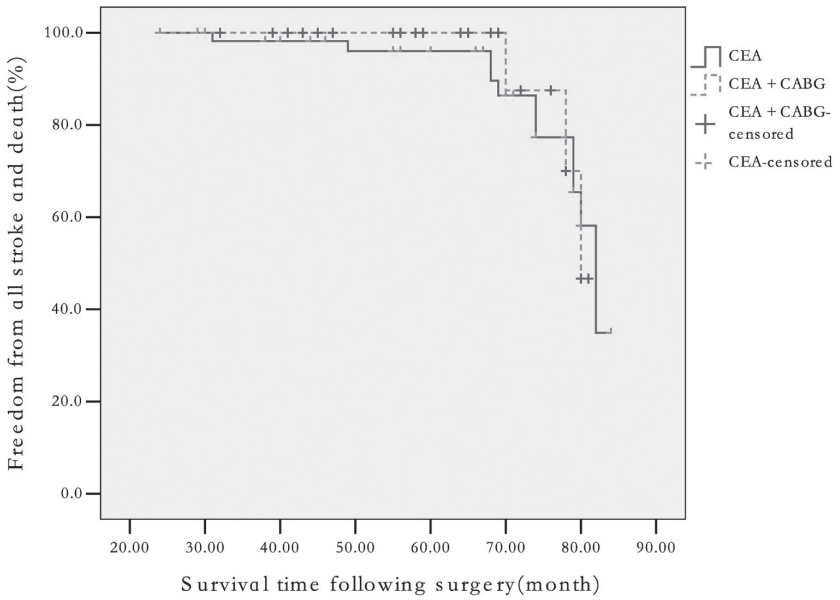

Fig. 1 Long-term survival of patients undergoing synchronous CEA/CABG versus solely CEA, no significant difference is found in both groups (P >0.05).
CEA: combined carotid endarterectomy; CABG: coronary artery bypass grafting

from colon cancer (n = 1), traffic accident (n = 1)and diabetic renal insufficiency (creatinine>15mg/dl) (n = 1) (**Table 2**). The Kaplan-meier analysis showed that the survival rate was 88%(22/25) in CEA/CABG group and 80.6% (50/62) in CEA group; there was no significant difference between the two groups (P>0.05) (**Fig. 1**).

One patient had stroke due to cerebral infarction on 5 years after CEA/CABG, the patient was treated medically with satisfactory. Meanwhile, five strokes occurred after solely CEA, of which 3 had cerebral hemorrhage and died afterward, the remaining two had non-disabling strokes and underwent CABG later.

Restenosis was found on ultrasonography in 4 patients in CEA/CABG, and 12 patients in CEA group, no statistical difference was found (P = 0.952).

CABG results

A complete revascularization was achieved with great saphenous veins during CABG procedure. IABP was used in 13/25 patients to maintain homodynamic stability and cardiac function. The patients were extubated within 24 hours after surgery. The neurologist consulted the suspected patients to evaluate neurological deficits. No mental disturbances were found in patients undergoing off-pump CABG, and no significant change was found on brain computed tomography following surgery. Of 5 patients undergoing on-pump CABG, 3 patients had transient psychological problems with disorientation on time, location and person, and resolved within 2–4 days without special treatment.

Discussion

Coronary artery bypass graft (CABG) has been accepted an effective procedure for patients with severe coronary artery diseases (CAD). There is a report[1,6] that about 3%–22% patients with CAD undergoing CABG coexisted with carotid artery stenosis and >70% internal carotid artery stenosis. Carotid artery disease causes approximately a third of post-CABG stroke. Postoperative stroke is a crucial cause of morbidity and mortality following CABG. A systemic review showed that 23% of patients suffering a stroke after CABG died,[7] and many more will become disabled.[7] As CEA has been considered as the gold standard of carotid artery revascularization, the NASCET trial showed that the symptomatic patients with disease >70% stenosis underwent CEA and had decreased the incidence of stroke,[2] thus concomitant CEA/CABG is addressed and more preferred in some institutions. Yet, there has been a controversial regarding the staged or concomitant CEA/CABG for severe CAD and carotid artery stenosis. Therefore, we compared the outcomes of concomitant CEA/CABG with solely CEA, and our findings indicated that no difference existed in the major risks of

Table 3 Comparison of outcomes in different combined procedures: literature review

Authors	Patient (n)	Mortality (%)	Stroke (%)	MI (%)
Combined CEA + CABG				
Naylor 4	7753	5.6	4.6	3.6
Naylor 5	5386	4.5		
Timaran 10	26197	8.6	3.9	
Mishra 11	192	1.6	2	
Abbasi 12	19	10.5	10.5	
Dick 13	134	1	4	0.7
Bilfinger 14	84	5.9	4.7	
Chiappini 3	140	6.4		
Combined CEA + CABG-off pump				
Naylor 4	324	1.5		
Mishra 11	166	1.2	0.6	
Staged CEA then CABG				
Santos 15	40	5	5	5
Naylor 4	917	3.9	2.7	6.5
Antunes 16	77	1.3	6.3	6.3
Chiappini 3	62	4.8		
Reverse stage CABG then CEA				
Naylor 5	302	2		
Naylor 4	302	3.9	6.3	0.9
Staged CSA + CABG				
Timaran 10	887	6.9	2.4	
Naylor 4	760	5.5		

CEA: combined carotid endarterectomy; CABG: coronary artery bypass grafting

surgery between patients undergoing concomitant CEA/CABG and those with solely CEA, the long term survival rate was similar in both groups. This showed that CEA/CABG could be safely performed as CEA.

There have been numerous observational studies[8–16] comparing the results of the staged versus concomitant surgery (**Table 3**). No conclusion has been reached on which approach is better than others.[8] The advantage of concomitant CEA/CABG is the lower cost, shorter hospital stay, and possible long-term lower stroke rate.[4] There is a report that concomitant CEA/ CABG has a high risk compared with other treatment groups.[8,9] Naylor's data show that there is a trend of decreased incidence of stroke in staged group. The higher stroke rate was found in the reversed staged procedure, CABG then CEA.[7,8] In comparison with solely CEA, our data indicate that combined CEA/CABG procedure is safe and feasible, addition of CABG to the CEA procedure did not induce extra surgical risk to patients undergoing CEA only.

Even only CEA per se might induce some risk of stroke and MI, depending on symptomatic or asymptomatic carotid artery stenosis and degree of stenosis, treatment of patients with concomitant coronary and carotid stenosis is rather difficult. We reviewed the literature in order to compare our results with others. The incidence of MI ranged in 0.9%–6.5%, the stroke rates after surgery were in the range of 0.6%–10.5% and mortality was in the range of 1%–10.5%. All these parameters varied with different approaches and institution (**Table 3**). In our patients undergoing CEA/CABG, no mortality and major morbidity occurred within 30 days after surgery. Our short-term results were comparable to those reported in literatures in terms of the rates of stroke, MI, and death. However, the long-term results after surgery are rarely reported. The long-term results in our series showed that the stroke rate was 4% in CEA/CABG group and 9.68% in CEA group. The survival rate in both group were similar with no significant difference, this means that combined CEA/CABG can be performed safely. Our data are in line with literature,[9,10] US National Inpatient sample (NIS) audit[11] suggests that staged carotid artery stenting (CAS) and CABG or synchronous CEA and off-CABG might become preferred options; however, in one pooled analysis, the combined incidence of death and stroke in patients undergoing CAS and staged CABG remains elevated. These results confirm that the presence of carotid

stenosis is, per se, a marker of risk that might persist independently of its treatment. A systematic or randomized evaluation is warranted.[17)]

Regarding the option of on-pump or off-pump CABG, Mishra et al.[11)] had compared the effect of both surgical approaches, and concluded that concomitant CEA/CABG is a safe and effective procedure in patients with significant coronary and carotid artery disease. Almost equally good outcomes after CABG had been achieved using on-pump or off-pump techniques, the patients had low morbidity, mortality, and good long-term results, even though there is a tendency of lower death rate and lower stroke rate in off-CABG group. In our series, 80% (20/25) patients were performed with off-pump CABG, and 20% patients undergoing on-pump CABG had psychological conditions after surgery. This could be caused by extracorporeal circulation, which induced contemporary ischemic injuries, cerebral, cardiac as well as hematological. Hypoxemia to the brain caused the transient psychological problem. In addition of this issue, no significant difference was found between patients undergoing CABG on-pump or off-pump.[11)]

Sternal wound infection following CABG is a serious and costly complication and may increase morbidity, mortality, and length of hospital stay. In our series, S. aureus had been cultured from the infected sternal wound after CABG, the infection rate is 12%, which is higher than 3.6%[18)] reported in the literature. We believe that careful sterilization of skin and careful manipulation of the wound closure and wound care may help reduce the risk of this serious complication after CABG.

The best medical therapy consisted of lipid-lowering agents(statins), antihypertensive (typically beta-blockers), and antiplatelet agents (aspirin), and lifestyle modification including smoking cessation, weight loss, and exercise. We always educate our patients to follow the best medial therapy to maintain the good effect of surgical procedures.

We have to acknowledged that our study was limited by number of patients, different composition of the patient populations, non-randomization, and possible bias in both groups. A large, randomized prospective study to compare staged CEA /CABG, combined CEA/CABG is warranted.

In conclusion, concomitant CEA and CABG can be performed safely, it could prevent stroke and would not increase the overall risk of surgery. The long-term survival rate in both groups is similar.

Disclosures

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