Egyptian Journal of Surgery Vol 25, No 2, April, 2006

ORIGINAL ARTICLE

TREATMENT OF ASSOCIATED CAROTID AND CORONARY DISEASE

By
Sherif Balbaa,[1] *Yehia Balbaa*[2]
[1]Department of General Surgery, Faculty of Medicine, Cairo University, [2]Department of Cardiothoracic Surgery, Faculty of Medicine, Cairo University, Egypt
Correspondence to: Sherif Balbaa, Email: sherifbalbaa@hotmail.com

Aim: ***The management of patients with combined carotid and coronary artery disease is controversial. Myocardial infarction is the most common cause of early and late mortality after carotid endarterectomy (CEA), and stroke after coronary artery bypass grafting (CABG) is a devastating and dreaded complication. This study aims to address different treatment strategies in patients with combined diseases.***
Methods: ***Thirty five patients with combined carotid artery stenosis and coronary artery disease were included in this case series. All patients were candidates for CABG, and their carotid status was either symptomatic or asymptomatic with critical stenosis. CEA either preceded CABG (the staged procedure) in 22 cases, was done in conjunction with CABG (the combined procedure) in 8 cases, or followed CABG (the reversed staged procedure) in 5 cases.***
Results: ***The mean age of study population was 71 ± 7.0 years. Five patients (14.2%) had suffered a previous stroke. The study had a single mortality (2.85%; cardiac in origin), one myocardial infraction, and 2 cerebrovascular strokes (5.7%). Two patients suffered temporary 12th nerve dysfunction.***
Conclusion: ***Patients with severe, symptomatic disease in both the carotid and coronary artery territories probably benefit from a combined revascularization. In patients with stable disease in one of the vascular territories, the choice of a staged, combined, or reversed staged procedure is more controversial.***

Keywords: *Cardiac bypass, cerebral ischaemia, endarterectomy.*

INTRODUCTION

Concomitant severe atherosclerotic disease in the carotid and coronary artery circulation is not uncommon, and the management is fraught with difficult decision making and the potential for significant complications.[1]

Advanced coronary artery disease is common in patients undergoing evaluation for carotid endarterectomy (CEA). Hertzer et al have showed that 28% of all patients presenting with extracranial cerebrovasulcar disease have severe correctable coronary disease,[2] and coronary artery disease is the leading cause of both early and late mortality after CEA.[3] Similarly, it is estimated that up to 22% of patients who are evaluated for CABG have > 50% diameter reduction of one or both carotid arteries, and that 12% have > 80% diameter reduction.[4]

The management of patients with severe disease in both the coronary and carotid circulations continues to be controversial. It has been established that CABG is effective in reducing mortality from symptomatic coronary artery disease[5] and CEA for high-grade carotid artery lesions is benfeficial in reducing stroke.[6]

Patients with co-existent carotid and coronary disease present in several ways.

The first, (and commonest) is the situation where a patient is scheduled for CABG, and severe asymptomatic carotid disease is discovered in the course of preoperative assessment.

Another scenario is that of a patients with symptomatic carotid disease (history of transient ischaemic attacks and / or stroke) who is a candidate for CEA (on the basis

of the findings from the North American Symptomatic Carotid Endarterectomy Trial (NASCET)).[6] During his evaluation, his cardiac condition is judged to be in need of coronary revascularization.

Finally, a third situation is that of a patient with severe asymptomatic carotid disease (discovered in a medical check-up) and is considered a candidate for CEA (in accordance with the findings from the Asymptomatic Carotid Atherosclerosis Study (ACAS)).[7] At the time he is also found to be with persisting cardiac symptoms despite medical care and / or angioplasty, and therefore in need of CABG.

Thus, for patients who are candidates for both coronary and carotid revascularization, the question would be which procedure would be performed first, or whether they could be performed simultaneously.

PATIENTS AND METHODS

Over a period from January 2002 to February 2006 35 patients with coexistent ischaemic heart disease and cerebrovascular disease were operated upon. The carotid procedure (CEA) either preceded the coronary procedure (CABG, the staged procedure), was performed simultaneously with it (the combined approach), or followed it (the reversed staged procedure). All patients had myocardial ischemia with persisting symptoms despite medical care and / or angioplasty and thus were candidates for coronary revascularization.

Inclusion criteria:

- For the carotid procedure:
  1. Symptomatic carotid artery disease.
  2. Asymptomatic carotid artery disease [critical (>80% stenosis) or bilateral (>150% combined stenosis)].
- For the Coronary procedure:
  1. Critical or unstable coronary artery disease.
  2. Persisting cardiac symptoms despite best medical care and / or angioplasty.

Preoperative assessment and patient selection: All patients had a carotid duplex evaluation using a 7.5 MHz probe in longitudinal and transverse planes with anterior, lateral, and posterior approaches. In addition, all patients with a history of stroke had computerized tomography brain scans.

Selection of patients for CABG was made on grounds of history taking [including cardiac symptoms and / or history of myocardial infarction (MI)], non-invasive studies including standard and stress electrocardiograms, echocardiography, radio-nucliide studies, and finally invasive evaluation through coronary arteriography.

Details of both the cardiac and the carotid procedures were explained the patients as well as the attendant risks and complications, particularly mortality, and stroke. An informed written consent was taken from all patients.

Choice of procedure sequence:

1. ***The staged protocol (CEA first):***

   For symptomatic or critical asymptomatic (tight or bilateral) carotid artery disease, in patients with stable coronary disease.

2. ***The combined protocol (CEA and CABG simultaneously):***

   For patients with symptomatic carotid disease with critical or unstable myocardial ischaemia.

3. ***The reversed staged protocol (CABG first):***

   For patients with unilateral asymptomatic carotid disease and critical myocardial ischaemia.

In other words, procedure sequence depended on which of the disease target sites was judged to be more critical.

The carotid procedure: In all staged procedures (CEA preceding CABG), carotid endarterectomy was performed under loco-regional anaesthesia with careful cardiac premedication and monitoring. After a standard incision along the anterior border of the sternomastoid, carotid artery exposure was obtained with vessel loop control of the three carotids and identification of the hypoglossal nerve. Adequate heparinization preceded vessel clamping and commencement of the endarterectomy. After carotid clamping neurological evaluation was conducted by the anaesthesist (through conversation and assessment of motor power). Any slurring of speech, confusion, and / or motor weakness on the contralateral side of the clamped carotid would mandate placement of an intraluminal carotid shunt. After completion of the procedure, patients were placed postoperatively in the cardiac ICU under close monitoring. In the staged procedure CABG followed CEA within a period of 7 days.

In the combined approach, carotid endarterectomy was performed with CABG (under the same anaesthetic but preceding the cardio pulmonary bypass). Neurological assessment under general anaesthesia was based on stump pressure evaluation; a pressure below 50 mmUg would indicate the need of a carotid shunt.[8] In the combined approach, the neck wound was left open after completion

of CEA, and closed only (with suction drainage) after completion of coronary revascularization and reversal of anticoagulation with protamine sulphate.

In the reversed staged procedure in patients with unilateral asymptomatic carotid artery disease, CEA followed CABG by a period of 7-10 days. The procedure was performed along the lines of the staged CEA.

In all CEA procedures, closure of the arteriotomy was done either primarily or using a knitted polyester patch in patients with narrow vessels.

The cardiac procedure: After standard median sternotomy, the pericardium was widely opened. After ascending aortic and right artial cannulation, cardiopulmonary bypass (CPB) was commenced under normorthermia. Heart was arrested using intermittent warm antegrade blood cardioplegia. Using radial artery and saphenous vein graft, distal anastomoses were performed first (end-to-side, and side-to-side) using polypropylene 7/0 and 8/0 sutures. The proximal aortic anastomosis was then performed to the ascending aorta. For the internal mammary graft (IMA), only a distal anastomsis (usually to the left anterior descending artery) (LAD) was required.

In 7 cases, "off pump" CABG was performed. Indications included single vessel coronary disease, heavily-calcified (porcelain) ascending aorta (as detected by plain chest x-ray or CT scan), and non-dialysis renal failure. After median sternotomy and pericardiotomy, elevation and stabilization of the heart was accomplished using 4 deep pericardial sutures with snare protectors. Coronary revascularization was achieved using the internal mammary artery and radial artery anastomosed to it (end of radial to side of internal mammary). No aortic side-occlusion clamping was done in any of the off pump CABGs.

As regards all coronary revascularizations, a mean of 3.4 grafts per case were required.

Statistics: All statistical analysis was performed using SPSS 11.5 for windows. Data were described as mean (percentage) or mean ± standard deviation (for age and percentage stenosis).

RESULTS

Over the study period, 35 patients underwent CEA and CABG operations. Most of the patients were referred for coronary revascularization and were then worked up for co-existent carotid disease.

Twelve patients had asymptomatic carotid disease with a history of transient ischaemic attack (7 cases) or cerebrovascular stroke (5 cases).

The study group ranged in age from 56-81 (mean 71 ± 7.0) and was mainly comprised of males (27, 77.1%). Hypertension, angina, and diabetes were the most prevalent co-morbidities Table 1.

Table 1. Demographic information and risk factors.

Age	mean ± S.D.	71 ± 7.0
	min - max	56 – 81
Male sex		27 (77.1%)
Diabetes		20 (57.1%)
Hypertension		26 (74.3%)
History of MI		7 (20%)
Peripheral vascular disease		9 (25.7%)

Table 2 details the characteristics of the carotid disease in the study groups.

Table 2. Characteristics of carotid disease (n = 35).

Previous carotid endarterectomy	2 (5.7%)
Previous permanent stroke	5 (14.3%)
Bilateral disease > 70%	7(20%)
Left CEA	19(54.3%)
Stenosis (mean ± SD)	85 ± 10.5%.
Right CEA	16 (45.7%)
Stenosis (mean ± SD)	88 ± 10.0%.

As regards the CEA procedure (35), 22 preceded CABG (staged; 62.8% of cases), 8 were performed concomitant with CABG (combined; 22.8%), and 5 followed CABG (reversed staged; 14.3%). All combined procedures were for symptomatic patients (stroke/TIA). All reversed staged procedures were for asymptomatic patients, while in the staged group (22 cases) the majority of the patients were asymptomatic (18/22). Table 3.

Table 3. Type of carotid patient in relation to procedure protocol (35 Patients).

Number N=35	Procedure	Carotid Symptomatology
22	Staged	18 asymptomatic
		4 symptomatic
8	Combined	All symptomatic
5	Reversed Staged	All symptomatic

During the CEA procedure, 2 shunts were utilized (both in the combined procedure), and a knitted polyester patch was used for closure in 2 cases, both females with narrow carotid arteries.

As for the coronary revascularization, the majority of patients (27, 77.1%) had between 3-4 grafts. Grafts included the great saphenous vein, internal mammary artery, and the radial artery. Off pump CABG was performed in 7 cases, 5 times in conjunction with CEA (the combined procedure), and twice as part of the staged protocol.

Operative outcomes are summarized in Table 4.

The single mortality in the series was myocardial in origin, in a patient with a history of myocardial infarction and requiring 4 grafts. The patients, who was part of the staged protocol, suffered a postoperative MI.

Table 4. Postoperative outcomes (n = 35).

Mortality:	1 (2.85%) myocardial infarction
Myocardial infarction:	1 (2.85%)
Cerebrovascular stroke:	2 (5.7%)
	(1) Permanent.
	(1) Transient completely resolved prior to discharge.
Nerve injuires:	2 (transient hypoglossal nerve palsy)
Neck haematomas:	3 (all managed conservatively)
Pneumonia:	1
Renal failure:	1
Reoperation for bleeding (chest):	1

Two cases of cerebrovascular stroke were encountered (5.7%). The first was a permanent stroke (ipsilateral to CEA) and was encountered post combined CEA/CABG. It is worth noting that the patient had bilateral carotid disease, and that an intaluminal shunt was utilized. The second stroke occurred 24 hours after CABG in one of the staged cases, was contralateral to the endarterectomized carotid, and was completely resolved prior to hospital discharge (2 weeks). No strokes were encountered in the setting of off pump coronary revascularization (7 cases). Thus the stroke rates for the subgroups would be 12.5% for the combined CEA / CABG, and 4.5% for the staged CEA / CABG, and 0% for the reversed staged protocol. Numbers of subgroups, however, are too small to be representative.

DISCUSSION

Neurologic complications of varying severity are unfortunately relatively common after cardiac surgery. These complications can have an important effect on the disposition and eventual outcome of affected patients.

Naylor et al.[9] in a systematic review observed that 3 carotid factors were associated with a significantly increased risk of stroke in CABG patients:

1. The presence of a carotid bruit.
2. History of prior stroke or TIA.
3. Carotid stenosis > 50%.

That study also observed that patients with 0-49% stenosis incurred a 1.9% risk of stroke after CABG, increasing to 6.7% in patients with 50-99% stenosis.

The presence of a symptomatic 70-99% stenosis does not automatically confer equivalent stroke risk in all patients and the clinician may have to be more discriminating in patient selection. Markers of increased long-term stroke risk include: male sex, irregular plaque, increasing age, 90-99% stenosis, contralateral occlusion, hemispheric as opposed to retinal symptoms, cortical stroke and > 6 months of recurrent symptoms.[10]

Roach and coworkers[11] in a prospective observational study of 2108 elective CABG procedures reported an incidence of adverse cerebral outcomes of 6.1%, nearly half of which suffered severe neurological sequelae with a high mortality.

Borger and colleagues[12] conducted a meta-analysis of CEA and CABG; the study identified 16 studies that contained combined and staged CEA/CABG patients. The most significant finding of the study was increased risk of stroke or death during combined procedures. This is in accordance with results of the present study, since in the combined protocol subgroup (8 patient) one patient suffered a postoperative stroke (he had symptomatic and bilateral carotid disease).

The meta-analysis conducted by Borger et al.[12] also noted that lack of randomization introduced a strong selection bias, as most surgeons tend to select the sicker, more morbid patients for the combined procedure.

The studies of Coyle and coworkers[13] and Rizzo et al.[14] illustrate that, although the combined procedure can be performed with reasonable safety, patient selection significantly affects the results, and those patients with severe bilateral (combined stenosis more than 150%) or symptomatic carotid disease in combination with severe symptomatic coronary artery disease are at high risk for associated complications.

Hertzer[15] studied 9714 patients who presented for CABG, and provided an analysis closest to a randomized trial. That study demonstrated that the stroke rate in the staged, reversed staged, and combined procedures was 4.2%, 14%, and 2.8% respectively. That suggested that the reversed staged procedure should be avoided and that the combined procedure can be performed with low stroke and mortality rates.

More recent studies, however, have established that the reversed staged procedure definitely has a role in the CABG candidate with a unilateral asymptomatic carotid disease.[1] In the present study none of the patients in the reversed staged protocol suffered from a postoperative stroke.

In contrast to the evidence supporting a causative role for carotid disease in the aetiology of post-CABG stroke, evidence was also provided that carotid artery disease (alone) was probably not responsible for the majority of post-CABG stroke.[10]

It has been found that carotid disease per se, might only ever be responsible for about 40% of all strokes. In the present study, one of the 2 strokes encountered post-CABG was in the hemisphere contralateral to the endarterectomized carotid in a patient with a unilateral disease.

Antunes and colleagues,[16] in their study, using multivariate logistic regression, identified the following variables as independent predictors of a postoperative cerebrovascular accident:

1. Cerebrovascular disease.
2. Number of periods of aortic cross-clamping.
3. Left ventricular hypertrophy.

Proximal aortic arch atherosclerosis at the site of aortic clamping for proximal coronary graft anastomosis has been associated with a 2.8 fold risk of stroke,[11] and presence of carotid artery stenosis was found to be associated with presence of aortic arch atherosclerosis.[17]

It is worth noting that 7 off-pump CABGs were included in this study (5 times in conjunction with CEA (combined) and twice as a part of the staged protocol); in none of these cases was aortic side-clamping used and no strokes were encountered. Radial artery grafts were anastomosed to the side of IMA, and then anastomosed to subsequent coronary stations.

Recently, carotid artery stenting (CAS) has been used as an alternative for CEA in the staged protocol; CAS followed by CABG. Randall et al. (18), in a study of 52 patients in whom carotid stenting (with cerebral protection) was followed by CABG noted that all patients remained stroke-free during and after the stent procedure. However, the combined 30-day outcomes for the carotid stenting procedure and cardiac procedure included 3 strokes (1 minor and 2 major), all ipsilateral to the stented vessel and occurring 24-48 hours after CABG, as well as 2 stroke-related deaths.

In conclusion, patient with symptomatic or critical asymptomatic disease having a stable coronary condition can undergo a staged procedure with careful haemodynamic monitoring and meticulous postoperative care.

Patients with concomitant symptomatic carotid and unstable coronary artery disease are recommended for the combined procedure. This would result in intermediate risks for both stroke and myocardial infarction postoperatively, rather than risking high rates if one procedure preceded the other.

A reversed staged approach can be advocated for patients with unilateral asymptomatic carotid disease but critical coronary condition.

In summary, this study has its limitations: the limited number of patients and consequently the limited number of the different subgroups and strategies. A multi-institutional, randomized trial can provide much more objective data. Until then, management of these patients should be guided by the relative severity of their carotid and coronary artery disease, and the surgeon's own results in the treatment of these patient populations.

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